People • Science • Regulation

# PDA Letter

Volume XLIX • Issue 10 www.pda.org/pdaletter November/December 2013


# Crossover Moves

## Making a Career on Both Sides of the Government/Industry Divide

32

# 2014 PDA ANNUAL MEETING

**April 7-9, 2014 | JW MARRIOTT SAN ANTONIO HILL COUNTRY | SAN ANTONIO, TX**

## CALL FOR POSTERS

The *2014 PDA Annual Meeting* Program Planning Committee encourages you to submit an abstract for a one-day poster presentation at the *2014 PDA Annual Meeting*, which will be held on April 7-9, 2014 in San Antonio. Abstracts must be noncommercial, describe developments, strategies or work and significantly contribute to the body of knowledge relating to biopharmaceutical manufacturing, process knowledge, quality management and technology. Abstracts related to sterile or related product manufacture are preferable, but those addressing other technologies are welcome. All abstracts will be reviewed by the Program Planning Committee for consideration.

Suggested topics include, but are not limited to:

### BIOLOGICAL SCIENCES

- Microbial Control in the Manufacturing Environment
- Bio-film
- Combination Products
- Container Closure Integrity
- Green/Sustainable Manufacturing
- PAT
- Cell Culture Processes
- Viral Clearance
- Purification Process

### STERILE PRODUCT MANUFACTURING

- Diagnostics
- Challenges in Quality for ACIs
- Challenges in Manufacturing
- Expiration of Products, Logistics and Shipping
- Stem Cells
- Single-use Technology

### QUALITY SYSTEMS

- Testing Characterization, Stability
- Room Decontamination and H202
- Upstream/Downstream: Chromatography
- Cold Chain
- Sterilization
- Bio-burden/Bio-film
- Mycoplasma/Virus
- Process Validation
- Cleaning Methods and Validation

**Abstracts must be received by January 17, 2014 for consideration.**

You will be advised in writing of the status of your abstract **by February 7, 2014**. Poster presenters are required to register as a *paid full conference attendee* at the rate of $1795 member/$2044 nonmember. *Exhibit only* registrants are eligible to present a poster by registering as a full conference participant.

In order to be listed in the final program, your full conference registration must be received no later than **March 3, 2014**. After March 3rd, the prevailing registration fees and policies apply.

Visit **www.pdaannualmeeting.org/2014CFP** to submit an abstract.

**Please include the following information with each abstract:**

- Presenter's name
- Presenter's professional title
- Presenter's full mailing address
- Presenter's e-mail address
- Presenter's phone number
- Take-home benefits
- Presentation objectives
- 2-3 paragraph abstract, summarizing your topic and the appropriate forum (case study, discussion, traditional, panel, etc.)

**For more information, please contact Tanya Allen, Coordinator, Programs and Registration Services via e-mail at Allen@pda.org or phone at (301) 656-5900 ext. 136.**

# Volunteer Opportunities at PDA

## Leadership

- PDA Executive Officers
- Director
- Scientific Advisory Board
- Biotechnology Advisory Board
- Regulatory Affairs and Quality Advisory Board
- PDA Committee Chair/Co-Chair
- Task Force Co-Chair

- Author/Contributor to the *PDA Letter*
- Author/Contributor to the *PDA Journal*
- Poster Presenter
- Attend Chapter Committee/Planning Meetings
- Technical Report Peer Reviewer

- Speaker
- Chapter Leader
- Task Force Member
- TRI Instructor
- Interest Group Leader

**PDA Committees:**

- Program Planning Committee
- Membership Committee
- PDA Letter Committee
- Education Committee
- Audit Committee

- PDA Membership
- Attend Global PDA Meetings
- Attend Chapter Events
- Survey Reviewer
- Interest Group Member
- Attend TRI Courses

## Getting Involved

**1,000** Over 1,000 volunteers worldwide actively carry out PDA's Mission

**volunteer@pda.org**

PDA Letter

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

# Cover



*Cover Art Illustrated by Katja Yount*

# Departments

## News & Notes



## People



## Science



## Regulation



## Programs & Meetings



## TRI — Education



## Voices of PDA

# Contents

## Features

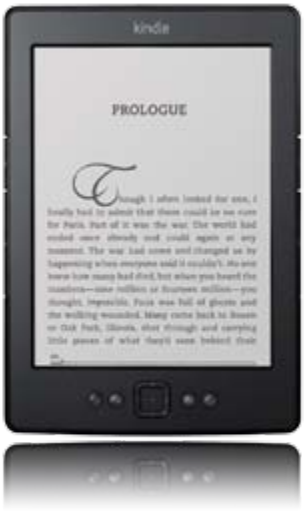


# Put Your Touch on the *PDA Letter*

The *PDA Letter* Editorial Committee is looking for active PDA members to provide ideas for, and comment on, articles for the *PDA Letter*. For more information about this 2-year volunteer commitment, please contact **Rebecca Stauffer** at stauffer@pda.org by December 30.

# Readership Survey Winner Announced

We are pleased to congratulate **Eric Webster** of PETNET Solutions whose name was drawn from a list of those who completed the 2013 *PDA Letter* Readership Survey. He received a Kindle e-reader courtesy of PDA.




***The* PDA Letter *wants to thank everyone who completed the survey***

We received close to 900 responses—almost 10% of our membership!

Keep an eye out for the next readership survey and PDA Pulse questions.

# Attention PDA Bookworms!

Vote for your favorite 2012 or 2013 PDA/DHI Technical Book at www.surveymonkey.com/s/authoraward13. The author who receives the most votes will win the PDA/DHI Technical Books Distinguished Editor/Author Award, which will be presented at the *2014 PDA Annual Meeting.*


### *BioPharm International*

June 1, 2013

"An Integrated Prefilled Syringe Platform Approach for Vaccine Development" —**Kingman Ng, Ronald Malone, Changyun Xiong** and **Xuefeng Yi**

tinyurl.com/mvjxt7o

### *BioProcess International*

September 2013

"Analytics and Quality"

tinyurl.com/mrfokl3

### *Controlled Environments*

August 20, 2013

"Interphex and PDA Announce Sponsorship Agreement"

tinyurl.com/msbmr9d

### *"The Gold Sheet"*

August 2013

"Difficulty Identifying Experts Seen as a Factor in Poor Investigations"—**Bowman Cox**

### *IPQ Monthly Update*

June 2013

"FDA Seeking Industry Input on Quality Metrics to Help Rationalize Its Review and Inspection System"

"Analyses of Defect Reports by Ireland's IMB and FDA Highlight Packaging and Labeling as Key Pharma Manufacturing Problem Area"

July/August 2013

"FMD Implementation in Europe Drives Better API Sourcing Knowledge and Interagency Communications"

"Revision of EU Annex 16 Clarifies QP Responsibilities in the Face of an Increasingly Complex Supply Chain"

"Burden of Pre-Inspection Submission Requests from Agencies Outside the US and Europe is Growing"

"NSF-IPEC 363 GMP Standard Will Provide Risk-Based Approach for Auditing and Certifying Excipient Manufacturers"

September 2013

"FDASIA Section 707 Draft Guidance on Obstructing Inspections Draws Industry Comments; Investigator Subjectivity Among Issues Raised"

"EDQM Amends CEP Submission and Revision Process; Starting Materials Remain at Issue; Risk-Based CEP Inspection Approach is Finding Problems"

### *IPQ News in Depth*

October 4, 2013

"CBER Focus Intensifying on Export Certification, Adverse Event Databases, and Lab Help in Product Development"

October 18, 2013

"Vetting of ICH Q3D Pre-Step 2 Impacts Final Draft; LVP and E&L Issues Could Warrant Further Public Comment"

October 24, 2013

"Comment Process on FDA's Proposed Rule on Product Detention During Inspections Reflects Industry Support"

October 30, 2013

"Joint Drafting of Contract Manufacturing Quality Agreements Needed to Reflect Shared Quality Ownership, FDA Stresses"

### *Pharmaceutical Technology*

August 2013

"PDA Training & Research Institute—Where Excellence Begins"

September 2, 2013

"The Elements of Training" —**Susan Schniepp**

tinyurl.com/kt3ulja

September 2, 2013

"Overcoming Limitations of Vaporized Hydrogen Peroxide" —**James Agalloco, James Akers**

tinyurl.com/kladgso

October 2, 2013

"FDA Seeks Metrics to Define Drug Quality" —**Jill Wechsler**

tinyurl.com/lpbbokk

### *PharmTechTalk*

September 19, 2013

"FDA, CDER Weigh Organizational Changes" —**Jill Wechsler**

tinyurl.com/kp6kbe4

October 24, 2013

"Industry Needs to Drive the Dialogue Regarding FDA's Quality Metrics Initiative" —**Walt Morris**

tinyurl.com/mcv9cew

### *Validation Times*

September, 2013

"Deficiencies in records and reports jump in number of 483 citations in '13; lab control problems still No. 1" —**Ken Reid**

"Hospira exec said firm had to 'drain the swamp,' but more warnings and 483s coming" —**Ken Reid**

# PDA Volunteer Spotlight

## Claudio Cappai Correa

- Global Supply Chain Quality Manager – LATAM & Canada
- *F. Hoffmann-La Roche Ltd.*
- Member Since | 2012
- Current City | Rio de Janeiro, Brazil
- Originally From | Belo Horizonte, Brazil

*Dreams are always important*

*In his spare time, Claudio enjoys growing orchids in his garden.*

**You recently attended the *2013 PDA/FDA Joint Regulatory Conference.* Why do you think it is important for PDA members to attend these types of conferences?**

For any professional, this is the opportunity to follow presentations and to understand the best practices in any area and, most importantly, ask questions directly to the inspectors and industry gurus. This makes this event worth PDA membership.

**How did you benefit from your attendance at the joint regulatory conference?**

The benefits of attending this PDA/FDA conference are being on top of the main discussions and having the opportunity to hear directly from the best sources any person in the industry can listen to. Not to mention networking, including meeting people/experts from other companies that are always willing to talk. This is valuable for any professional.

**Why did you choose to join PDA?**

PDA was looking for someone that could represent Latin America and Canada for the Regulatory Affairs/Quality Advisory Board. At this time, the chair of the RAQAB contacted me; by coincidence I was attending a PDA course at the headquarters in Bethesda, Md. The chair knew about my professional background and suggested me for the team. I did some interviews and was accepted to the RAQAB and then joined PDA as a formal member.

**What did you gain from being a PDA member?**

The greatest value I get from being a PDA member is the opportunity to share knowledge and interact with the best scientific and technical minds in the industry.

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

Be curious and passionate about what you are doing. Do not be afraid to ask questions.

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

As a child, the only thing that I could think or dream about was travelling the world. In a way, due to my work, I have been able to visit a large portion of it.

# Metro Chapter Examines Warning Letter Trends

**Anthony Grilli, Focus Scientific**

On Oct. 8, **Debra Pagano** presented "Recent Inspection Trends" to PDA's Metro Chapter. Pagano, a former U.S. FDA inspector, gave a cogent analysis of recent FDA warning letters issued to pharmaceutical and API manufacturers.

The first surprise was that of the 28 warning letters issued for drug cGMP violations in the past 12 months only one company was located in the United States. India received the highest number of warning letters, followed by Germany and Canada. These numbers confirm FDA's heightened surveillance of foreign manufacturers.

The most cited observation was inadequate product failure investigation—13 firms were cited. While root cause analysis and CAPA implementation have become standard practice for most U.S. firms, Pagano showed several examples of companies not getting to the root cause of stability failures, unknown chromatography peaks and sterility test failures. The next most cited observation was inadequate establishment of excipient or API vendor's product quality. Several manufacturers were only conducting ID tests, others were not even doing this much.

The warning letters also listed quality deficiencies in process validations and testing programs. There were also several incidences of partially released batches with no formal risk analysis regarding the safety of released product. As some of these companies were contract manufacturers and research organizations, interested attendees asked about sponsor company responsibilities for these violations. Pagano pointed out that a warning letter to a contract manufacturer provided sponsor information, underscoring the importance of a sponsor's due diligence.

Finally, Pagano revealed that a company within the last few months received a warning letter for failing to self-identify as a Generic Drug User Fee Amendment manufacturer. This may be the start of a new trend. The warning letter indicated that since the GDUFA fees were not paid, the drugs were in fact misbranded. Since it is a violation of federal law to ship misbranded product, the company faced possible product injunction or seizure.

### PDA Who's Who

**Debra Pagano,** President of DLP/FDA Consultants, LLC

(l-r) Debra Pagano, DLP/FDA Consultants; Jim Agalloco, Metro Chapter Nominations Chair

# Singapore Becomes Latest PDA Chapter

Recently, 45 pharmaceutical professionals formed the Singapore chapter of PDA, bringing to 24 the number of chapters across the globe. The chapter held its first official meeting in September and elected the following officers:

**President:** **Maureen Hertog**

**President-Elect:** **Sateesh Yelisetti**

**Treasurer:** **Chia Phei Kok**

**Secretary:** **Wayne Lee,** PhD

As the chapter begins planning and hosting new events for pharma professionals in this region, please monitor the chapter's Web page for updates: www.pda.org/singapore.

### PDA Who's Who

**Maureen Hertog,** PharmD, Novartis Singapore Pharmaceutical Manufacturing Pte Ltd

**Sateesh Yelisetti,** Baxter

**Chia Phei Kok,** Visentic Solutions Pte Ltd

**Wayne Lee,** PhD, Pall

chapter update

# UK Chapter's Single-Use Systems Workshop Proves Worthwhile

**Mark Gibson, AstraZeneca**

On September 19, PDA's UK Chapter organized a workshop on single-use technology hosted by Fujifilm Diosynth Biotechnologies at Billingham, U.K. The planning committee, led by UK PDA Chapter board member **Luke Heaven,** Sartorius Stedim Biotech, provided a stimulating program starting with a table-top exhibition and a networking opportunity for the attendees. This was followed by an afternoon of presentations from invited speakers with a focus on overcoming the challenges of implementation of single-use systems in the biopharmaceutical arena. Over 50 members and guests from the United Kingdom and some from the rest of Europe participated in the workshop, proving it to be a very worthwhile event.

**Peter Large**, Fujifilm Diosynth Biotechnologies, welcomed everyone to his site at the start of the presentations and led guided tours of the facilities at the end of the afternoon. He also gave a very engaging presentation about his personal experience on the design of the single-use operation at Fujifilm, discussing both the benefits and the challenges that they had overcome.

**Dave Wolton,** PM Group, chaired the workshop science sessions, introducing single-use systems and offering a presentation on the project management of single-facilities and disposables.This was followed by a presentation from Luke Heaven on material management and sourcing for single-use. **Arnaud Schmutz,** Sourcin S.A., then discussed knowledge management systems for training of single-use based processes.

There was time after the presentations for a panel discussion with the presenters and other experts who answered questions from the audience that had not been raised earlier. This resulted in a lively discussion and open debate among the attendees and served to share knowledge and experiences in the challenges of single-use implementation.

One overwhelming topic of the day was the theme of standardization of single-use, both in terms of technologies, approaches and data packages offered by the vendors. The current state of standardization and ongoing initiatives were of interest to end users and vendors alike. This was a timely discussion in light of the upcoming PDA technical report on the topic.

Judging by the number of attendees who stayed to the end and toured the facilities, there remains a great deal of interest in single-use technology.

# PDA Conference Recordings – Interactive Online Learning

PDA's Conference Recordings allow you to affordably hear from today's top presenters in the bio/pharmaceutical industry with no traveling!

**Recordings from PDA's 2013 events are now available for purchase. The events include:**

## 2013 PDA/FDA Joint Regulatory Conference

Recordings from the entire conference are available for purchase for **$400 Member/ $440 Nonmember**. Price of recordings includes:

- Seventeen (17) recorded sessions from the 2013 PDA/FDA JRC and five (5) recorded sessions from the Improving Investigations Workshop
- Access to 45 downloadable presentation handouts
- Unlimited access to all session recordings for **90 days from receipt of login information.**

## 2013 PDA/FDA Improving Investigations Workshop

Recordings from the entire workshop are available for purchase for **$400 Member/ $440 Nonmember**. Price of recordings includes:

- Five (5) recorded sessions from the 2013 PDA/FDA Improving Investigations Workshop and seventeen (17) recorded sessions from the 2013 PDA/FDA JRC
- Access to 45 downloadable presentation handouts
- Unlimited playback of the recordings for **90 days from receipt of login information.**

## 2013 PDA Visual Inspection Forum

Recordings from the entire conference are available for purchase for **$240 Member/ $280 Nonmember**. Price of recordings includes:

- Eight (8) recorded sessions from the 2013 PDA Visual Inspection Forum
- Access to 14 downloadable presentation handouts
- Unlimited playback of the recordings for **90 days from receipt of login information.**

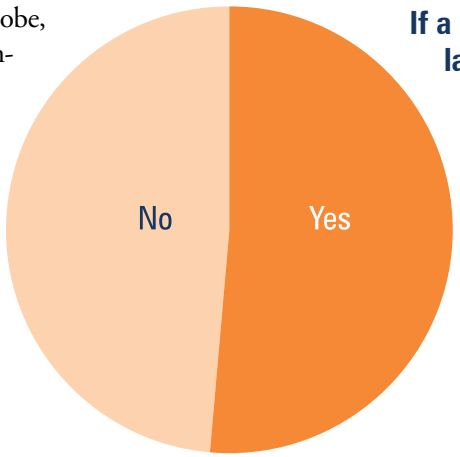
**For more information on all PDA conference recordings please visit: www.pda.org/onlinelearning**

PDA Pulse

# Hiring Managers 50/50 on Foreign Language Proficiency

PDA members come from all across the globe, and, naturally, many speak more than one language. In light of this, we asked if proficiency in a foreign language served as a deal breaker during the hiring process. Just over 51% indicated language proficiency would have an impact on whether to hire someone while over 48% said it would not.

**If a candidate lists proficiency in a foreign language, does that impact your decision to hire the person?**



# PDA/FDA JRC "Neophytes" Provide Real-Time Updates

**Rebecca Stauffer, PDA**

For the *2013 PDA/FDA Joint Regulatory Conference,* the *PDA Letter* decided to follow around two new participants of the Association's largest meeting to gather real-time feedback. **Anne Ravelo,** Alexza Pharmaceuticals was attending her second PDA/FDA conference, and **Chitra Sharma,** gCompliance, was a bonafide rookie participant. Both graciously and patiently answered questions posed by **Rebecca Stauffer,** who practically tailed the two as they experienced the 2013 event.

### Monday, Sept. 16, 2:45 p.m.

***PDA Letter:*** How are you finding it so far?

**Ravelo:** I'm finding this conference to be highly informative and a very good resource for a number of different reasons. One, is to find out what some of the trends are, and what the area of focus is for the specific regulatory bodies but also to kind of get solutions or ideas for moving toward a quality-driven culture, and recognizing that there are hurdles, and knowing how to overcome them.

**Sharma:** I think this conference was very enlightening from the get-go. That people were very science-driven and they gave specifics. And I liked how the case studies were laid out, examples set and there was no need to point at anybody or anything, in particular, but to give all the specifics. And that to me—I mean, I'm a big detail person—and so to me, that was the biggest thing. A gift, so far, is that whether it's a regulatory body or whether it's a person from the industry, they're able to speak about specifics freely and scientifically. And that's great value.

***PDA Letter:*** So, you'd say its meeting your expectations?

**Sharma:** It's *totally* meeting my expectations! I am so driven to be here tomorrow again.

***PDA Letter:*** What are you looking forward to tomorrow and for the rest of the sessions today?

**Ravelo:** I'm particularly interested in not only the bigger plenary sessions but more of the interest groups, and spending some time face-to-face and more intimate time and personal, interactive time with some of the key people in the interest groups.

***PDA Letter:*** So, what are you looking forward to, Chitra?

**Sharma:** I'm also looking forward to the interest groups and more specifics and I'm also attending the workshop on improving investigations. I've always been credited with doing investigations well or liking investigations but I'm all about learning and I'm sure with new approaches to investigations, one only gets better. So, I'm really looking forward to it.

### Tuesday, Sept. 17, 2013, 2:45 p.m.

***PDA Letter:*** Chitra, to start us off, how has the second day been so far?

**Sharma:** Excellent. I enjoyed the conference in terms of all the GMPs and all the regulators' talks today. It was very interesting to hear the CDRH perspective on combination drugs. And it's been a great day.

***PDA Letter:*** So, Anne, what have you liked so far?

**Ravelo:** The two key takeaways from today was the presentation that **Erwin [Vanhaecke]** gave—it had a lot to do with quality metrics and being able to institute a quality culture in an organization. And then like Chitra said, there's very detailed information about the combination products because I'm in that space too. So, there's a lot of guidance we can utilize and leverage.

***PDA Letter:*** And both of you yesterday were excited about going to the interest group sessions. How did that go?

**Sharma:** Very good. Very good. So, I did go into the Quality Systems Interest Group meeting, and **Rick Friedman** was there, and there were a couple of other people. And I really enjoyed asking some questions. And at one point I asked a question to Rick who later said it's a tough question!

**[Editor's Note:** See p. 42 for an overview of the Quality Systems Interest Group meeting at the conference.**]**

***PDA Letter:*** Did you attend that one as well, Anne?

**Ravelo:** That one I attended too. And that one I'm familiar with too because I think **Jennifer Magnani** runs that one and she presented last year, and it was good to see her again, kind of enforcing and strengthening some of the key concepts.

***PDA Letter:*** What are you both looking forward to about tomorrow, the last day of the conference?

**Sharma:** I'm looking forward to starting my workshop.

**Ravelo:** The Compliance Update is a good one to go to. And actually these presenters were here last year too. It's all the authorities that are up there on the panel.

### Wednesday, Sept. 18, 10:45 a.m.

***PDA Letter:*** So, Chitra, what have you thought of the conference so far?

**Sharma:** It's extremely informative. And I think I have met some key people who make decisions at the U.S. FDA., and I've heard from them. And physically also had an opportunity to go meet them before or after the sessions. But even listening to them speak very clearly and very methodically about each of the events or programs that they have at the FDA, it's very useful. A lot of times you get inundated by information on the industry side, and it's so hard to parse the differences but when each division comes and speaks so eloquently, it kind of parses it for you.

***PDA Letter:*** Would you attend this conference again?

**Sharma:** It's probably going to be on my annual list of conferences. I've already followed up with the PDA organization to volunteer actively because I really think that this is very well aligned with what I do professionally, and that I can contribute to this organization, if I were to volunteer.

## About the Experts

**Anne Ravelo** is Sr. Manager, Quality Systems, Documentation and Data Management at Alexza Pharmaceuticals. Previously, she was a Senior Business Analyst at the company, focusing on process and systems at the company.

**Chitra Sharma** is a biopharmaceutical consultant with over 15 years of experience in quality and regulatory affairs in both small and large molecules. She authors and reviews regulatory submissions, leads regulatory inspections and provides input, strategy and advice on the regulatory path forward for companies through the pharmaceutical development of the product.

### Call for Volunteers!

If you're planning to attend the *2014 PDA/FDA Joint Regulatory Conference* and would like be interested in speaking with the PDA Letter throughout the course of the conference, please contact **Rebecca Stauffer** at stauffer@pda.org

# TOOLS FOR SUCCESS

Brought to you by the PDA Career Center.
Go to www.pda.org/careers for the latest opportunities.

# Crash and Burn: Toxic Errors in a Resume

**Perry Newman**

HERE are five errors in a resume that can cost you a job and sometimes much more.

1 Sometimes job seekers with extended gaps in their background try and fill them in by extending actual dates of employment by adding an extra month (and sometimes more) onto both sides of the position. This is dangerous. Some feel it is right to extend a date on a resume when it represents only a few days, i.e., a layoff occurred on April 25 and they put May on the resume as the final month of employment. I do not recommend this tactic. For me, the best way to cover lengthy gaps in employment is to just put down years of employment, i.e., 2002 to 2007.

If you no longer work for a company, however, but are still on the payroll after you left the job, I do not consider it lying to say you are still employed up until your final severance date has been reached.

2 Personally, as a hiring authority the error I hate the most in a resume is misrepresenting skill sets by adding ones you do not have just because I desire them. Just as egregious is to intimate proficiency at something when it's not so, or overstating a skill set or the amount of experience you have working with it when it is not the truth.

3 The dumbest error I have seen, and the one that has come back to haunt more people after they got the job, is to lie about education and certifications. Almost as bad is stating you have completed training courses you began but did not finish.

4 Everyone knows a top notch resume must include Achievements, but listing achievements that are not true is not the way to go. I have seen too many people overstate achievements and accomplishments, or take credit for things they have no right to claim as their own. This is foolish, and in most cases people are tripped up during the interview process when the interviewer tries to confirm these claims. To me, the hardest part of writing a resume is gathering information and properly wording an achievement to sound as strong as possible, without crossing the line between fact and fiction.

5 While on the topic of Achievements, this final point is one people (and professional resume writers) often fail to consider, and it can be potentially costly if you're caught. For many of you, especially in sales, or in positions related to the sales process, and for managers and top executives, your achievements may be extraordinary but they may also be proprietary information. When you convey these achievements in writing you must be careful not to disclose information that you can be sued for, or that others may consider unprofessional, i.e., client names, specific contacts and proprietary figures as related to sales volume, revenue and specific contract figures, etc. Some information may be protected in an employment contract and using it to boost your value may be grounds for a lawsuit against you.

## About the Author

**Perry Newman,** CPC/CSMS, is a nationally-recognized career services professional; an executive resume writer and career transition coach, certified social media strategist, AIPC-certified recruiter and a straight-shooting blogger on how to conduct a successful job search.


# 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

2013 PDA/FDA
Joint Regulatory Conference

Plenary Sessions

**Opening Remarks and Opening Plenary**
(l-r) Anders Vinther, PhD, Genentech; Susan Schniepp, Allergy Laboratories; Daniel Kraft, MD, FutureMed; Janet Woodcock, MD, U.S. FDA; Joyce Bloomfield, Merck; Richard Johnson, PDA


**P4: A Patient's Perspective**
Rick Roberts, University of San Francisco

**P2: Quality Culture and Partners**
(l-r) Joyce Bloomfield, Merck; Mary Oates, PhD, Pfizer; Janet Stevens, Hospira; David Jaworski, Lachman Consultant Services

**P3: Understanding Good Manufacturing Practices**
(l-r) Rick Friedman, U.S. FDA; Cathy Burgess, Alston & Bird; Erwin Vanhaecke, PhD, Novartis; Mary Malarkey, FDA; John Ayres, PhD, Eli Lilly

**P5: Compliance Update**
(l-r) John Finkbohner, PhD, MedImmune; Martine Hartogensis, U.S. FDA, CVM; Steven Silverman, FDA, CDRH; Mary Malarkey, FDA, CBER; Ilisa Bernstein, FDA, CDER; Armando Zamora, FDA, ORA



**A1: Quality Agreements**
(l-r) Rebecca Devine, PhD, Consultant; Paula Katz, U.S. FDA; Shane Killian, J&J


**A2: GMP for API's, Excipients and Components**
(l-r) Alicia Mozzachio, U.S. FDA; Janeen Skutnik-Wilkinson, NSF

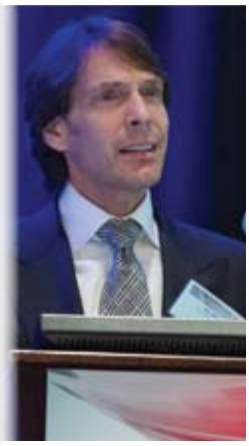

**B1: New Facility Design Options**
(l-r) Pankaj Amin, U.S. FDA; Morten Munk, CMC Biologics

**B2: FDASIA**
Mark Walderhaug, PhD, U.S. FDA


**C1: Beginning of Lifecycle [Development]: FDA's Expectations for a Submission**
(l-r) Ramesh Sood, PhD, U.S. FDA; Jeffrey Baker, PhD, U.S. FDA

2013 PDA/FDA
Joint Regulatory Conference

Breakout Sessions



**C2: Integrated Approach to Product Lifecycle: Development and Technical Transfer**
(l-r) Alton Johnson, PhD, Pfizer; Renee Kyro, AbbVie; J. David Doleski, U.S. FDA

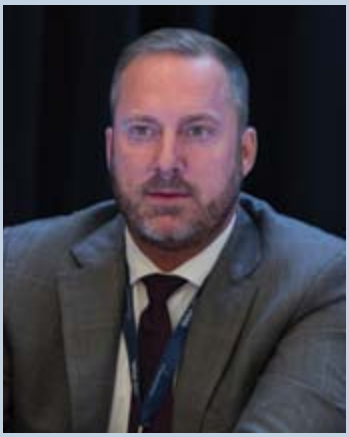


**A3: Good Distribution Practices**
(l-r) Riekert Bruinink, IGZ; David Ulrich, AbbVie; Steven Mendivil, Amgen


**A4: International Trends: Inspection and Collaboration**
(l-r) Raphael Brykman, U.S. FDA; Carmelo Rosa, FDA



**C4: Lifecycle Towards Commercial Manufacturing**
(t-d) Maik Jornitz, G-Con; E.J. Brandreth, Althea; Ian Elvins, Elvins & Associates



**A5: Post Inspectional Follow-up**

(t-d) Ernest Bizjak, U.S. FDA; Douglas Campbell, InterPro QRA

**B3: Outsourcing Innovation**

(l-r) Susan Schniepp, Allergy Laboratories; Laurie Norwood, U.S. FDA; Ian Elvins, Elvins & Associates


**B4: Combination Products and Companion Diagnostics**

(l-r) Patricia Love, MD, U.S. FDA, Isabel Tejero, MD, PhD, FDA; Stanley Liu, FDA

**C5: Continuous Improvement**

(l-r) Grace McNally, U.S. FDA; Sharon Bourke, PhD, Eli Lilly; Mahesh Ramanadham, FDA

## 2013 PDA/FDA Joint Regulatory Conference

### Exhibit Hall


### Visiting Chapters

**Brazil Chapter**

Members of the Brazil Chapter pose for a photo outside the Gala Reception.

**Japan Chapter**

Members of the Japan Chapter pose with PDA President Richard Johnson (third from left, top row) and PDA Europe SVP Georg Roessling, PhD (first from right, top row).

Jade Chin, J&J, took home a bottle of fine Midleton Irish Whiskey gifted from Complya Consulting

Timothy Michler, GSK, won an iPad from NSF International

Annette Post of Novo Nordisk won the iPad furnished by PDA

Adnan Kadiri of Bausch + Lomb took home a Dell laptop from Commissioning Agents, Inc.

Máire Colhoun of Mylan walked away with a Kindle Fire from NSF-DBA

Lizzie Leininger won a Kindle Fire HD from Associates of Cape Cod

snapshot

# Risk Assessment During Drug Product Design: Being Proactive

**Jahanvi (Janie) Miller, PDA, and William Harclerode, Forest Research Institute**

Medical device design is often improved and optimized (even after launch) to reduce risk to patient. For drug products, however, once the drug is initially designed and has gone through clinical trials, it is not common practice to revisit the original design once the product is commercialized. The U.S. FDA released their guidance, *Safety Considerations for Product Design to Minimize Medication Errors,* in Dec. 2012 for comments. This guidance discusses various considerations for the design of both the drug product and the user interface in order to prevent medication errors (the most common type of error in healthcare). But what corrective actions or risk management is industry implementing to reduce patient risk to address the concerns that were raised in this guidance?

There are many aspects of drug product design and development that can be assessed for risk (including: sizing, dosing form, delivery method and labeling) to improve patient safety. Proactive risk assessments have long been discussed during the early stages of drug development but many pharmaceutical companies have yet to develop formal plans to execute these assessments and further improve the quality of drug products. It is critical to implement a safety by design practice during drug design and development, and to update the design as necessary after commercialization. Since patients can vary widely in their state of health, it is also good practice to utilize analytical approaches to investigate (and potentially minimize) possible user-related risks. It's of added value to take learned lessons from marketed drug products and implement corrective and preventative action plans for new drug designs.

This year PDA has published three technical reports which are heavily focused on ensuring drug product quality during manufacturing to reduce risk to patients. We will continue this effort by channeling knowledge of our membership and industry subject matter experts in an effort to expand our portfolio of risk-based technical documents to include the design of drug products.

*Technical Report No. 54: Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations*

*Technical Report No. 54-2: Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations, Annex 1: Case Study Examples for Quality Risk Management in Packaging and Labeling*

*Technical Report No. 54-3: Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations, Annex 2: Case Studies in the Manufacturing of Pharmaceutical Drug Products*

# Journal *Preview*

## November–December Issue Includes Three Parts on Leak Detection of a Parenteral Proteinaceous Solution

This issue includes a three-part exploration of leak detection of parenteral proteinaceous solutions from **Dana Guazzo,** PhD, **Mats Rasmussen, Rasmus Damgaard, Peter Buus** and **Brian Mulhall.** Part 1 looks at method development and validation and Part 2 explores method performance while Part 3 examines chemical stability and visual appearance.

*Editorial*

Govind Rao, "Mens Sana in Corpore Sano"

*Commentary*

Christoph Herwig, et al, "Risk-based Process Development of Biosimilars as Part of the Quality by Design Paradigm"

*Research*

Harry Yang, et al., "A Risk-based Approach to Setting Sterile Filtration Bioburden Limits"

*Technology/Application*

Dana Morton Guazzo, et al., "High-Voltage Leak Detection of a Parenteral Proteinaceous Solution Product Packaged in Form-Fill-Seal Plastic Laminate Bags. Part 1. Method Development and Validation"

Dana Morton Guazzo, et al., "High-Voltage Leak Detection of a Parenteral Proteinaceous Solution Product. Part 2. Method Performance as a Function of Heat Seal Defects, Product–Package Refrigeration, and Package Plastic Laminate Lot"

*Case Studies*

Tim Sandle, Barbara Gebala, "Comparison of Different Fungal Agar for the Environmental Monitoring of Pharmaceutical-Grade Cleanrooms"

Nuala Calnan, et al., "Enabling ICH Q10 Implementation—Part 1. Striving for Excellence by Embracing ICH Q8 and ICH Q9"

Mansoor Ahmad, Nudrat Adil, "Stability Studies of Two Different Polygelin (Haemaccel and Gelofusine) According to ICH Guidelines"

Dana Morton Guazzo, et al., "High-Voltage Leak Detection of a Parenteral Proteinaceous Solution Product. Part 3. Chemical Stability and Visual Appearance of a Protein-Based Aqueous Solution for Injection as a Function of HVLD Exposure"

Kiyoshi Fujimori, et al., "Development of an Inductively Coupled Plasma Mass Spectrometry Method for Quantification of Extracted Tungsten from Glass Prefilled Syringes Used as a Primary Packaging for Pharmaceutical and Therapeutic Protein Products "

# Tech *Trends*

## Autoinjectors Present Challenges and Future Outlook

**Geralt Williams, PhD, Aptar Pharma**

Currently, there is an increase in the demand for, and approval of, biologic therapies and this is predicted to accelerate over the next few years. Autoinjectors have been employed for several years to deliver biologics treatments for chronic diseases such as multiple sclerosis and rheumatoid arthritis. Self-injection of prescription medicines has helped make "normal life" accessible to increasing numbers of patients.

Despite autoinjectors being available for a number of years, many patients and healthcare workers remain unfamiliar and somewhat dissatisfied with these devices. Because of the different treatment needs for specific diseases, which are sometimes chronic, the delivery device must be aligned with specific therapies in order to get the best outcome for each patient group.

Since autoinjectors are often used infrequently, patients tend not to develop familiarity with these devices. Manufacturers must keep in mind usability and functionality factors such as ease of training, repeated and consistent usage and reliability.

With increased pressure on healthcare costs worldwide, elements such as cost per dose as well as adherence and compliance are becoming key considerations in autoinjector product developments. It is widely accepted that important factors include ease of use and training as these are closely related to issues of adherence/compliance which in turn affect clinical outcomes and ultimately the overall costs.

Pharmaceutical companies are the engine driving the effort to meet the increased demand for biologics in the future. They will be key in pulling together all the above elements all the way from the biological new molecular entities to the finished product, which should ultimately fully meet the patient's needs and provide life changing opportunities to many people.

Meeting regulatory standards is also an obligation for these products and specific regulations applicable in the autoinjector device domain include usability engineering, human factor considerations, and risk assessments.

### About the Author

**Geralt Williams,** PhD, is Director, Scientific Affairs, Aptar Pharma, Prescription Division, in France. He is in charge of scientific affairs and has contributed to the development of several new devices for nasal and inhaled drug products. Aptar unveiled a new line of autoinjector products at the PDA *2013 Universe of Pre-filled Syringes and Injection Devices conference in Basel.*

# Task Force *Corner*

## Blow/Fill/Seal Task Force Promises "Robust" TR

**Rebecca Stauffer, PDA**

Members of the Blow/Fill/Seal Task Force met face-to-face in Boston, Oct. 2–3, after the Blow-Fill-Seal International Operators Association (BFSIOA) meeting there. Task force members began outlining the upcoming BFS technical report with some assistance from BFSIOA. This organization represents individuals, primarily in pharma, who work with BFS technology, and has even provided a "Points to Consider" document which the task force is using as a starting point in developing the technical report.

"We're not starting this project from ground zero thanks to their generosity," **Ken Muhvich,** PhD, Principal Consultant, Micro-Reliance, and task force leader, said of BFSIOA. "They want a really robust technical report to be out in the industry sooner rather than later."

Ultimately, the technical report will address the lack of process understanding among regulatory authorities and the lack of available guidance for new and existing users of BFS technology in addition to providing meaningful environmental monitoring for BFS processes.

"There's a universal dearth of readily available information on this subject," Muhvich said. "Our approach is to give an even-handed look at the technology and provide guidance for people [and] try to educate the regulators a bit about areas of the technology they may not know."

The task force consists of 15 members, including five from Europe. The team will also reach out to various regulatory authorities for input as well.

While the technology itself is not new, Muhvich pointed out that companies in emerging markets such as China, India and some South American countries are buying BFS machines but have little experience with the technology.

The task force hopes to have a final draft of the report ready for review by the PDA Board of Directors in September 2014. Muhvich expressed confidence that the report will provide industry with scientific-driven information on BFS technology.

"Depending upon the equipment used and the sterile manufacturing process itself, BFS technology can be considered advanced aseptic processing," he said. "We hope to give the pharmaceutical industry a ready reference which gives the reader a realistic view of BFS capabilities, benefits and limitations."

### About the Author

**Ken Muhvich,** PhD, is the Principal Consultant for Micro-Reliance LLC, which specializes in microbiology and regulatory compliance consulting. He has conducted numerous mock prior approval audits of sterile manufacturing facilities.

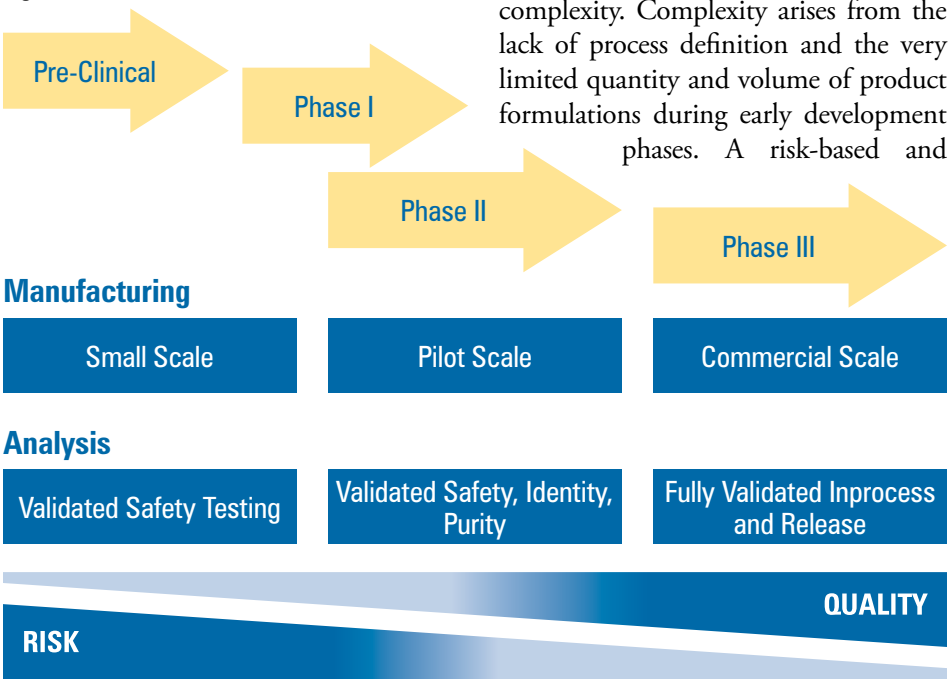
# Validation and Qualification of Sterile Filtration for INDs

**Ross W. Acucena, EMD Millipore**

The manufacture of investigational medicinal products presents additional challenges and complexity in comparison to commercially manufactured and marketed products. By definition, the word "investigational" implies that there is an effort to achieve a further understanding through additional knowledge. It is the acquisition of process understanding and process knowledge that drives a development effort to build quality into the process and product by effectively mitigating risk and unknowns. The application of QbD is intended to eliminate risk and build a foundation of quality into the product and process as it moves along the development continuum **(Figure 1).** Therefore, patients participating in clinical trials are exposed to higher risks as compared to patients treated with marketed products.

Regulatory guidance on investigational products is intended to minimize this risk. This recommendation involves evaluating the manufacturing setting to identify potential hazards and take appropriate actions to eliminate and mitigate them with the intention to safeguard the quality of the investigational drug ***(1).*** Some patient safety risks such as toxicity, unintended side effects or the efficacy of the product are inherent to the nature of drug development, and exist as a result of the lack of process understanding and validation at early phase development. Per the U.S. FDA, "Product sterility is a critical element of human subject safety, you should take special precautions for phase 1 investigational drugs that are intended to be sterile" ***(1).*** For aseptically prepared drug products, the sterilizing filtration process is a critical unit operation in providing sterility assurance to the manufacturing process.

**Figure 1** QbD Continuum




Qualification and validation requirements for the sterilizing filtration of liquids of commercial drug products are clear and well understood. *PDA Technical Report No. 26 (Revised 2008) Sterilizing Filtration of Liquids* is a valuable reference which clearly details how sterile filtration validation should be conducted in order to comply with regulations. Determining the appropriate qualification and validation activities and methodologies for the filter sterilization of investigational medicinal compounds is an area of much less clarity and greater complexity. Complexity arises from the lack of process definition and the very limited quantity and volume of product formulations during early development phases. A risk-based and phase-appropriate strategy for the qualification and validation of filter sterilization is a sound mechanism to overcome these challenges and to ensure that as a product advances through development stages, risk is continually displaced by a foundation of quality. Therefore, one can look to regulatory guidance documents to better understand the requirements for validation of sterilizing filtration of early phase medicinal products. Two such documents that can be referenced in this case are the FDA's *Guidance for Industry: CGMP for Phase 1 Investigational Drugs* and *Eudralex Vol. 4 Good Manufacturing Practice Guidelines*.

A review of these documents for guidance specific to the qualification and validation of the sterilizing filtration of liquids provides numerous insights.

The FDA document ***(1)*** proceeds to list out a number of manufacturing controls that should be considered; this list includes controls such as media process simulation, environmental monitoring, sterilization of components and devices, aseptic technique training and quality control requirements for product release. The topic of liquid sterilization by filtration, however, is not directly addressed or emphasized as a process control that should be focused upon during phase 1. One could conclude that validating the efficacy of the filter's ability to produce a sterile effluent is not required at this stage.

In contrast to the FDA guidance, the European guidance ***(2)*** makes a strong recommendation that liquid sterilization by filtration should be validated to the same standard as commercially marketed products. During early development stages such as phase 1 this could be difficult to achieve due to product volume limitations that could prevent the normal course of work that is a prerequisite to filter validation such as filter capacity and sizing trials.

It can be concluded that neither the FDA nor EU guidance provides detailed

insight on how the critical operation of sterilization by filtration should be handled in development phases. In reality, from the perspective of a sterilizing-grade filter supplier and validation service provider, we see sterile filter validation occur at a variety of development stages from as early as phase 1 and up to late phase 3. Thus, the question is often raised "what is the right time to validate the sterile filtration process." The answer, like most validation questions, is, "it depends." In general, many drug manufacturers' lifecycle management processes require filter validation to occur in phase 2.

There are of course exceptions, however, such as difficult to filter sterilize formulations which could warrant validation at an earlier time or development of a highly similar products where the acquisition of existing knowledge can be leveraged. Still, filter validation can be considered as a lifecycle process in and of itself and not as a discrete action. This concept will be elaborated upon with recommended actions to mitigate risk from the sterile filtration process as early as practically possible to align with the concept of quality by design and the overall objective of producing safe clinical products. The recommendations that follow will focus on the three main facets of sterilizing-grade filter validation: chemical compatibility, bacterial retention, and Extractable and Leachable substances evaluation. The objective of each recommendation is to acquire as much knowledge as practically possible in regard to the efficacy of the filtration process, and thus remove risk and unknown and build quality into the process. In essence, the activity of sterilizing filtration process design and validation should be treated as a lifecycle process not an event that occurs at a single point in time.

## Early Phase Development

**Chemical Compatibility:** It is critical even as early as phase 1 to start the evaluation of chemical compatibility because a noncompatible fluid and filter combination has a much higher likelihood to result in particulate or leachable contamination and/or bacterial passage both of which are unacceptable. The successful use of a sterile filter in early phase as defined by product quality and filter integrity testing is not a suitable replacement for evaluating chemical compatibility. The reason is, with small batch sizes the filter/product contact time could be a very short duration, and therefore, evidence of a noncompatible filter may only be detected during full validation at a later stage of the product development. Once the process has become more defined and fixed, the replacement of a critical device with a large product contact surface area becomes a greater challenge.

Drug product availability may not afford a full compatibility test of the filter device. Therefore, a paper-based assessment is the optimal starting point were the product solvent, active ingredient and excipients can be assessed against material handbooks and supplier-published information, as well as knowledge obtained from the development and qualification of highly similar product formulations. If a paper-based assessment points toward any suspected incompatibility, testing should follow. This could be testing of only membrane coupons in order to limit use of valuable drug product or testing of a full device using a placebo if the compatibility concern is related only to the solvent or excipients. Despite the fact that the filtration process may not be well defined, a compatibility testing design space could be easily arrived at by assuming that the total filter/product contact time would not exceed the length of time that an aseptic filling process is qualified for, and a similar design space decision could be made for temperature assuming the maximum temperature of a typical filling suite for products filtered at ambient temperatures or just below the maximum temperature at which a product would remain stable for a product that is heated prior to filtration.

The lack of a fixed final product formulation is another challenge of determining compatibility during early development. Design space strategy, however, can be implemented to overcome this challenge. Here, a hypothetical product could be formulated on the basis of the maximum quantity of individual ingredients and pH limits and thus serves as a basis for a worst-case formulation from which compatibility of a filter device can be evaluated.

**Microbial Retention:** It is critical at early development stages to evaluate the risk of not having an efficacious sterile filtration process. When evaluating microbial retention, a drug developer who has experience developing highly similar formulations, such as MAbs for instance, has the advantage of relying on the filtration efficacy results of highly similar drug product filter combinations where critical parameters that influence microbial retention can be compared such as surface tension, osmolarity and physical parameters such as: pressure and time. Table 6.3-1 in *PDA Technical Report No. 26 (Revised 2008) Sterilizing Filtration of Liquids* is a good starting point from which highly similar product formulations could be risk assessed in order to use the prior knowledge gained by validation of one or more formulations to assess with some degree of confidence that a new formulation/filter combination is efficacious. At which point a proper validation of microbial retention should commence as the product formulation and filtration design space become more clear and fixed by establishing the required parameters from which to design a meaningful process and product specific validation: defined product formulation, filter capacity, flux, maximum pressure, maximum contact time, expected bioburden and filtration mode (constant pressure or constant flow rate).

In contrast, the developer of a novel drug formulation with no existing knowledge should make every effort to prove sterile filtration efficacy as early as practically possible. In particular, a new formulation which contains a surface active ingredient that reduces surface tension or a nanoparticulate formulation such as a liposomal vaccine presents additional risk. Per Folmsbee and Moussourakis:

> "A review of field and laboratory bacterial retention validation data for a variety of fluids and challenge conditions suggests that low surface

tension fluids, such as many adjuvants and adjuvanted vaccines, present a higher risk of the occurrence of a bacterial penetration event during sterilizing filter validation. Among the classified solutions examined, liposome solutions represent the highest risk, followed by lipid and finally surfactant solutions" ***(3).***

During early phase development when product volume is scarce it may not be practical to complete a process and product specific microbial retention test at the same standard as required for marketed products. A modified approach, however, can provide the drug developer with an early indication that sterilizing filtration efficacy will be effectively validated later in the development effort. The typical approach to microbial retention studies could be modified to use only one challenge filter as opposed to the typical set of three or by use of membrane discs that are smaller than the often used 47 mm size. Additionally, filter manufacturers and validation service providers can be consulted for advice on test setups and arrangements that are designed to limit the amount of product volume required. In general, an opportunistic approach should be employed to seize opportunities to acquire additional knowledge of the liquid sterilization process as early as practically possible.

**Extractable and Leachable Substances:** As is the case with chemical compatibility and microbial retention, numerous opportunities exist to acquire knowledge and reduce risk along the development path. Essentially, the E&L evaluation starts as early as initial filter device selection where only devices that meet compendia and other qualification standards should be selected examples include conformance to USP Class VI, materials that meet indirect food additive requirements per 21 CFR 177–82, and are nonfiber releasing. Verifying acceptable compatibility between the process conditions, process fluid, and filter increases the likelihood that selecting well qualified materials will result in an acceptable E&L evaluation that is not additive to the product to an extent that would pose a health risk to the patient.

The practice of performing extractable substances studies with model solvents is an advantage for early phase development because these studies do not require valuable and perhaps nonexistent formulated drug product. In the case where the drug manufacturer is developing highly similar formulations, it is likely that previous model solvent studies utilizing the same filter type would be applicable to new formulations. Additionally, suppliers may publish some basic extractable substances information in the form of white papers or validation guides which can be leveraged at an early stage to assess the expected overall quantity of extractable substances, and also review identified compounds for toxicological assessment and potential to react with the API or other drug ingredients.

A rationalized design space taking into consideration the sterilization process, the maximum expected contact time, and temperature is generally all that is required to select relevant model solvent data from which to evaluate a particular process if unsure of the most appropriate model solvent the worst case one could be selected. Thus, qualification information and extractable substances evaluation will provide a strong indication that the selected filter device will not adversely impact the product. Further confidence is built upon the utilization of the same materials of construction throughout development to ensure through clinical trials and stability studies that no adverse reaction is occurring between filter leachable substances and the product. Additional evidence of safety and quality can be demonstrated by conducting a leachable substances evaluation during the later stages of drug development when the precise formulation becomes fixed; the filter that will be used in commercial production is selected, sterilization method and process is defined, and any mitigation steps such as preflush of filters has been defined.

## Conclusion

The treatment of filter validation as a lifecycle process and a process validation effort will help to ensure that the right level of quality is being designed into the sterile filtration process. When treated in this manner a drug developer is in a much stronger position from which to demonstrate due diligence in protecting patient safety. This can be a challenge within the context of regulatory guidance that points towards the importance of sterility assurance controls as early as phase 1 but is very nondescript on the manner in which the validation of the sterile filtration process should be conducted at such an early point in the drug development effort.

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3. Folmsbee M. and Moussourakis M. "Sterilizing Filtration of Liposome and Related Lipid-Containing Solutions: Enhancing Successful Filter Qualification." *PDA Journal of Pharmaceutical Science and Technology* 66 (2012): 161-167.


## About the Author


**Ross Acucena** has over 13 years of combined experience in pharmaceutical manufacturing and validation. His work experience includes manufacturing of both API and sterile drug products.


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# ATMPs Offer Exciting Drugs, Face Age-Old GMP Challenges

**Walter Morris, PDA**

The tone of the 2013 PDA Europe *Advanced Therapy Medicinal Products* conference in Florence, Italy, last June, was set early with a presentation by **Harald Petry,** PhD, Chief Scientific Officer, uniQure, a Dutch company that just so happens to own the first EMA-approved gene therapy in the western hemisphere.

Excitement in the room over the newly approved therapy was palpable, and led conference participants and speakers to ponder if a revolution in advanced therapy medicinal products (cell and gene products) was on the horizon similar to the one for monoclonal antibodies (mAbs) several decades ago.

PDA Europe's **Georg Roessling,** PhD, Sr. VP, suggested as much in his questions directed to conference co-chair and first speaker, **Giovanni Migliaccio,** PhD, Director, Research, Instituto Superiore di Sanita, following his talk, "The Long and the Short Way to Clinical Use in Europe for ATMPs."

Migliaccio replied to the "big question," noting that in the end, it will come down to costs versus benefits. Nevertheless, he noted that there are lessons for ATMP developers in the history of mAb marketization. The first product took longer to get on the market than the next, and subsequent approvals took less time, because "now everything written was done. You had the handbook and you could go faster."

Like ATMPs today, cost was an issue for mAb products at first, Migliaccio explained. When it became clear "that antibodies were very effective, more effective than previous care, so we accepted the costs and everyone was happy."

Today, companies developing ATMPs must ask if they are creating therapies for which people will pay.

"My suggestion is let's start from the low-hanging fruit. Something that is very effective, change life, and everyone is willing to pay a high price because you get better and it is less expensive than paying for care for life."

Another strategy is to target an untreated rare medical condition, like lipoprotein lipase deficiency (LPLD), which is one of the genetic diseases targeted by uniQure, the successor company to Amsterdam Molecular Therapeutics.

According to the July 19, 2012 EMA assessment report ***(1)***, "*Glybera* (Alipogene tiparvovec) is a replication-deficient adeno-associated viral vector designed to deliver and express human LPL gene variant LPLS447X."

The drug substance is produced using a baculovirus expression system transduced into insect cells. Three different replicating baculovirus vectors are transduced, "either expressing the recombinant AAV vector genome carrying the LPL cassette, the AAV rep gene or the AAV cap gene." These vectors replicate in the insect cells to produce AAV components resulting in recombinant AAV particles, which are released from the cells by incubation in lysis buffer, purified, concentrated and filtered. The drug product is in the form of a sterile injection delivered in a single-use vial.

Approval of the marketing application took over three years, a journey that included several recommendations against approval by the EMA's Committee for Medicinal Products for Human Use (CHMP).

In his talk, uniQure's Petry discussed a few of the process-related issues that arose during application review. Demonstrating to the regulators "control of this natural process of the cell," he explained.

"This is quite challenging to do to make sure that this process in the cells which is not really totally controlled is consistent and robust and always delivers the same products with the same specifications that we set."

Although the downstream process was "relatively straightforward" compared with the upstream process, Petry noted that the regulators wanted increased measures to ensure there was no viral contamination from the baculovirus.

"Because baculoviruses are infectious," Petry said, the company had to "really make sure our product is free of baculovirus." The company, therefore, added an additional chromatography step for increased "security and safety."

The company also had to tweak the sensitivity of the impurity assays. "We've come to a stage with regulators where impurities are more important than your product itself," quipped Petry. While showing the identity of the product was "relatively easy," developing and validating impurity assays was a "big hurdle." Petry attributed the difficulty to the fact the company was using "cutting-edge technology" for the assays.

To be successful, he said, "You need a strong interaction with regulators to explain to them what is cutting edge technology, really, and what you can do on the side of validation so you can get to an agreement with them. If you don't get agreement, then you have a hard time."

The company also spent a lot of resources validating and comparing the evolving processes to past processes. "We are now on process 6," Petry explained. The first few processes were developed a decade ago, and "those people were long gone."

The reviewers wanted the company to show comparability with the past processes used for clinical purposes. In the end, Petry said, the process "does not have to be the same [and] if you find differences, it is fine as long as you can explain what the differences are and where they are coming from."

Each iteration of the process resulted in testing of the product "in very different ways," each of which had to be validated. "Most of you know what validation means; it means a lot of time and money," remarked Petry. In the end, he recommends that other companies developing ATMPs "try to develop as few processes as possible."

### Raw Materials a Concern

Microbial contamination and impurities are big concerns for cell and gene products, particularly because options for sterilization and impurity removal are limited.

**Jaana Vesterinen,** Senior Researcher, Supervision and Licenses, Finish Medicines Agency and Chair of the Working Party, talked about the importance of high-quality raw materials for advanced therapies and the progress of the EDQM's newly established Raw Materials for the Production of Cell-Based and Gene Therapy Products Working Party. The group was formed in 2012 following calls for harmonized guidelines in this area.

Guidance in this area is needed, Vesterinen explained, because many "if not most" of the hundreds of the raw materials used for ATMPs are available only in research grade. "It makes it difficult to assess the quality, safety and consistency of these raw materials and also the implications of these aspects to the medicinal products."

Particularly concerning is the lack of data for full traceability and exact composition of the raw materials in many cases, she said. "This places the manufacturer of cell-based or gene therapy products into a difficult situation because they must fulfill the legislative requirements and provide enough adequate and reliable information on the origin and composition of the raw materials."

Clinical-grade raw materials, when they exist, "are often very expensive and they may hinder the development or use of these advanced medicinal products."

The Working Party seeks to develop an overarching text outlining quality requirements for ATMP raw materials. The scope will include biologically active raw materials of biological origin, such as serum, growth factors, cytokines, antibodies and enzymes. Quality attributes to be covered include origin, traceability, composition, viral safety, identity, product-related variance and biological activity.

An audience participant asked Vesterin if there was impetus to harmonize with the USP <1043> "Ancillary Materials for Cell, Gene, and Tissue-Engineered Products." Vesterinen replied, "First we integrate our own opinions in Europe, and we need to consider what is needed here and what is relevant. And then we can have a next step to harmonize. It doesn't mean necessarily that it is in contradiction."

She said the Working Party believes the risk-based approach promulgated by USP has to be "built in the quality criteria rather than taken as the natural approach."

Raw materials is one of the areas of focus for PDA's new Gene and Cell-based Therapeutics (GCBT) Task Force, which held a meeting at the June conference. Besides tackling ancillary materials, the group also wants to clarify GMP expectations for GCBT products and other regulatory concerns in the European Union and United States.

**Valerie Pimpaneau,** PhD, Voisin Consulting Life Sciences, and **Michelle Myers**, PhD, Product Leader, GlaxoSmithKline, are co-chairs of the task force. The two spoke with the *PDA Letter* during the meeting. It was clear that the group was in a transitional phase as it decided to merge three previously created sub-groups into one main group to tackle issues one at a time rather than concurrently.

The first project tentatively aims to address manufacturing and control strategies for cell therapy-based products. The team is looking at the A-MAB and A-VAX case studies, developed from the cooperation of several large biotech companies. (For more information on the GCBT Task Force, contact PDA's Joshua Eaton, eaton@pda.org).

The remainder of the ATMP Conference delved deeply into clinical and financial concerns for this nascent product category.

All in attendance agreed that the meeting was an important one as the age of gene and cell-based products is upon the industry. In the opening to her presentation on raw materials, **Jean Stanton,** Director, Compliance, Janssen Pharmaceuticals summarized the mood best:

"The more I see topics being covered like this at the level of PDA it just warms my heart....You can feel the progress. We are in the state of transition, coming out of the lab and moving into the clinics."

### References


1. Assessment Report: Glybera, European Medicines Agency: July 19, 2012 www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002145/WC500135476.pdf


### Gene and Cell-based Therapeutics (GCBT) Task Force

**Ricardo Jimenez**

**Theo De Natris,** bioMerieux Industry, Inc.

**Viktoria Graf,** CELLGENIX GmbH

**Robert Shaw,** FinVector Vision Therpies Oy

**Dorit Harati,** Gamida Cell

**Otto-Wilhelm Merten,** Genethon

**Audra Riley,** GlaxoSmithKline Biologicals S.A.

**Dirk Groenewegen,** Glycostem Therapeutics

**Annigje Rietveld,** Health Care Inspectorate, the Netherlands

**Kellathur Nadathur Srinivasan,** Health Sciences Authority

**Manuel Carrondo,** IBET - Instituto de Biologia Experimental e Technologica

**Shuyuan Zhang,** Intrexon Corporation

**Ofra Axelrod,** Israeli Ministry of Health

**Allen Burgenson,** Lonza AG

**Patrick Stragier,** Masthercell S.A.

**Nigel Stapleton,** MicroSafe Laboratories

**Niels Guldager,** NNE Pharmaplan A/S

**Zorina Pitkin,** OrganoGenesis, Inc.

**Alice Varga,** OXiGENE

**Harvey Brandwein,** Pall

**Rich Levy,** PDA

**Ailyn Kandora,** PDA Europe

**Hannelore Willkommen,** Regulatory Affairs & biological Safety (RBS) Consulting

**Kevin Slatkavitz,** Think Quality, LLC

**Hanna Kankkonen,** University of Tampere/ Regea (Institute for Regenerative Medicine)

**Stephen Brown,** Valneva

**Vera Franzen,** Vera Franzen Consulting AB

# 2014 PDA UPCOMING EVENTS

## JANUARY EVENTS

**28-29**
**Joint Regulators/Industry QbD Workshop**
London, UK
https://europe.pda.org/EMA2014

## FEBRUARY EVENTS

**18-19**
**Pharmaceutical Microbiology**
Berlin, Germany
https://europe.pda.org/Microbio2014

**20-21**
**2014 PDA PIC/S Q7 Training**
Bethesda, Maryland

## MARCH EVENTS

**11-12**
**Parenteral Packaging**
Brussels, Belgium
https://europe.pda.org/ParPack2014

**18-20**
**Interphex 2014**
**PDA Premier Sponsor**
New York, New York

**25-26**
**Modern Biopharmaceutical Manufacturing**
Lyon, France
https://europe.pda.org/Biopharm2014

## APRIL EVENTS

**7-10**
**2014 PDA Annual Meeting and Bioburden and Biofilm Workshop: Contamination Control**
San Antonio, Texas
www.pdaannualmeeting.org

**28-29**
**Vaccines & Beyond**
Brussels, Belgium
https://europe.pda.org/Vaccines2014

## MAY EVENTS

**19-20**
**2014 PDA Knowledge Management Workshop – Enabler for ICH Q8 & Q11, QRM and Continued Process Verification**
Bethesda, Maryland
www.pda.org/QRM2014

**20-21**
**2014 PDA Packaging Conference**
Washington, D.C.
www.pda.org/packaging2014

## JUNE EVENTS

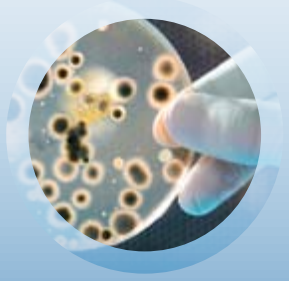
**3-4**
**2014 PDA/FDA Supply Chain Conference**
Bethesda, Maryland
www.pda.org/supplychain2014

**3-4**
**Advanced Therapy Medicinal Products**
Madrid, Spain
https://europe.pda.org/ATMP2014

**9-11**
**PDA/FDA Virus & TSE Safety Conference**
Bethesda, Maryland
www.pda.org/viral2014

**17-18**
**2014 PDA Aseptic Sterilization Conference**
Chicago, Illinois
www.pda.org/aseptic2014

**24-25**
**Parenteral Manufacturing**
Istanbul, Turkey
https://europe.pda.org/ParMan2014



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**8-10**
**2014 PDA/FDA Joint Regulatory Conference**
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www.pda.org/pdafda2014

**10-11**
**2014 PDA Drug Shortage Workshop**
Washington, DC
www.pda.org/drugshortage2014

**16-17**
**Pharmaceutical Freeze Drying Technology**
Brussels, Belgium
https://europe.pda.org/FreezeDrying2014

**24-25**
**7th Workshop on Monoclonal Antibodies**
Basel, Switzerland
https://europe.pda.org/Monoclonal2014

**29-30**
**Mycoplasma**
Berlin, Germany
https://europe.pda.org/Myco2014

## OCTOBER EVENTS

**6-7**
**2014 Universe of Prefilled Syringes and Injection Devices**
Huntington Beach, California
www.pda.org/prefilled2014

**13-15**
**2014 PDA Biennial Human Performance & Human Error Reduction Training Conference**
Bethesda, Maryland
www.pda.org/humanfactors2014

**14-15**
**Pharmaceutical Cold & Supply Chain Logistics**
Berlin, Germany
https://europe.pda.org/SupplyChain2014

**16-17**
**Interphex Puerto Rico**
**PDA Premier Sponsor**
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**20-22**
**PDA 9th Annual Global Conference on Pharmaceutical Microbiology**
Bethesda, Maryland
www.pda.org/microbiology2014

**21-22**
**Visual Inspection**
Berlin, Germany
https://europe.pda.org/Visual2014

## NOVEMBER EVENTS

**4-5**
**Parenterals**
TBD
https://europe.pda.org/Parenterals2014

## DECEMBER EVENTS

**2-3**
**Outsourcing/Contract Manufacturing**
Berlin, Germany
https://europe.pda.org/Outcon2014


# Crossover Moves

## Making a Career on Both Sides of the Government/Industry Divide

**Rebecca Stauffer and Walter Morris, PDA**

# In basketball,

## All agreed that the mission to serve the public does not change on either side of the divide

a well-executed crossover move gives the ball handler a clear path to the basket. There, she can either dish off for an assist or score an easy layup. The *PDA Letter* staff has identified another kind of crossover move—the career crossover. This happens when a professional with a long track record in the industry leaves to join a regulatory agency, or vice versa. When played well, this crossover opens up a clear path to professional growth and fulfillment. The *PDA Letter* editors interviewed six individuals who executed this move in recent years.

While each of our participants had unique situations and career aspirations, there were surprising similarities across the board. These "crossover moves" show that while there are clear differences between the private and government sectors, the folks who make this move adjust to the new environment fairly quickly and pursue their new career with as much, if not more, vigor as in their previous role.

### Giving Back, New Challenges Drive Crossover Moves

**Cesar Matto** moved to the Agency after 25 years in industry. Originally from South America, joining the U.S. FDA allowed him to fulfill a lifelong goal: providing a service to his country.

"I had a set of goals that I wanted to fulfill, and one of them was basically providing a service to my community, to my country; and that in itself was a tremendous motivator," he said.

For **Yuexia Li,** her move to FDA after a lengthy private-sector career offered an opportunity for her to use her skills as a quality assurance expert to have a bigger impact and meet a personal goal.

"First of all, I always wanted to work for the FDA. For maybe the past ten years," she said. "And I think with my education, my training, and experience in the industry as a scientist in a management role, I can really make a difference in the FDA to contribute to the drug regulations."

**Jeff Baker** saw the opportunity to work for FDA as a new professional challenge following a quarter century working for pharma companies.

"The move is both squarely in my comfort zone, building upon 25 years in development and manufacturing of bioproducts and both technical and managerial leadership roles, and presents a rich environment to learn new things, new perspectives, and hopefully help out in new ways," he said.

Taking a position with Amgen following a two-decade career at FDA, offered a new professional challenge for **Kris Evans.**

"I started as an investigator and spent 16 years doing that," he said. "Then I went to CDER, Guidance and Policy, where I was able to use a lot of that investigative experience to then work on some interesting initiatives—the aseptic guidance and the GMP of the 21st Century Initiative, which were big programs....And as those were winding down, it felt like a good time to go. I was enjoying my job; I loved it. I wanted to leave while I still enjoyed it....It was time to take those experiences to a company to see how I could help make a difference there."

**Moheb Nasr** said joining GlaxoSmithKline after a 22-year career at FDA provided him an opportunity to expand his horizons through the company's diversity of products.

"As a global and diverse company, it provides a lot of opportunities to meet my many interests," he said.

Even though one can gain varied experiences at FDA, Nasr said he wanted to gain new knowledge and work with a diversified set of products.

"Looking for a company that was global, that has diversity of drug products—small molecule, large molecule, vaccines, consumer health—different therapeutic areas—respiratory, oncology, antiviral, antibiotics, cardiorenal, diabetic drugs—so this was the kind of diversity I was referring to that made me select GSK as an employer," he explained.

A "good offer" that included "opportunities to contribute and learn" prompted **Renita Johnson-Leva** to join Advanced Bioscience Laboratories following years working for both the FDA and U.S. National Institutes of Health.

"ABL is a great company with really talented people, terrific scientists. It's a great combination with really interesting work," she indicated.

### Motivations Remain the Same Despite Career Switches

Interestingly, money was not a major motivating factor leading to these career transitions for our six crossover specialists.

"Earning potential is only part of the equation," said Johnson-Leva. For her, "wanting to go to work and making a difference" serves as her main motivation.

Nasr affirmed that salary was only a minor consideration, but was not "fundamental" to his decision to join GSK. Evans said there is more money in the private sector, but that didn't motivate him. He cited other benefits to working for FDA besides money, such as job security and work/life balance, which were much more valuable to him while raising a family.

For Li, public service also serves as a motivator.

"I really work for the American public and what I do every day, directly or indirectly, impacts the American public. I think this is a very good feeling," she said.

Baker's motivation remains unchanged now that he is with FDA.

### Article at a Glance

- Motivation to deliver safe, effective drugs the same regardless of role
- "Crossover Moves" do require some adjustment
- Personal connections made at earlier roles missed

## Back to School for a Career in Academia

**Rebecca Stauffer, PDA**

While our cover story focuses on career transitions between industry and regulatory, occasionally individuals within either area "cross the court" to a third option: academia.

In May, **John Ferreira** joined Blinn College as Director of the Therapeutics Manufacturing Program. Previously, he spent several decades within industry, working for a number of biotech companies.

While he "thoroughly enjoyed" his prior role as SVP, Quality for Kalon Biotherapeutics, he admitted that teaching was an area that always lay at the back of his mind.

He further described his role as the "perfect opportunity for someone who has been a 'practitioner' for so many years to transition into academia to build courses and refine curriculum specially designed to support the industry in which they worked."

Like the others the *PDA Letter* interviewed, Ferreira felt that his initial motivation—ensuring product safety—changed little.

"My role here at Blinn College is not that different than the roles I have had in private industry," he said. "Here at Blinn College, I have the task of developing a curriculum comprised of courses in manufacturing and quality that will prepare students for positions in a FDA-regulated environment."

He warned anyone considering a career in academia treat it like any new other role that requires learning new knowledge and skills.

"If you do make the jump to academia, keep in mind 'teaching' is a skill." Ferreira said. "Recall your own academic experiences, and which instructors, teachers or professors were engaging and which teachers were just there."

Despite his joy at teaching, he said he also relished his career within industry. He pointed to his work at Kalon, in particular the hard work and dedication of his coworkers.

"We spent many hours and sleepless nights in the first year developing and refining project proposals, simultaneously designing and implementing the firm's manufacturing and quality programs to support the company's business goals," Ferreira said.

He plans to use this experience, as well as earlier project work, to provide his students with "practical knowledge in addition to their academics that will hopefully lead to successful careers in an industry dedicated to treating, preventing or curing disease."

Although the earning potential within academia can be lower, Ferreira said this is offset by the "personal satisfaction of knowing that you may have contributed in some small way to the future success of a graduating student. And when a student thanks you for your efforts… there is no greater reward."

### About the Expert

**John Ferreira** was hired in 2009 by G-CON in College Station, Texas as Director of Quality. He then took a position with by Kalon Biotherapuetics as SVP, Quality. He is now the serving as the Program Director for Blinn College's new Therapeutics Manufacturing Degree Program.

"Throughout my career I've been driven to broaden the impact of biotechnology and manufacturing sciences in general. That was my motivation in industry, and actually it remains my motivation in government service," he said.

All agreed that the mission to serve the public does not change on either side of the divide.

"I personally strongly believe that there is a common shared goal between industry and regulators, and that common goal is developing and delivering high-quality medicine to the nation," Nasr explained. "There is a shared goal that regulators and industry work hard to achieve. They have different roles in achieving such goals."

In describing the shared mission, Johnson-Leva said, "It's a different seat at the table. I think the table is round. We're all looking at the same thing."

Moving to government or to industry can expand horizons.

Nasr put it this way: "When I worked in the Agency, the goal would be how can I assure quality based on what is in the file… What was missing for me was the earlier part of drug discovery, drug development and manufacturing," he said. "I think my work here at GSK will provide me with depth of knowledge in the areas of drug discovery, development and manufacturing that I did not see much of while I was working at the agency."

Matto said he felt more limited with industry.

"While I was in industry and working for a specific company—and I've worked with some very large corporations and some medium-sized corporations—and while I was addressing problems specifically at a site, they were just site-specific issues. My radius of influence was limited to a set number of applications, a set number of issues, what area the site is responsible for—but with the FDA, my radius of influence has expanded tremendously," he said. "And that was one of the other issues that motivated me—the sphere of influence I would have bringing this wealth of experience that I had in industry, that would definitely have an impact into a larger group as opposed to just one single company."

#### Adjusting to a New Culture

Although motivations for the most part remained unchanged, those interviewed pointed out there are differences between the two work environments, even if they wouldn't say one environment was better than the other.

"Definitely there is a cultural difference in the government," Li said. "Because you can lead a project but you don't have a carrot or you don't have a stick. You have a very limited way to promote people doing a good job…you [also] have a very limited way to get rid of the nonperformers."

She went on to mention that she has found that when leading a project for FDA, she seeks buy-in from her team, such as pointing out how the initiative or project will make their jobs easier.

Matto noted that adjusting to the FDA culture was not dissimilar to moving from one company to another.

## It's a different seat at the table. I think the table is round. We're all looking at the same thing

"You go into a new organization, you're going to learn new systems, you're going to have to learn about the people, [and] how to interact with the folks," he said. When moving from industry to government, he allowed, "The level of complexity certainly *is* higher."

Baker also did not find it a disruptive change.

"Both FDA and industry participate in sophisticated decision-making processes that manage both opportunity and risk," he said. "It was not as disruptive a transition as one might imagine."

While he feels he has adapted pretty quickly, Baker hopes to avoid complacency in his job.

"I hope I never really get fully comfortable because that can lead to complacency or perhaps a lessening of drive. We need to be a continuously learning organization. We need to always be changing and improving."

Most of the individuals interviewed adjusted fairly quickly to their new environments. Li and Matto indicated it only took about six months for them to get settled into their new roles at FDA.

Those joining industry after lengthy stays with the FDA felt it took a little longer: one year for Nasr and even longer for Evans.

"Oh, I'm still getting used to it," Evans said. "The transition is a challenging one. It's not that easy to go, probably, either way from FDA to industry or vice versa. And there's a lot to learn, and a lot to unlearn, at first, so that you can kind of be open to understanding not just your own view of the world but working within a complex business environment with a lot of things to think about."

For Nasr, it took time to adjust to experiencing all aspects of the product lifecycle, from early stage development to manufacturing, the diversity and complexity of GSK's products and its culture.

"It took me about a year to really be able to better understand the working pieces in industry," he said.

On the other hand, Johnson-Leva who has alternated between working for the National Institutes of Health, FDA, and industry, said her periods of transition have varied but her approach to it hasn't.

"I always viewed it as an adventure," she said.

As far as differences, each identified aspects of the government bureaucracy as a clear differentiator.

Among the things he really likes about working in the private sector, Nasr listed less bureaucracy, streamlined administration and the number of experts he can reach out to.

Matto said there is a clear difference in the "speed" of processes between the private sector and government.

"I understand now, having worked four years at FDA, we have to be also very careful in our communication. So, there are different levels of review. I do miss that in industry, we perhaps move a little bit faster," he explained.

Li said, "I would say the incentive aspect of the private sector is very good, because they really have a different measurement to distinguish high performers to low performers. But in government, those are very limited. However, in the government, you do have that sense of a feeling you are working for the public and what you do, the impact is nationwide. And that is a very satisfying feeling."

Hierarchy might be less rigid in the private sector, too.

According to Li: "For my previous jobs, I usually reported directly to the CEO or the president, so I always had the top access to the top boss."

Evans put it this way: "Our company is what we call very matrixed—it's not very hierarchical. So, there's interactions…you can find yourself interacting with a senior vice president the first couple of days on the job. And so we don't have to kind of interact through a chain of command."

Surprisingly, the group identified some similarities in the working environments.

"There's lots of similarities," Baker said. "But both FDA and industry participate in sophisticated decision-making processes that manage both opportunity and risk. Whether the impact of a decision is personal and immediate or whether it's not, that can be viewed quite differently in the private sector or in public service and give rise to different views of what's acceptable risk and benefit. Nevertheless, both FDA and the regulated industry use data-driven science to bridge that cultural divergence and find that common ground and providing access to medicines."

Johnson-Leva concurred, "I think they're very complementary."

Evans also identified similarities: "Well, certainly similarity in terms of the mission. We're both serving patients and public health and that's a nice goal to have regardless of where you work, in government or in industry…very similar."

Evans feels the well of opportunity is deep within the Agency.

"So, at FDA, it was a place where you can go and work really hard and have limitless opportunities, if you're willing to take the initiative....That's a huge advantage. Not a lot of disadvantages really. You could take that investigator job as far as you were willing to go," he said.

### Personal Connections Missed/Enjoyed Most

All participants missed the relationships they built in their former professional lives.

Like a point guard on a new basketball team, Evans said, "I clearly miss my former teammates, if you will. I think there are a lot

of dedicated, hardworking employees at FDA—public servants." Evans also added that he missed his FDA badge.

Nasr provided almost an identical response: "I think I miss my colleagues and friendships that I developed over the years. I think this is the part is what I miss the most. I also miss not being able to assist with urgent public health issues."

In the end, while they missed the personal connections made in previous roles, the six individuals interviewed expressed the belief that by executing their "crossover moves," they opened up themselves up to new career opportunities. Their experiences also show that just because someone might work for many years on one side or the other, it is never too late to execute such a crossover move, opening up a path to a fulfilling and exciting second career.

People entering the pharmaceutical industry can look forward to opportunities both in the private and public sectors. While there are differences between the two fields in terms of bureaucracy and hierarchy, the environments do share similarities. Ultimately, the decision to make a crossover move comes down to evaluating the options available and determining if such a move aligns with your career path.

## About the Expert

**Jeffrey Baker,** PhD, joined the Office of Biotechnology Products as Deputy Director in 2011. He spent over 20 years at Eli Lilly in both bioprocess development and in manufacturing science and technology, participating in the development, launch, and stewardship of several bioproducts.

**Kris Evans** is currently the Executive Director of Quality Sciences at Amgen. In 2007, he retired from the U.S. FDA after serving for 20 years as a Field Investigator and later in CDER's Office of Compliance on the Guidance and Policy Team.

Since 2004 **Renita Johnson-Leva** has been an integral contributor for regulatory, quality and technical matters at Advanced Bioscience Laboratories. She has ten years of regulatory experience at the U.S. FDA including experience as the Primary Scientific and Regulatory IND Reviewer for over 60 IND products, over 170 BLA and supplements for licensure and postmarketing.

**Yuexia Li,** PhD, has been with the U.S. FDA for a little over three years. She was hired by the Office of Generic Drugs as the Sr. Quality Assurance Specialist to set up the Quality Management System (QMS) for OGD. Li is a molecular biologist by training and spent 15 years in the private sector in various capacities as Sr. Scientist, Project leader, QC Director and Sr. Director, Quality System.

**Cesar Matto** joined the Office of Compliance, in the Office of Manufacturing and Product Quality, U.S. FDA, in 2009. He spent over 25 years in the private sector assuming various roles with increasing level of responsibilities in the areas of quality control, quality assurance, compliance and manufacturing. Immediately prior to joining FDA he was Corporate Director, Quality Assurance at Pharmaceutics International, Inc.

After 22 years at the U.S. FDA, **Moheb Nasr,** PhD, joined GlaxoSmithKline in September 2011 as VP, Global CMC Strategy. He is responsible for the development and the execution of GSK's CMC regulatory strategy. Prior to joining GSK, Nasr served as the Director of the Office of New Drug Quality Assessment (ONDQA), CDER.

The conversation continues online with the November *PDA Letter* Podcast. Hear more of our interviews with **Jeff Baker, Cesar Matto** and **Yuexia Li.** This and all our 2013 podcasts are available at www.pda.org/pdaletter.

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# A SAMPLING OF SOUGHT-AFTER INDUSTRY/U.S. FDA JOBS

In light of our cover story, "Crossover Moves," the *PDA Letter* reached out to recruiting firm FPC of Atlanta who identified some in-demand jobs the company is seeing recurring within industry. We also took a look at some recent FDA job postings at the USAJOBS website (www.usajobs.gov).

## JOBS

### FDA

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**Operations Research Analyst (CDER)**

As an Operations Research Analyst within CDER, you will plan, organize and carry out various operations research studies involving the substance of major programs and the policies associated with those programs.

**Pharmacist (CDER)**

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**SUPERVISORY INTERDISCIPLINARY SCIENTIST (CDER)**

As the Division Director for the Division of Medication Error Prevention and Analysis within CDER's Office of Surveillance and Epidemiology, you will oversee the planning, managing, organizing, and directing of all the post-marketing operations/functions and activities of the Division.

**Biologist (CDRH)**

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# Reports from the *2013 PDA/FDA*

## Growing a Quality Culture

**Janmeet Anant, PhD, EMD Millipore Corporation**

Around 1300 people participated in the *2013 PDA/FDA Joint Regulatory Conference*, held in Washington, D.C. Sept. 16–18. This was the highest attendance figure in the history of this annual event, as asserted by PDA Chair, **Anders Vinther**, PhD, during the opening plenary session. Subsequently, Vinther reviewed ongoing changes in the pharmaceutical arena from various aspects, including industry, health authorities, technologies, organizations and people. Since the conference was titled "Driving Quality and Compliance throughout the Product Life Cycle in a Global Regulatory Environment," he emphasized that in this complex and dynamic environment, manufacturing quality continues to be the top priority for the pharmaceutical industry.

In contrast to Vinther's highlight of changes within the pharmaceutical industry, **Janet Woodcock,** MD, Director, CDER, U.S. FDA, began her presentation at the opening plenary by stating that manufacturing experts from the 1950s would easily recognize today's drug manufacturing processes. Woodcock compared the current situation regarding unreliable pharmaceutical drug quality, along with resulting drug shortages, with the recent history of hospital services and medication errors. She referenced a self-regulation report titled, *To Err is Human: Building a Safer Health System* ***(1).*** From this report, she highlighted key lessons that could mitigate current pharmaceutical manufacturing quality issues, such as avoiding "a shame and blame game" and "denial of collective responsibility." In the end, Woodcock sees reliable drug quality occurring when organizations and the industry look beyond just compliance and start moving toward a culture of quality.

She also presented examples of quality culture in terms of systems, risk management, metrics and specialization. As a positive example, Woodcock cited that quality metrics-based surveillance has reduced drug shortages by about 50% from last year. Everyone, she envisions, including suppliers, repackers, relabelers, manufacturers, regulators and others, should be part of the quality culture, whereby focus on clinically relevant specifications is critical. She then emphasized that establishing international standards and improving QbD will drive production of quality drugs from the start of the manufacturing process. In addition, a shift towards continuous manufacturing will make processes more flexible and efficient.

This opening plenary session introduced the main focus of the *2013 PDA/FDA Joint Regulatory Conference*, where more detailed presentations and discussions occurred during the three session tracks:

**(1) Quality and Compliance —** One of the biggest challenges in the pharmaceutical industry is the implementation of a quality system, especially across multiple sites within a global company.

**(2) Industry and Technology —** There is a need for ongoing innovation, where regulatory oversight is one factor in the lack of industry adoption of modern manufacturing technology

**(3) Product Lifecycle —** There is an emphasis on continuous process verification, starting during the process development phase all the way through product discontinuation

Like me, attendees took full advantage to learn, discuss and network with FDA experts, decision makers as well as industry professionals who were willing to share their insights and experience.

### Reference


1. Kohn, L.T., Corrigan, J.M. and Donaldson, M.S. eds. 2000. *To Err is Human: Building a Safer Health System.* Washington, DC: National Academy Press.


### About the Author

**Janmeet Anant,** PhD, is EMD Millipore's Regulatory Advocate, focused on interpreting the impact of regulatory guidelines and requirements for biopharmaceutical manufacturing.

## U.S. FDA, Industry Emphasize Robust Quality Systems

**Kerstyn Bryce, GSK**

As a new member of PDA, the *2013 PDA/FDA Joint Regulatory Conference,* was the first PDA-sponsored conference that I have ever had the pleasure of attending.

**Janet Woodcock,** MD, Director, CDER, U.S. FDA, kicked off the opening plenary, discussing the current regulatory perspective of quality systems, QbD and drug shortages. Woodcock introduced a theme which resonated throughout many sessions: by establishing a robust knowledge management system throughout the product lifecycle, issues can be anticipated and mitigated before they occur. She emphasized that quality systems should be flexible and operate with a minimum of regulatory oversight. The focus of an investigation should not be blaming indi-

# Joint Regulatory Conference

viduals but instead using well-developed metrics to evaluate the state of process. Identifying the correct metrics will result in anticipating how products might fail in the future based on tracking recurring failures and identifying potential risk. With regards to manufacturing, she underscored a familiar message that in order to provide high-quality products for patients it starts with personal accountability.

The session about continuous improvement presented by **Grace McNally,** Senior Advisor, CDER, and **Sharon Bourke,** PhD, Advisor, Technical Services/Manufacturing Sciences, Eli Lilly, expanded on Woodcock's message. McNally and Bourke discussed how increased process understanding throughout product lifecycle can be leveraged to ensure product quality. Bourke discussed how the increase of process knowledge throughout technology transfer from development to manufacturing can be used to develop effective quality controls. The establishment of a monitoring system leads to better process understanding and a reduction in process variability. A process monitoring dashboard facilitates timely data analysis and issue identification. McNally focused on the knowledge management of a postapproval process. She advised that changes to a process should not be unexpected but also to not adversely react to individual events.

The conference concluded with **Rick Roberts,** Adjunct Professor, University of San Francisco, with the perspective of a patient. His poignant personal story of receiving a contaminated drug reminded us that the drugs we produce and develop have a direct impact on a patient's quality of life. It is our responsibility to ensure that our products are manufactured to the highest possible standards.

## About the Author

**Kerstyn Bryce** is a Biopharmaceutical Associate at GlaxoSmithKline and part of a Technical Development Program in Global Manufacturing and Supply.

## Industry Faces Changing Times

**Patti Rossman, Globiox**

I came to the *2013 PDA/FDA Joint Regulatory Conference* to learn more about what the speakers had to say on changes occurring in our industry as well as to network with colleagues. I was struck by the attention focused on two particular topics, both by speakers and attendees.

One of these topics, first introduced at the conference in **Janet Woodcock's** keynote address, is the concept of fostering a "culture of quality, not blame." This paradigm is based on the notion that compliance through regulations is no longer sufficient as a sole driving force on the road to quality. The idea of promoting a culture of quality throughout the industry involves the U.S. FDA reorganizing their inspection program and using a more consistent risk-based approach for inspections. The Agency believes that a culture of quality has to start at the top of a company.

Quality culture was also a major topic from industry speakers. According to them, a "culture of quality" means that companies do things in a manner that produces high-value products and protects patient safety not just to comply with regulations but also because it is the way they should do business. Industry representatives recognized the quality challenges associated with the increased complexity of supply chains and global manufacturing operations. **Mary Oates,** PhD, VP, Global Quality Operations, Pfizer, stressed that it is important to do business with partners who have the same quality culture as you do.

A second major recurring topic at the conference was innovation, which will bring great changes to the industry. FDA is publicly encouraging innovation. In the past, companies have been afraid to be the first to innovate because they did not know if their innovation would be accepted by FDA. I think it will still take time for the Agency's changes in attitude to filter down to the inspectors. I believe the FDA is realizing that it cannot keep up with the fast pace of current innovation, such as the many mobile apps that fit the traditional definition of a regulated medical device.

Interestingly, on Sept. 25, the FDA issued its guidance on mobile medical applications. This document explains the Agency's oversight of mobile medical apps as devices and their focus only on the apps that present a greater risk to patients if they don't work as intended, and on apps that cause smartphones or other mobile platforms to impact the functionality or performance of traditional medical devices.

I left the conference convinced that big changes and challenges are ahead for all of us, and that leadership at the regulatory agencies and companies must work together to rethink and reinvent ways in which to deal with quality and the protection of patients.

## About the Author

**Patti Rossman** is President of Globiox, a consulting company that specializes in validation, quality systems, remediation and compliance.

snapshot

# Interest Group *Corner*

## Clinical Trial Materials IG Explores Outsourcing Models

**Rebecca Stauffer, PDA**

During the Clinical Trial Materials Interest Group meeting in September at the *2013 PDA/FDA Joint Regulatory Conference,* three speakers addressed issues relating to the outsourcing or insourcing of clinical trial materials development. Interest group leader **Galen Shi,** PhD, Director, Global Clinical Trial Material Manufacturing, Eli Lilly, explained that he wanted the meeting to address aspects of the relationship between the client and the outsourcing company and the development of working outsourcing/insourcing models.

**Jodi Smith-Gick,** Director, Global Clinical Trial Packaging and Comparator Sourcing, Eli Lilly, and a colleague of Shi, discussed how to create effective partnerships with third party organizations. Before working with a third party organization, it is important to determine your strategic rationale for outsourcing. Capacity, capability, geographic reach are some considerations that should be factored into the strategy. The relationship/partnership with the third party should have master service level agreements, quality agreements, governance structure, and tactical instructions/processes developed in order to be effective.

In conclusion, she summarized that the breadth and complexity in the area of clinical trial material manufacturing and associated services lends itself to multiple opportunities for effective outsourcing. Partnership with third parties is essential to maximize benefit and to mitigate risk.

For the perspective of a CMO, **David Brown,** Account Executive, Patheon Pharmaceuticals, outlined a list of items that companies should expect from a CMO. One key item: in person meetings at the CMO facility.

"Part of being a partner is being there and being present," he said. "The reality is it's really irreplaceable to go visit the site and in that way build a more integral team."

He tied site visits to the overall theme of "thinking, speaking and acting like a full partner" in the client/CMO relationship.

**Susanne Resatz,** PhD, Manager, Process Development and Manufacturing, Vetter, a contract development and manufacturing organization, agreed that there must be a consistent relationship between the customer and the contract development and manufacturing organization.

"It is really important that all parties including the customer, client, and the CDMO share the same overall approach to quality. Having the same understanding ensures that all interests are taken into account. The customer wants the CDMO to have a good understanding and approach to quality, and the CDMO does not want to have a customer that encourages practices that could cost its reputation," she said.

*Continued at right of page 51*

# Interest Group *Corner*

## Metrics Should be "Meaningful," Advises Regulator

**Rebecca Stauffer, PDA**

The discussion at the Quality Systems Interest Group meeting naturally turned to the topic of quality metrics following a presentation delivered by **Rick Friedman,** Associate Director, Office of Compliance, CDER, U.S. FDA, at the *2013 PDA/FDA Joint Regulatory Conference* in September.

Friedman's presentation touched upon metrics in the context of ICH Q10, noting that metrics by themselves are not a solution.

"Metrics should be meaningful," he said. "They can be misapplied, misinterpreted or promote unintended behaviors."

Takeaways from last year's ICH Q10 workshop included an overview of purposeful metrics, such as right first time, lack of repeat occurrence, CAPA adherence and supporting a "speak up" culture.

"If you can make a metric around that," Friedman said, "that's really important."

Other examples of "metrics that work" from the workshop, Friedman noted, involve near misses, "no surprises" audit and inspection outcomes, forecast metrics, backlog creation/reduction and organizational health metrics that measure a company's quality of culture.

He then provided examples of metrics that don't work. These are "performance metrics that exclusively focus on timeliness or cycle times, metrics linked to punitive measures and metrics that discourage self-identification and reporting."

As an example of the latter, Friedman referred to metrics that encourage "no reds," such as no 483 observations. During the following Q&A, an audience member inquired as to why this is considered an inappropriate metric.

"The fact is that in our risk model, we do factor it in," responded Friedman, pointing out that lack of a 483 can also engender complacency, thereby undermining the quality system.

Also during the Q&A, the question of how to measure CAPA effectiveness arose. An audience member cited her company's experience manufacturing a product that showed potential to form a dimer. Recognizing this, the company analyzed the formation through several internal stability studies, developing a test method and then used the same test method as an in-process assay. This enabled a proactive CAPA.

Anyone interested in joining the Quality Systems Interest Group is encouraged to contact PDA at volunteer@pda.org.

### About the Expert

**Rick Friedman** is the Associate Director, Office of Manufacturing and Product Quality, Center for Drug Evaluation and Research (CDER), Office of Compliance, FDA.

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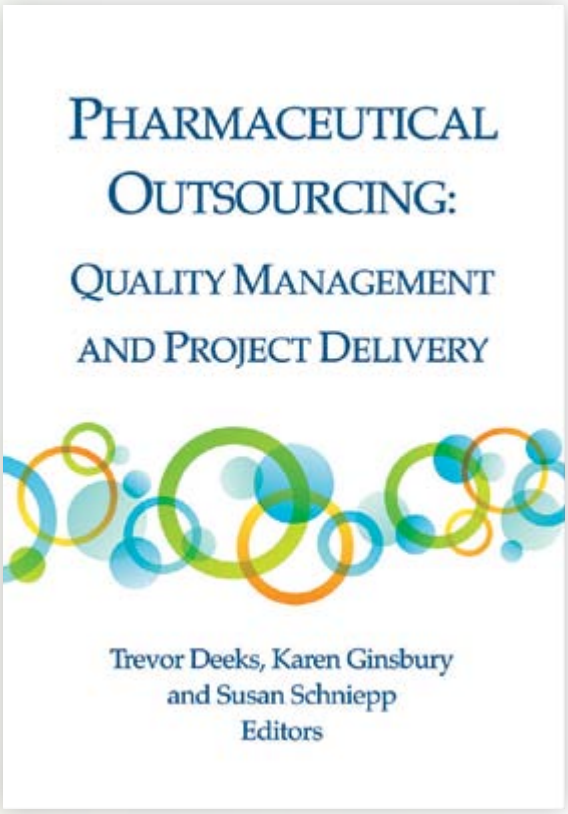


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## Pharmaceutical Outsourcing: Quality Management and Project Delivery

**Edited by Trevor Deeks, Karen Ginsbury and Susan Schniepp**

There has been a significant amount of activity and growth in contract operations. Contract organizations have services that range from research activities to clinical trial management and oversight to manufacturing of the clinical supplies and commercial product to packaging and labeling as well as product testing. Virtual companies may have multiple contracts with multiple service providers for multiple phases of the drug development process and the drug manufacturing process. To complicate the matter, there is little guidance from regulatory authorities regarding the use of contract providers, and the relationship between a client and a contract provider is important and complex. This book is intended to set forth and explore the best practices for contract organizations from various perspectives: the contract organization, the contracting organization and the regulators.

## Key Topics

Overview of Outsourced Operations
Legal Aspects of Contract Manufacturing
Points to Consider for the Outsourcing of High Value Manufacturing — A Customer's Perspective
Best Practices in Implementing Quality Agreements
Management of Outsourced Operations
Quality Management System for Outsourced Operations
Outsourced Services
Outsourcing Process Development
Outsourcing Analytical Methods
CMOs for Early Phase Biologicals Production: Process and Analytical Development
CMOs for Early Phase Biologicals Production: Contract Manufacturing and Control
Contract Manufacture of a Commercial Biological Product
Auditing the CMO
Outsourced Qualification, Validation, Calibration, and Maintenance Activities
Outsourcing IT Services and Consulting: Benefits and Pitfalls
Tools for the Management of Outsourced Operations

**www.pda.org/outsourcing**

# FDA Public Meeting Addressed FDASIA Supply Chain Provisions

**Rebecca Stauffer, PDA**

This July, industry representatives gave feedback to U.S. FDA officials on Title VII of the Food and Drug Administration Safety and Innovation Act (FDASIA), specifically Sections 713 and 714, which pertain to standards of imported drugs and registration of commercial importers along with development of Good Importer Practices. The meeting was held at the Agency's headquarters in Silver Spring, Md.

Before delving into Sections 713 and 714, members of industry and the FDA spoke about the development of FDASIA and its impact on pharma.

FDA Commissioner **Margaret Hamburg,** MD, said that "FDASIA does even more through provisions that enhance FDA engagement with stakeholders, promote innovation and address and prevent drug shortages."

But more importantly, she emphasized that Title VII "provides FDA with new authorities needed to better oversee our drug supply chain; a chain that is aggressively more complex and more global."

Later that morning, **Martin VanTrieste,** Sr. Vice President, Quality, Amgen, current Rx-360 board member and former PDA board member, said that industry's main responsibility is supplying safe medicines to patients.

"Without a doubt, this responsibility has grown more complex and challenging due to globalization of our supply chain," he said. "Globalization is impacting most industries and the biopharmaceutical industry is no exception."

That afternoon, **Jean McCue,** Regulatory Counsel, Office of Compliance, CDER, FDA, offered a more nuanced view of Section 713, which authorizes the Agency to require importers to provide information that demonstrates drugs being imported comply with FDASIA. The FDA must issue regulations that clarify this section by Jan. 9, 2014.

She specified that Section 713 lists information demonstrating the drugs regulatory status, facility information, indication of compliance with cGMP, testing results, certifications relating to status, among others as required information.

Still, FDA continues to seek public outreach regarding key aspects of 713.

"We were interested in receiving public input on how we should define importers under Section 713," she said, adding, "should there be overlap with the term 'commercial importers' as it is used in Section 714?"

Additionally, she explained that Section 713 permits the Agency to offer expedited clearance for importers voluntarily participating in a partnership program for compliant companies.

Following McCue's presentation, **Brian Pendleton,** Senior Policy Advisor, Office of the Commissioner, spoke about Section 714.

"So, what does Section 714 do?" He asked. "It requires the Agency to issue regulations requiring the registration of commercial importers of drugs, included among that would be a requirement for the commercial importer to specify its unique identifier for its principal place of business. It also directs the Agency to establish a unique facility identifier system for commercial importer registrants. And, finally, it directs the FDA to issue GIP regulations."

Like Section 713, Section 714 has also raised some questions, according to Pendleton. The biggest is how to define a "commercial importer" as well as what constitutes appropriate exemptions and how to minimize the burdens of registration.

Some of the issues raised by Sections 713 and 714 were addressed by various stakeholders during the public comments session.

**David Schoneker** from IPEC-Americas started off the comments by addressing requirements for the importation of excipients.

"We believe that excipients should be exempted from additional import requirements under FDASIA based on the level of oversight already required on the part of the end user," he said, explaining that additional requirements at importation would be redundant. As far as Section 714, he further explained that commercial importer registration requirements are again redundant as end users of excipients are already subject to FDA facility registration.

Following Schoneker's presentation, **Roger Murry** from the Certified Importer Program Coalition spoke about the Coalition's intention to develop a partnership program for compliance companies, enabling imports from these companies to be released by the Agency.

"The goal of the coalition is to eliminate the competitive advantage of noncompliance," he said.

Next, **Ben Firschein** with the U.S. Pharmacopeia offered USP's comments on Sections 713 and 714.

"Our overall message here today is demonstration of plans with standards should be part of standards for admission of imported drugs under Section 713," he said.

Firschein also emphasized that while USP does not have a verification program, current programs could be expanded to serve as an independent verification program enabling risk-based importation processes. Additionally, USP believes the FDA should require importers to provide Certificates of Analysis to demonstrate adherence to requirements.

Representing Six Degrees Counterfeit Prevention, **Reid Graves** addressed how his company offers the ability to ensure certificates of analysis (COA) using military grade encryption originally used to protect

*Continued at bottom of page 56*

# Another Successful ICH Q10 PDA/FDA Workshop —

## How do we Improve Investigations?

**Jennifer Magnani and Anders Vinther, PhD, Genentech**

The *2013 PDA/FDA Improving Investigations Workshop* was the latest in the ICH Q10 series of workshops that the U.S. FDA and PDA developed with the objective of discussing relevant topics pertaining to the pharmaceutical quality system, implementing it within industry and sharing best practices. In a subsequent issue of the *PDA Letter,* we will discuss key themes and summaries of the many plenary presentations.

Inadequate investigations continue to be one of the FDA's top five inspectional findings from inspections of domestic and foreign companies. This is also consistent with inspectional findings from many other health authorities around the world. A few examples of inadequate investigations include: lack of adequate detail, scope not broad enough, inadequate rationale for batch disposition, lack of root cause analysis, failure to address issues at CMOs, and complaints not substantially investigated or trends not detected.

Speakers at the workshop included both senior FDA officials and industry leaders. More than 200 FDA and industry subject matter experts attended the highly interactive workshop to share ideas, best practices and knowledge. FDA provided very good insight into industry deficiencies related to investigations, showed examples and also discussed with the attendees how improve investigations so that observations in this area decrease.

The structure of the workshop followed the "flow" of a quintessential investigation. After keynote presentations were delivered on the topic of "Expectations and Benefits of a Well-Executed Investigation," by **Rick Friedman,** Associate Director, CDER, FDA, **Juan Torres,** SVP, Quality, Biogen Idec, and **Martin VanTrieste,** SVP, Quality, Amgen, we went straight into discussing staffing and scoping an investigation. Following two presentations on the topics "Forming an Investigation Team" by **Swroop K. Sahota,** PhD, VP, Quality Operations, Catalent, and "Deviations, Complaints, QC Failures, and other Investigations... How to Gauge Risk, When to Act, and Who to Inform" from **Jacques Zimmowitch,** VP, Quality – Drug Product Operations, Americas/Asia, Eli Lilly, the attendees were broken into three groups (lab investigations, manufacturing investigations or supplier investigations) where they participated in a mock Quality Review Board. They were then tasked with scoping and forming an investigation team, and along the way, capturing lessons learned and making edits to the investigation's Points to Consider list.

An essential element that each of the investigation groups noted was the importance of having the right people/competencies involved from the beginning of the investigation as in many cases investigations can be very complicated—getting to the root cause and finding good solutions requires people with the right background. Also, sometimes team composition changes when new knowledge is discovered. Being open minded and not going straight to solutions without looking at all relevant data were two other key points that the participants noted. Senior management and health authority notification processes were also discussed, particularly in terms of timing and level of detail provided.

After two more presentations covering the topics of "Essential Components of a Thorough Investigation" by **Thomas Arista,** National Expert Investigator, FDA, and "Getting to Root Cause," by **Shane Ernst,** VP, Quality, Hospira, the investigation groups met again to discuss execution of the investigation. As part of this discussion, participants agreed that following a structured and methodical process is important. One should strive to identify and work on several hypotheses instead of just jumping to the most obvious one. While deadlines are important, it is also most important that the investigation is well executed with enough attention from management. Checklists can help, but one should not overrely on them.

After a third round of plenary talks, "Reactive vs. Vigilant Quality Culture Outcomes," **Lori Hirsch,** Managing Counsel, Merck, "Handling Customer Complaints," **Meera Khullar,** Lead Director, Pharma Quality Operations, U.S. Sites, Hospira, "Identifying the Right Corrective Actions," **Sharon Timmis,** VP, Operational Excellence, Pfizer and "How do you Assure Effective Corrective Actions?," **Veronica Cruz,** PhD, VP, Quality and Compliance, McNeil, teams met to identify CAPAs, including effectiveness checks. Participants acknowledged that successfully concluding an investigation is dependent on effectively getting to the root cause; effective CAPAs should prevent repeat deviation. Effectiveness monitoring is very important to ensure that the corrective action drives the right behavior and solution.

Internal company communication was highlighted and the importance of sharing and documenting the knowledge gained and lessons learned in a more structured way through the quality system.

The combination of plenary presentations and breakout discussions received positive feedback as all attendees had opportunities to share, learn and network about conducting better investigations. These discussions show that most investigations have similar elements that need to be covered, yet there are many ways of conducting a thorough investigation.

In addition to the value of the presentations, discussions, and networking, each

*Continued at bottom of page 57*

# PDA Comments on What Constitutes Limiting Inspections

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

September 13, 2013

Division of Docket Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Reference: FDA Draft Guidance for Industry Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection

Dear Sir/Madam,

PDA appreciates the opportunity to comment on this draft guidance which strengthens the FDA's ability to conduct necessary inspections to ensure manufacturing site are in conformance with GMPs.

Because this guidance includes the possibility of FDA requesting documentation in advance or in lieu of inspections, PDA suggests that FDA provide a secure electronic system to receive these documents comparable to the system for receiving electronic submissions. PDA also notes there is nothing in the guidance discussing company and FDA interactions if documents are requested in lieu of an inspection. PDA recommends FDA provide additional clarification in this guidance such as whether a 483 would be issued and how the company, who is the subject of the inspection, is given the opportunity to respond to any FDA questions or conce4rns when an inspection is conducted by review of submitted documentation.

PDA also suggests FDA provide clarification that response times for records requests may be negotiated depending on the urgency and nature of the request, volume of the records requested, and logistical considerations.

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

If there are any questions, please do not hesitate to contact me.

Sincerely,
Richard Johnson,
President, PDA

CC: Rich Levy PDA; Denyse Baker, PDA

## PDA Commenting Task Force

**Denyse Baker,** PDA (Chair)
**Jeffrey Hartman,** Merck
**Edwin Rivera-Martinez,** Sanofi
**Stephan Roenninger,** Amgen
**Anil Sawant,** PhD, J&J
**Susan Schniepp,** Allergy Laboratories

# Regulatory Briefs

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

## North America

### U.S. FDA Proposes Drug Shortages Plan

On Oct. 31, the U.S. FDA announced a proposal to alleviate drug shortages. This plan would require companies manufacturing medically important prescription drugs to notify the Agency six months in advance of any changes that might lead to shortages. This new plan expands requirements passed last year under the Food and Drug Administration Safety and Innovation Act; these requirements target companies who are the sole manufacturer of a drug while the FDA's new proposal encompasses manufacturers of any "life supporting, life sustaining" medication. Comments are due Jan. 3, 2014.

### U.S. FDA Rule Requires Unique Identifier for Devices

Effective Dec. 23, the U.S. FDA requires a unique device identifier for medical devices. This new system is supposed to adequately identify devices throughout distribution and usage. Device labelers must submit product information to the Agency's Global Unique Device Identification database. This information, including the UDI, must be submitted in plain text and in a format allowing for automatic identification and data capture. Additionally, UDIs must be included on the label and device package.

### Legislation Targeting Compounders in Senate

In early October, the U.S. Congress released a proposed bill, the Drug Quality and Security Act, which includes language tightening U.S. FDA oversight of compounding pharmacies. The bill creates a class of compounders, called "outsourcing facilities," that would be regulated by the Agency. This classification will be voluntary; if enacted, hospitals and clinics would have the option of choosing to use either the FDA-regulated pharmacy or one that is not.

The bill also creates a "track and trace" system for following the movement of prescription drugs across the supply chain. This system would require bar codes on packages of drugs shipped.

### U.S. FDA to Close Jordan Office

In December, the U.S. FDA will close its office inside the U.S. embassy in Amman, Jordan. Staff currently stationed at the office will be transferred to the Agency's headquarters in Silver Spring, Md. This post was not involved in manufacturing facility inspections and the closure is not expected to impact inspections of facilities in the region. FDA personnel at the post were primarily involved in leading training efforts for Saudi Arabian regulators.

## Europe

### New EC Device Rules Allow Random Inspections

On Sept. 24, the European Commission officially adopted two measures for improving the safety of medical devices. Within these two measures, is a requirement that allows for EU member states to conduct random, unannounced audits of manufacturing facilities.

In addition, the new measures require EU member states to designate a "notified body" following a joint assessment conducted with EC experts and other member states. These notified bodies will fall under the supervision of the member states, who will conduct monitoring and surveillance to ensure notified bodies conduct the random audits.

### EMA Releases Variations Q&A

The EMA released a Q&A document in September outlining practical considerations involving the implementation of variations guidelines. These variations concern the terms of marketing authorizations for medicinal products. The Q&A document specifically clarifies procedures that must be conducted in relation to implementation of the revised guidelines, including general considerations, new classification categories, revised classification categories and impact on postauthorization measure submissions.

# The PDA Journal of Pharmaceutical Science and Technology (The Journal) Journal.pda.org

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# Reinvent the Future in April at the *2014 PDA Annual Meeting*

**Michael VanDerWerf, Shire**

*"The best way to predict the future is to invent it."*
***–Alan Kay (American computer scientist/inventor)***

**2014 PDA Annual Meeting • San Antonio, Texas • April 7–11 • www.pdaannualmeeting.org**

Our industry faces many challenges in the 21st century, particularly some challenges that we have never been confronted with before. Dried up pipelines, pressures on prices and unexpected cost effectiveness analyses are three noteworthy difficulties facing biopharmaceutical companies. The future will be driven by innovation and new ways of thinking about manufacturing to achieve efficiencies and healthcare delivery. Like the computer industry, it is up to the biopharmaceutical industry to reinvent itself to meet today's challenges and create the future.

PDA has established a long reputation of championing innovation and quality in the manufacture of biopharmaceuticals and sterile products. The theme of the *2014 PDA Annual Meeting*, "Biopharmaceutical and Sterile Manufacturing – Embracing Innovation to Meet Global Challenges," is indicative of PDA's commitment to support the industry and be the forum for knowledge exchange.

The *2014 PDA Annual Meeting* planning committee is formulating an exciting program addressing the current issues of our industry. As a snapshot here is a sampling of some of the topics that will be presented:

- Innovative drug development approaches, and how transparent health technology assessments can recognize and reward the added value of new medicines while maintaining an innovation-friendly environment.
- Six keynote speeches given on major topics, like patient access to drugs, manufacturing innovation to address the cost of drugs, new approaches to drug development, and serving emerging markets. Leaders will share their views on the forces shaping our industry and their visions for reinventing the development and manufacturing of drugs to make cures available to the global markets.
- The planning committee has designed a program with three main tracks: "Biological Sciences," "Product Manufacturing" and "Quality Systems." There will be over 30 talks given in these three tracks. The topics to be discussed range from biosimilars, to globalized supply chains, support for aging facilities, inspection trends, investigations, process validation, aseptic processing, protection strategies for biologics, technology transfer and process analytical technologies. These talks are designed to provide information and knowledge to the attendees, but also to stimulate discussion and the exchange of ideas on topics related to manufacturing technologies and quality approaches. During the sessions, there will be ample opportunity to ask questions, pose problems, and present ideas.
- Numerous PDA interest groups will meet during the two and a half day meeting and will provide interactive forums for discussion on the most recent developments and trends in their respective subject matter expert areas. The interest groups are the place to work directly with colleagues to explore new ideas and develop initiatives, which will be the basis of future efforts to educate, guide, and improve our industry.
- Six breakfast sessions are planned to discuss topics such as human performance and human error reduction, pharmaceutical compounding, fundamentals of shipping validation and endotoxin testing and career development. Breakfast sessions are typically lively (with lots of caffeine served!) and interactive.
- Finally, and perhaps most importantly, this conference will provide us with the opportunity to meet and network directly with industry professionals, your peers.

After the conference, PDA TRI will be hosting courses from April 10–11 on biosimilars, quality risk management, process validation and verification, product development basics for combination products, and moist heat sterilization processes.

On behalf of the planning committee, please accept our invitation to join us and many of your colleagues this coming April. Together we will reinvent the future of our industry.

# Maximize Your Knowledge

**Program Planning Committee Chair Christopher Smalley, PhD, Merck & Company**

We all know *training* is important, in fact, crucial. But where do we get the content of that training?

**2014 PDA Knowledge Management Workshop • Bethesda, Md. • May 19–22 • www.pda.org/KM2014**

We all know that *finding* the *root cause* is necessary as part of an investigation, but where does that root cause and the information obtained during an investigation reside—could you find it again?

We all know that *data collection* is an integral part of our job. But after collecting volumes of data, do we really know anything more about the product or process?

The *2014 PDA Knowledge Management Workshop* has been designed to answer these, and many more, of your questions. Designed by the task force that is preparing the technical report on knowledge management, this symposium will address very old concepts such as why is it difficult to continue manufacturing when senior personnel have been lost in work force reductions or retirements. But it will also address very recent questions, such as how is knowledge management an enabler of the pharmaceutical quality system as envisioned in ICH Q11?

The planning committee behind the workshop has assembled a faculty representing a breath-taking array of expertise on knowledge management. This includes expertise outside of the biopharmaceutical industry, offering an opportunity to learn from other science-based industries.

An exciting feature of the symposium will be two breakout working groups, where you will be able to meet and network with your colleagues as you identify the issues and topics important to you alongside speakers and regulatory representatives.

This is very new, and I believe very important to becoming efficient and effective at biopharmaceutical manufacturing. I hope to see you there!

PDA TRI will be hosting three courses to complement this very important workshop:

- Integration of Risk Management into Quality Systems (May 21)
- Technology Transfer – *New Course* (May 22)
- Learning, Knowledge Management and Impact: Moving from Theory to Practice (May 21–22)

# Biopharm Manufacturing Conference Keeps Pace

**Jean-Luc Clavelin, Consultant, and Christophe Grimm, Sartorius**

Next year, the 2014 PDA Europe *Modern Biopharmaceutical Manufacturing* conference will take place for the 10th consecutive time. This time, the event will be hosted in Lyon, France March 25–26.

**Modern Biopharmaceutical Manufacturing • Lyon, France • March 25–26 • https://europe.pda.org/biopharm2014**

During these past ten years, while keeping its focus on the regulatory and quality aspects of biopharmaceutical production, this annual event has attempted to educate and provide guidance to attendees working in a fast changing and highly regulated environment.

The need to constantly improve patient needs while satisfying both regulatory and reimbursement agencies results in a high pressure environment. The consequence is the need to implement more cost-effective and flexible solutions in order to speed up time-to-market, but also a reduction in the cost of goods during manufacturing. Many concepts have been initiated and developed to achieve these goals. Major ones center on production facility design (dedicated vs. multiproduct facilities, increased flexibility, single-use systems, etc.) and process improvement and simplification (QbD, continuous processing, single-use systems, etc.).

As 2014 is our 10-year anniversary, we continue to focus on practical approaches to challenges in the development and manufacturing of biopharma and biotech products in the current GMP environment. Among innovations and evaluation of novel developments that offer solutions to some of these challenges, the 2014 conference will also address the move towards continuous processing for biopharmaceuticals. The concept of continuous production is a topic of high interest not only for an industry that sees it as a high potential for reducing cost of goods while increasing flexibility, but also to regulators as a path to improving product quality.

The planning committee is looking forward to another successful event and warmly invites you to join us in Lyon in March 2014.

*Interest Group Corner continued from page 42*

**[Editor's Note:** See the cover story, "Roadmap to External Manufacturing Partnerships," September *PDA Letter*, p. 28 for a guide on developing and maintaining an outsourcing relationship.**]**

Anyone who is interested in joining the Clinical Trial Materials Interest Group is encouraged to contact PDA at volunteer@pda.org.

## About the Experts

**David Brown** has been a business manager and account executive with Patheon Pharmaceuticals, Inc. for two and a half years. Prior to that he held management roles in several emerging innovator companies where he was responsible for both in-house and contract development and manufacturing services.

**Susanne Resatz,** PhD, heads the Process Development and Manufacturing function at Vetter's clinical production facility in Chicago. Her expertise includes designing and implementing highly efficient, high quality manufacturing processes for early stage products.

**Galen Shi,** PhD, has worked in Eli Lilly for almost ten years, with experience in solid dosage form formulation/process development, parenteral bioproduct process development and clinical trial manufacturing. Prior to that, Shi worked in Merck and Bend Research for five years in preformulation, formulation and drug delivery areas.

**Jodi Smith-Gick** is a Registered Pharmacist, from Purdue University. She has expertise in Integrated Drug Development, Portfolio Management, CT Material Manufacturing and Associated Services, Dry Product Manufacturing, Quality Assurance, and Quality Control. She is currently the global head of clinical trial packaging and comparator sourcing.

# Parenteral Packaging No Longer an Afterthought

**Dana Guazzo, PhD, RxPax**

**2014 PDA Europe: Parenteral Packaging • Brussels, Belgium • March 11–12 • https://europe.pda.org/parpack2014**

Approximately 30 years ago, **Dr. Nicholas Lordi,** the graduate school dean for Rutgers University's pharmacy school, recommended that I pursue packaging engineering in conjunction with my pharmaceutical sciences major. At the time, my research interests included parenteral product formulation and manufacturing. He patiently explained that no parenteral product exists without a properly designed and assembled package. His point seems so obvious today, when an entire PDA Europe conference is dedicated to parenteral packaging. But three decades ago, packaging was often an afterthought, if it was considered at all!

The conference planning committee and I encourage you and your colleagues to join in attending what promises to be an exciting event, as well as the preconference workshop and postconference training courses, making for a full week of packaging immersion!

The meeting will open with a session on regulatory designed to delve into the dynamic regulatory landscape for pharmaceutical container closure systems and combination products. Presentations will provide an overview of recent and upcoming global pharmacopeial changes relating to elastomeric closures and polymeric containers.

The next session, "Material and Quality," will begin with case study results comparing cyclic olefin polymer vials to glass vials for storage and delivery of stem cells, radio pharmaceuticals, high pH drug products and biotherapeutics. Then findings from the longest running study of its kind on prefilled glass syringe functionality will be described, exploring the impact of siliconization, stoppering, and storage variables on syringe break loose and extrusion forces.

The third session will focus on the processing, handling and assembly of packaging components into parenteral container/closure systems. New ways to employ advanced packaging nesting tools will be explained, designed to make for more flexible equipment and smaller product runs, compatible with multiple package types.

Day 2 will begin with a blow/fill/seal session, which promises to provide insight into two current hot topics in this technology.

The conference will conclude with a session on new technologies. First, the use of computer simulation tools for improved design of package components and processes will be discussed. Another topic to be explored is the coating of standard container materials to improve their chemical inertness and/or to avoid the use of materials that might contribute to package system leachables. Thirdly, testing package functionality or usability from the customer's point of view is a trend that will be considered.

# Upcoming Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

## JANUARY 2014

### Environmental Mycology Identification Workshop
January 22-24 | Bethesda, Maryland
www.pda.org/mycology

## FEBRUARY 2014

### Aseptic Processing Training Program, Session 1 – February 3-7
Week 2, March 3-7 | Bethesda, Maryland
www.pda.org/2013aseptic

### An Introduction to Visual Inspection – Session 1
February 20-21 | Bethesda, Maryland
www.pda.org/visual

## MARCH 2014

### Recommended Practices for Manual Aseptic Processing – Session 1
March 11-12 | Bethesda, Maryland
www.pda.org/map

### Fundamentals of Aseptic Processing – Session 1
March 17-21 | Bethesda, Maryland
www.pda.org/apfundamentals

### Aseptic Processing Training Program, Session 2 – March 31-April 4
Week 2, May 5-9 | Bethesda, Maryland
www.pda.org/2013aseptic

## APRIL 2014

### 2014 PDA Annual Meeting Course Series
April 10-11 | San Antonio, Texas
www.pdaannualmeeting.org/courses

- Risk-Based, Product Development Basics for Combination Products: Harmonizing Design Controls and Quality-by-Design in Product Development and Market Authorization Documents (April 10)
- Biosimilars: Understanding the CMC Challenges of Meeting 'Similarity' (April 10)
- Implementation of Quality Risk Management for Commercial Pharmaceutical and Biotechnology Manufacturing Operations (April 10-11)
- Process Validation and Verification: A Lifecycle Approach (April 10-11)
- Quality Control and Quality Assurance of Cell-Based Therapeutic Products (April 11)
- Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Validation and Ongoing Control (April 11)

### Validation of Moist Heat Sterilization Processes
April 15-17 | Bethesda, Maryland
www.pda.org/moistheat

### PDA Biotechnology Week
April 21-25 | Bethesda, Maryland
www.pda.org/bioweek2014

- Biopharmaceutical Manufacturing under Regulatory Compliance: Process Strategies, CGMP Considerations and Facility Requirements (April 21-22)
- CMC Regulatory Compliance of Biopharmaceuticals (April 23-24)
- Biosimilars – Understanding the CMC Challenges of Meeting 'Similarity' (April 25)

### Management of Aseptic Processing
April 28-30 | Bethesda, Maryland
www.pda.org/apmanagement2014

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

Laboratory Courses

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

# 2013 – Another Good Year for PDA TRI

**Bob Dana, PDA**

As summer ends and we move into the fall, my favorite season, some things seem the same every year. In baseball, the World Series is upon us; and yes, the Red Sox are in it. College football and the National Football League are well into their schedules. The leaves are changing color and the air has a certain crispness to it. In short, all the signs tell me another year is drawing to a close.

And so, just as for the past four years, it's time for me to reflect back on 2013 and see what kind of a year 2013 was for PDA's Training and Research Institute.

Our courses at our Bethesda, Md. training facility did quite well. We had another year keeping the facility busy with our flagship Aseptic Processing Training Program, taught by lead instructors **Dave Matsuhiro** and **Hal Baseman** and capably supported by almost 20 other faculty members. Dave and some of the other instructors also teamed up to present "Practical Aspects of Aseptic Processing" to several U.S. FDA staff members in July. And speaking of FDA, we also held a one-day training session for 38 FDA investigators covering aseptic processing **(Dave Matsuhiro),** environmental monitoring **(Dona Reber),** filter sterilization **(Wayne Garafola** and **Maik Jornitz)** and particulate matter **(John Shabushnig).**

We expanded our aseptic processing training offerings in 2013 to include two new courses. Combined with "Quality Systems for Aseptic Processing" and the Aseptic Processing Training Program, we now have a more complete range of courses designed for all levels and depths of involvement with aseptic processing.

The facility played host to a number of other lab-based training courses in 2013. As a first for TRI, our "Introduction to Visual Inspection" course proved so popular that we added a third session, taught on Friday and Saturday following the *2013 PDA Visual Inspection Forum* in October. Thanks are due to instructors **Ron Leversee, Matt Ostrowski** and John Shabushnig, as well as to the 19 students who stayed on for this extra offering.

A couple of years ago, we introduced the concept of theme weeks at TRI. During these weeks, multiple courses on related topics are offered at reduced registration rates. One such week in 2013 was Lyophilization Week, with "Fundamentals of Lyophilization" taught by **Ed Trappler** and "Validation of Lyophilization" taught by **Barbara Berglund** and **Karen Bossert** being presented to 22 and 19 students respectively, 15 of whom enrolled in both courses.

Our second theme week this year will be Filtration Week. This week features two courses, a basic one and an advanced one taught by long time instructors Wayne Garafola and Maik Jornitz**.** The basic course, as I'm sure you can guess, provides a foundation in filtration theory and concepts, while the advanced course gives the students a chance to apply these concepts when things go wrong.

All told, we held over 20 different courses in our TRI facility this year, keeping TRI staffer **James Wamsley** plenty busy!

While James was busy with the courses in our facility in Bethesda, his colleague **Stephanie Ko,** was also busy and racking up frequent flier miles. In April, she was in Orlando, Fla. for the *2013 PDA Annual Meeting* course series. Of the six courses presented in Orlando, three ["Validation of Moist Heat Sterilization Processes," taught by **Mike Sadowski** and **Kevin Trupp**, "Recommended Practices for Manual Aseptic Processes" **(Carol Lampe)** and "Process Simulation Testing for Aseptically Filled Products" **(Hal Baseman)**] exceeded our planned registration numbers.

While in Orlando, we were pleased to present two of our long-time faculty members, **James Cooper,** and **Dale Seiberling**, the James P. Agalloco Award. This award is presented for excellence in teaching as determined by student evaluations and assessments by the TRI staff with the concurrence of the PDA Awards Committee. Closer to home, in May, Stephanie was busy with "Utilization of Statistical Methods for Production Monitoring" (a new course taught by **Jason Orloff)** and "Process Validation and Verification: A Lifecycle Approach" **(Scott Bozzone** and **Wendy Lambert),** courses at the *2013 PDA/FDA Process Validation Workshop* in Bethesda.

In June, Stephanie was off to Chicago for the course series held in conjunction with PDA's *2013 Aseptic Processing-Sterilization Conference*. All three courses held at this conference were highly successful. "Validation of Moist Heat Sterilization Processes" (Sadowski), "Parametric Release" (Sadowski) and "Validation of Dry Heat Processes" (**Debbie Havlik**) all exceeded our planned attendance.

In September, Stephanie was just down the road in Washington, D.C. for the six courses held in conjunction with the *2013 PDA/FDA Joint Regulatory Conference*. Thanks to the hard work of **Rich Levy,** SVP, Scientific and Regulatory Affairs, PDA, and **Josh Eaton, Morgan Holland** and **Janie Miller** of Rich's staff, we had course materials ready and were able to present four interrelated courses on risk management. On Thursday, the parent "Quality Risk Management" course was presented by **Jeff Hartman** and **Emma Ramnarine.** Then, on Friday, we presented three courses amplifying on the concepts in the parent course—"Quality Risk Management: Case Studies, Drug Products" **(William Harclerode),** "Quality Risk Management: Case Studies, Biotech Bulk Drug Substances" **(Scott Rudge)** and "Quality Risk Management: Case Studies, Packaging and Labeling" **(Ghada Haddad).** The other courses, "GMP for Manufacturers of Sterile and/or Biotech Products" **(Michael Anisfeld)** and "CMC

Regulatory Requirements in Drug Applications" (**Zi-Qiang Gu**) held at this conference were equally successful.

This year, we renewed our relationship with the pharmaceutical industry in Russia. We have been working with members of the St. Petersburg Chemical and Pharmaceutical Academy to help them develop a GMP training center in Russia. In October, four delegates from the Academy spent a week with us learning how we utilize our facility to complement the learning process. PDA faculty **Rebecca Brewer,** Dave Matsuhiro, Maik Jornitz, **Igor Gorsky** (who also helped with translation as necessary) and PDA staff **Denyse Baker, Bob Dana,** Stephanie Ko and James Wamsley all provided valuable insight to help the delegates understand some of what they will be facing as they move forward with this project. Incidentally, if you are interested in supporting this initiative, PDA would love to talk with you. See PDA President **Richard Johnson's** message in the upcoming January 2014 issue of the *PDA Letter,* or refer to p. 7 of the May 2013 issue for more details.

2013 was a busy year for our in-house training programs as well. We brought PDA training to eight companies.

This year, we brought four of our courses to China. In June, Kevin Trupp presented two courses on moist heat sterilization in Nanjing and Shanghai. In October, Hal Baseman presented courses on aseptic processing and validation in Shanghai.

This year we welcomed some new TRI staff as well. **Oscar Bermudez** joined us at the beginning of the year as our new Coordinator, Laboratory Education. He's done a great job helping PDA prepare for the laboratory portions of our courses. In addition, we have been fortunate to have **Bethanne Bond** continue to support us in a temporary, part-time role. She has applied her skills to our course materials, working with PDA staff and our instructors to create a dynamic "family" appearance to our PowerPoint slides. We were also fortunate to have a summer intern again this year. **John Shank** worked with us for two months this summer before returning to his studies at West Virginia University.

So, another year has passed; one which was very successful for our education programs. None of what we accomplished would have been possible without the participation of our students who enrolled in our education programs. Our staff and instructors invest a lot to ensure you receive a quality experience when you enroll in a PDA course. And once again, my thanks to my hard working and dedicated staff.

I'd like to close by wishing each of you a safe, healthy and prosperous New Year. I hope to see you all at one of our TRI courses in 2014.

## PDA's Who's Who

**Michael Anisfeld,** President, Globepharm

**Denyse Baker,** Senior Regulatory Advisor, PDA

**Hal Baseman,** COO, ValSource

**Barbara Berglund,** Manager, QA, AMRESCO

**Oscar Bermudez,** Coordinator, Laboratory Education, PDA

**Bethanne Bond,** PDA

**Karen Bossert,** PhD, VP, Lyophilization Technology

**Scott Bozzone,** PhD, Sr. Manager, Quality Systems and Technical Services-Validation, Pfizer

**Becky Brewer,** President, Validation and Compliance Partners

**Jim Cooper,** PharmD, Consultant, Endotoxin Consulting Services

**Bob Dana,** SVP, Education, PDA

**Josh Eaton,** Sr. Project Manager, Scientific and Regulatory Affairs, PDA

**Wayne Garafola,** Application Specialist, Sartorius

**Igor Gorsky,** Associate Director, ValSource

**Zi-Qiang Gu,** PhD, Independent Consultant

**Ghada Haddad,** Associate Director, Engineering, Biosterile Validation, Merck

**William Harclerode,** Associate Director, Forest Laboratories

**Jeff Hartman,** Director, Validation Quality Assurance, Merck

**Debbie Havlik,** Research Investigator, Hospira

**Morgan Holland,** Coordinator, Scientific and Regulatory Affairs, PDA

**Richard Johnson,** President, PDA

**Maik Jornitz,** COO, G-Con

**Stephanie Ko,** Senior Manager, Lecture Education, PDA

**Wendy Lambert,** Divisional Validation Leader, Novartis

**Carol Lampe,** Independent Consultant

**Ron Leversee,** QA External Operations, Perrigo

**Rich Levy,** SVP, Scientific and Regulatory Affairs, PDA

**Dave Matsuhiro,** President, Cleanroom Compliance

**Janie Miller,** Sr. Project Manager, Scientific and Regulatory Affairs, PDA

**Jason Orloff,** Statistical Engineer, PharmStat

**Matt Ostrowski,** Pfizer

**Emma Ramnarine,** Head, Global Biologics, Genentech

**Dona Reber,** Sr. Manager, Laboratory Operations, Pfizer

**Scott Rudge,** PhD, COO, RMC Pharmaceutical Solutions

**Mike Sadowski,** Director, Sterile Manufacture Support, Baxter

**Dale Seiberling, Retired**

**John Shabushnig,** PhD, Consultant, Insight Pharma

**John Shank,** Intern, PDA

**Ed Trappler,** President, Lyophilization Technology

**Kevin Trupp,** Principal Consultant, Sterilization Technology and Compliance

**James Wamsley,** Senior Manager, Laboratory Education, PDA

Ursula Busse, PhD, Novartis

## Enhancing Value for Our Global Membership

It has almost become a truism that the world has grown much smaller, particularly within our very own industry. Communication is a large part of this paradigm shift; it takes only a few minutes for an email to go around the world. We're truly involved in an interconnected industry. But with global expansion comes greater challenges as well.

The PDA Board of Directors recognizes this and has expanded efforts to enhance global communications with our members along with outreach to regulatory agencies in a number of counties. We truly want to emphasize the value of our global membership, ensuring that members around the globe remain connected on issues of importance.

First, we've expanded the number of PDA chapters worldwide. Over the past few years we've established new chapters in India, Singapore and Texas. The Singapore chapter is our newest chapter (see p. 9) and will expand PDA's footprint in East Asia. We're also increasing our support for our existing chapters. To provide greater outreach, the board is reaching out to chapters, so expect to see occasional board members at your chapter's upcoming meetings and events!

Our technical reports are becoming global documents as well. We're working to translate five technical reports into Chinese.

On the training side, PDA's Training and Research Institute is working with the St. Petersburg Chemical and Pharmaceutical Academy to support the development of a training center in St. Petersburg, Russia. This facility will be similar to the TRI facility at PDA's headquarters in Bethesda, Md.

And lastly, but certainly not least, we're implementing a new communication tool for members. This new platform will be a social networking software that enables users to build online communities that can be accessed using various mobile devices. This new platform will provide members with greater opportunities for dialogue around the world. Phase I of the implementation will be focused on building online communities for PDA interest groups and chapters.

This is an exciting time in the history of our industry and PDA. I look forward to seeing how many new members we can recruit and how we can continue the international growth of our publications and training. PDA is truly a global organization that provides value and connects members no matter their location.

*FDA Public Meeting Addressed FDASIA Supply Chain Provisions continued from page 44*

the medical records of Israeli soldiers.

"Protecting our patients is our primary importance," he said. "We would like to customize and fully secure and create a cloud-based system to sponsor this type technology"

Next, **David Gaugh,** SVP of Sciences and Regulatory Affairs, Generic Pharmaceutical Association, emphasized that the Agency should consider clarifying expectations regarding standards of importation and their "final recommendation is about partnership…we think this is paramount to the success of the program."

Finally, **Sarah Spurgeon,** Assistant General Counsel, Pharmaceutical Research and Manufacturers of America, urged the Agency to take into account differences among importers, using "these differences to establish risk-based standards for the submission of information."

Additionally, she urged FDA "not to make arbitrary decisions about the level of risk posed by the imported drug."

Her group also encourages FDA to work together with the U.S. Customs and Border Protection to streamline the importation process.

**Steve Solomon,** Deputy Associate Commissioner for Regulatory Affairs, then concluded the meeting, noting that information will continue to be updated on the Agency's FDASIA website "as we make progress on implementing this very important piece of legislation."

# President's Message

Richard Johnson

2013 will end up being the most successful year in PDA's history. Our conferences and workshops enjoyed higher attendance; we added more members and new chapters, and PDA completed and published a record number of publications. Just as important, the quality of our activities and the response from our members, attendees, and readers has been very high.

In 2014 we will continue this momentum across all of our activities, maintaining our focus on our strategic plan initiatives, "Connecting People, Science and Regulation." We know that the world, and the pharmaceutical/biopharmaceutical industry, is changing. PDA is changing along with these changes, and focusing our combined efforts to help lead the way to continuous improvement.

We will continue to improve our member benefits, with new tools for communication and collaboration among members; increased outreach in emerging markets; and enhancing the volunteer experience.

PDA will continue to connect "People, Science and Regulation" through our conferences and workshops worldwide, including:

- The 68th Annual Meeting in San Antonio, Texas in April
- The *Universe of Prefilled Syringes and Injection Devices* conference in Huntington, Calif. in November
- Key regulatory conferences, including the 24th *PDA/FDA Joint Regulatory Conference* in September; workshops and conferences with U.S. FDA, PIC/S and other health authorities on subjects including QbD, supply chain and drug shortage prevention.
- PDA will begin as Premier Sponsor for Interphex in New York City and Puerto Rico
- Other large and small events in the United States, Europe and Asia

We will be expanding our training to industry and regulators worldwide, building on our prominence in aseptic processing and our growing portfolio in quality systems. We will continue to maintain the highest standards of content and educational delivery in all of these programs.

We will continue expanding our portfolio of technical reports that are leading the way to practical science-based implementation of technologies and quality systems, including new topics like bioburden and biofilms and comparison of global sterile GMPs. We will continue to make these invaluable resources available to members as a member benefit.

PDA has been, and will continue to be a very busy association. Our strength is in our members/volunteers. The PDA staff is committed to maintaining the high level of service that you deserve. I hope to see you soon.

*Another Successful ICH Q10 PDA/FDA Workshop continued from page 45*

attendee received all the case study materials, a summary of the lessons learned (generated by all the attendees), an example of a detailed Points to Consider list for conducting investigations, and a simple root cause analysis tool guide. Of course, the intention of this is to help each other conduct better investigations, ensure a reliable supply and at the end of the day, provide patients with high quality medicine.

## About the Authors

**Jennifer Magnani's** areas of responsibility include management of global quality portfolios, strategic global quality projects, and GMP document governance for all of Roche's technical operations, strategic communication, global quality training program and quality council governance.

**Anders Vinther** is responsible for the Biologics Technical Operations at Roche and Genentech. This includes operational quality leadership for ten biologics sites and for Roche and Genentech's biologics products.

# Closing Out a Year of Transitions

The November/December issue always marks the end of the year for the *PDA Letter* and its staff, even though we are putting it together in October and November. By the time it publishes, however, we are already diligently gathering content for the first issue of the following year. New editorial topics, calendars and even new volunteers on the *PDA Letter* Editorial Committee are being sought.

As 2013 comes to an end, we want to thank the hard work and contributions of **Vince Anicetti, Hal Baseman, John Paul Bevel, Mitchell Ehrlich, Karen Ginsbury, Mike Long, Rainer Newman, Kathleen O'Sullivan** and **Sarah Thomas.** Whether providing insightful critiques of articles, finding authors to contribute, or burning the midnight oil themselves, each of them have been valuable members of the committee and will be missed. Of course, the PLEC is a rotating membership committee, so anyone can apply to rejoin after one year off the committee.

We are looking for new volunteers, so if you are interested in helping shape the *PDA Letter* in 2014 and 2015, contact us (stauffer@pda.org) for more details.

The Letter has had a great year with the introduction of a regular InfoGraphic, Podcasts, and a commitment to producing predictably sized editions. We strived and succeeded for the most part to provide tighter, more impactful content. And, by midyear, we launched our first comprehensive readership survey—the results of which will inform even more changes in 2014.

The PDA membership experiences change regularly, both in their work environments and their careers. This month, we fulfilled a long-time goal of the Editors and the PLEC to interview members of our community who made the leap from government to industry and vice versa. We strongly believe that the information we gleaned from these interviews will help inform your future career decisions. This was one of several career-oriented feature articles published in 2013. Look for more in 2014!

We also tried to capture some highlights from the *2013 PDA/FDA Joint Regulatory Conference,* which was the most successful PDA conference ever. This time, **Rebecca Stauffer** followed two attendees the meeting to get "real-time" feedback on their experience. And, instead of producing staff reports from the conference, we enlisted PDA members to provide reports about sessions they found particularly helpful. Again, you can relive the meeting in our six-page PDA Photostream.

Well, we think we are ending the year with an issue as strong as the one that kicked it off. We look forward to providing even better issues in 2014!

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

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

**PDA Letter**

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# Bio/Pharmaceutical Publications

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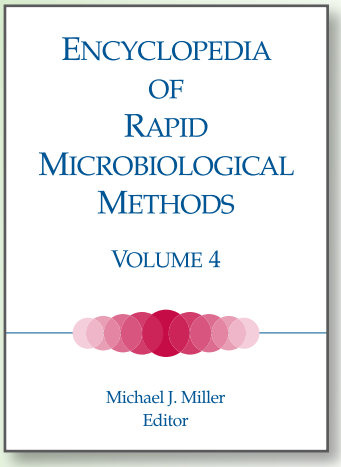


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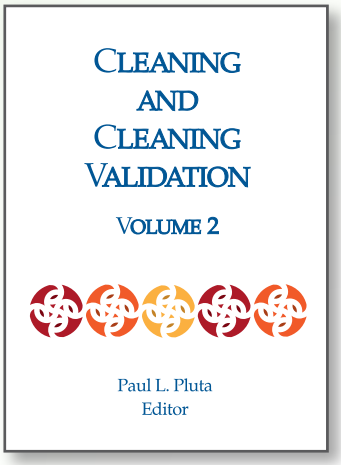


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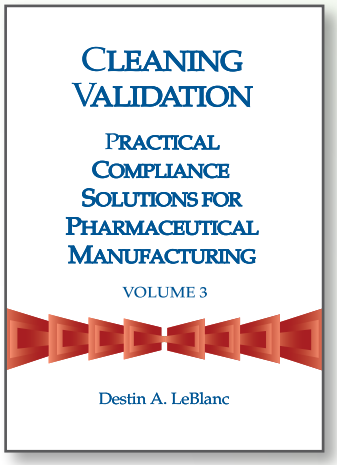


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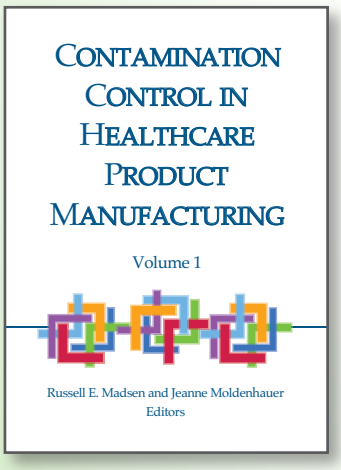


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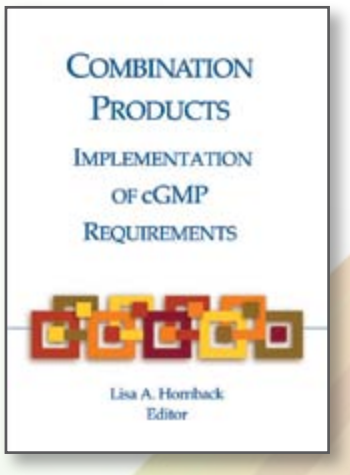


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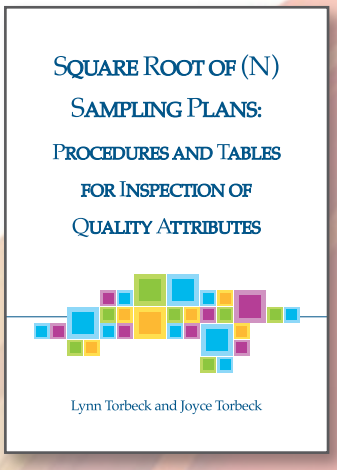


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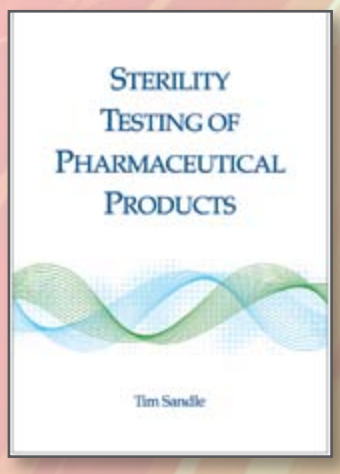


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*The Parenteral Drug Association presents...*

## 2014 PDA Europe

# Modern Biopharmaceutical Manufacturing

*Manufacturing of the Future*

The annual conference will particularly address burning topics relevant to a fast changing and highly regulated environment such as Dedicated Facilities, Continuous Processing, Multi-Product-Lines as well as Flexible and Single-Use Factories. Practical approaches to the challenges in development and manufacturing of biopharmaceutically and biotechnologically derived products in the current GMP environment, and Quality by Design perspectives will also be discussed.

The rapidly evolving international environment in which biopharmaceutical industry is working confronts us with new challenges daily. Innovations and new developments offer solutions to some of these challenges.

A host of international experts will share their experiences by presenting the latest practices, methods and Case Studies associated with the industrial development and production of vaccines & biopharmaceuticals. Risk Management concepts applied to these new technologies and innovative operations will be discussed as well.

If you are operating in the biopharmaceutical business, whether in a large or small firm, this annual international survey of current best practices makes for the ideal lead into 2014, and an opportunity to network with opinion leaders and experts in these fields.

There will be plenty of time for questions and discussion, making for a very interactive and fruitful meeting.

We will be pleased to meet you in March 2014, and would also like to take this opportunity to celebrate the 10th anniversary of the French PDA Chapter.

**Jean-Luc Clavelin,** *Co-Chair, Consultant*
**Christophe Grimm,** *Co-Chair, Sartorius Stedim Biotech*

## 25-26 March 2014
## Lyon | France

**CONFERENCE** 25-26 Mar | **EXHIBITION** 25-26 Mar | **TRAINING COURSES** 27-28 Mar

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