

# PDA Letter

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[www.pda.org/pdaletter](http://www.pda.org/pdaletter)

October 2011



## Personalized Medicines: The Next Big Thing in Healthcare

18





The Parenteral Drug Association presents...

# PDA's 6th Annual Global Conference on Pharmaceutical Microbiology & TRI Courses

## *Challenges Facing Pharmaceutical Microbiology in the 21st Century*

**October 17-19, 2011**

**EXHIBITION:** October 17-18 | **COURSES:** October 20-21  
Bethesda North Marriott Hotel | Bethesda, Maryland

"The conference was an invaluable opportunity for me to meet the foremost experts in the field (scientists, regulators, vendors, colleagues). The whole conference was an inspiring event."

D. Govezensky, PhD,  
Bio-Technology General Ltd.

The 6<sup>th</sup> Annual Microbiology Conference has an impressive agenda filled with a strong lineup of leading regulatory and industry speakers addressing today's most important challenges. Issues to be discussed include the latest industry and regulatory trends, new technologies to improve testing and improved quality by avoiding contamination by "objectionable" microorganisms.

Preview this year's leading speakers:

- **Keynote Presenter: Dennis E. Guilfoyle**, PhD, Pharmaceutical Microbiologist International Expert, *ORA, FDA*
- **James Akers**, PhD, Chair, 2010-2015 *US Pharmacopeial Microbiology Expert Committee*
- **Tony Cundell**, PhD, Director, Analytical Sciences – Microbiology, *Merck Sharp & Dohme Corporation*
- **Claudio D. Denoya**, PhD, Research Fellow, Analytical Development, *Pfizer, Inc.*
- **Rudolf R. Eggers**, PhD, Group Leader, Immunization Services Strengthening, *WHO*
- **Marc W. Mittelman**, PhD, Senior Managing Scientist, *Exponent®* and Visiting Scientist, *Harvard University School of Engineering and Science*
- **Judith Noble-Wang**, PhD, Team Lead, Environmental and Applied Microbiology, Clinical and Environmental Microbiology Branch, *CDC*
- **Bryan S. Riley**, PhD, Microbiology Reviewer, *OPS, CDER, FDA*
- Lieutenant Commander **Destry Sullivan**, Director Regulatory, *CBER, FDA*
- And many more.

Four related training courses are being offered immediately following the conference for your extended learning purposes.

For details and to register, visit

[www.pda.org/2011microbiology](http://www.pda.org/2011microbiology)





# Calling All Active PDA Members Vote Now!

## Online Voting Opens September 6th for the 2012 PDA Officers & Board of Directors Election

PDA members, online voting will open on September 6th for the 2012 **PDA Officers & Board of Directors Election**, we encourage you to take a moment and vote for your candidates of choice.

To vote is easy, just follow the instructions below. You will need your PDA Member ID and last name to log in.

All PDA members in good standing as of **midnight on August 25, 2011 are eligible to vote**. Voting for this election will close at **11:59 p.m. EST on November 11, 2011**. All votes cast after this date and time will not be accepted.

If you need assistance please contact the PDA Membership Service Department at +1 (301) 656-5900 ext. 119 or [howe@pda.org](mailto:howe@pda.org).

## Thank you for being a valued PDA member and voting!



### Vote by Using Your Smartphone.

Download a free QR Code App and scan this barcode.

### Instructions for Voting:

- Go to [www.pda.org/vote](http://www.pda.org/vote)
- Log into the system using your PDA Member ID and last name
- Please read the instructions for each question carefully
- Review the choices for each position then select a candidate for that position
- When you are done voting, review your selection and then check the participant consent box and click on the "SUBMIT" button
- You have now completed the voting process
- You can view and print your receipt or exit the PDA eBallot System

**Thank you for your participation in this important election process.**

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There are always benefits to going the extra mile or two in anything you do, and now pharmaceutical manufacturers who want to pursue the enhanced approach to licensing filings, including fully supported design space, will benefit from increased flexibility to enact post-approval changes.

Cover Art Illustrated by Katja Yount

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Recently there has been a huge increase in interest within the pharmaceutical and drug delivery community around "human factors" (HF), or usability.

## PDA's MISSION

To develop scientifically sound, practical technical information and resources to advance science and regulation for the pharmaceutical and biopharmaceutical industry through the expertise of our global membership

## PDA's VISION

To be the foremost global provider of science, technology, and regulatory information and education for the pharmaceutical and biopharmaceutical community



Connecting People, Science and Regulation®

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## PDA BOARD OF DIRECTORS

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## Vote Now for 2012 PDA Officers and Directors

It is time for PDA members to choose the volunteer leadership for 2012/2013. Officers up for vote are the **Chair Elect, Secretary and Treasurer**. Four Director positions are also up for election. Below are the nominees for each position with abbreviated personal statements. Full personal statements and bios are available at the "online voting booth," [www.pda.org/vote](http://www.pda.org/vote). Polls are open until November 11.

### Chair Elect



#### Harold (Hal) Baseman

It is an honor to be nominated as the Chair Elect of PDA Board of Directors. I am thankful to be a part of this great organization and to work with such fine staff, volunteers, members and leadership. Through its efforts PDA has met the business and technical challenges our industry has faced in the past years and enhanced its position as the premier organization for connecting science, regulation and business. PDA stands as the leader in technical publications and reports, conferences and meetings as well as education and training. PDA is the most trusted source of information and gives insight into scientific understanding and regulatory expectations. In order to maintain and improve our position and ability to provide unparalleled service, we will need to follow our strategic plan and be prepared to adapt to further changes and challenges...

### Secretary



#### Steven Mendivil

It has been my privilege to have served on the PDA Board over the past six years, as PDA provides an important voice for the biopharmaceutical industry on scientific and regulatory matters. If elected as an Executive Officer, I will assure that PDA is actively involved in biotech and GMP issues that serve the membership and provides opportunities for discussion and clarification between industry and regulators on critical issues. I believe it is important that new GMP and submission initiatives take into account specific technologies, scientific attributes and unique aspects of biologic, drug and combination products...

### Treasurer



#### Rebecca (Becky) Devine

It has been a great pleasure serving on the PDA Board as Secretary, and I am very appreciative to be nominated to serve as PDA's Treasurer. Being part of the PDA family continues to be one of the most rewarding experiences of my career...I will work with the PDA leadership to be sure we continue to look to the future to find ways to keep the organization well positioned to serve our

members. Assuring the financial strength of the organization will allow PDA to continue its excellent programs, conferences, training and technical guidance. I will also work to see that the Training and Research Institute remains strong and that we continue to find new and innovative ways to leverage this important resource...

### Board of Directors



#### Ursula Busse

It is a great honor to be nominated for a position on the PDA Board of Directors. Challenging, yet interesting times lay ahead of us, driven namely by changes in healthcare environment, demographics and globalization....I will enhance PDA's role in innovative technologies delivering patient-specific medicines, advanced therapy medicinal products, drug device combination products and biologics. I want to ensure that PDA continues to be recognized as a provider of high-quality information adapted to the needs of its members, including emerging markets. Finally, I want PDA to become the prime forum for open scientific dialogue between industry, regulators and other institutions worldwide.



#### Ian Elvins

As a long time attendee of PDA conferences I have always recognized the tremendous value that these meetings offer to everyone who cares about the quality of pharmaceutical products....PDA is about far more than just organizing great conferences. I believe that one of the greatest contributions that PDA has made to advancing progress within our industry has been the collaboration with the regulators....If elected to serve on your board, I will work passionately to further advance the great work that has already been done. My long and varied experience has included chemical API manufacture, biotechnology, lyophilized products and pre-filled syringes. I have also been privileged to work in many different countries and feel that this has given me a deep appreciation of the cultural issues which can sometimes lead to misunderstanding...

## Read each candidates full statement & Bio and Vote at [www.pda.org/vote](http://www.pda.org/vote)



### John Finkbohner

I am very honored and delighted to be nominated to the PDA Board of Directors. Nearly 20 years ago, the depth and quality of the science found in PDA technical reports and other publications inspired me as a new reviewer in the FDA to actively seek opportunities to participate in PDA activities. PDA is the common thread that spans my personal transition from FDA reviewer and inspector to working in the biopharmaceutical industry, and, more broadly, our shared transition to the new demands of market globalization....If selected by the members to join the Board of Directors, I would continue to serve with the philosophy of maintaining the high level of scientific and technical excellence of PDA...



### Norbert Hentschel

The nomination for the 2011 Board elections is a great honor for me. I have been a PDA member for almost 20 years and found PDA to always be an invaluable source of information....This knowledge was provided by other PDA members, who felt that it is important to share their expertise with the entire membership community. Their shared expertise helped me to make my job better and motivated me to get actively involved in PDA activities....I hope that I will get the opportunity to serve on the Board of Directors and will do my best to contribute to PDA's efforts to provide scientifically sound, practical technical information...



### William (Bill) Miele

It is an honor for me to be nominated to the PDA Board of Directors. Serving in such a capacity would be a professional challenge for me in my career and an opportunity to bring to my fellow industry colleagues, and bring to this strategically placed organization, an increasingly inclusive perspective. To meet this challenge, I would endeavor to better shape PDA's service to its participating membership, to the industry, and to the global patient community as a whole.... As a member of the Board of Directors, I would endeavor to bring my diverse background and experiences, along with those of my PDA colleagues, together to foster a pragmatic and comprehensive direction for the Parenteral Drug Association...



### Junko Sasaki

If elected again, I will continue to promote the values and mission of PDA by using my powers to increase the communication between Asia and other countries. I will contribute by representing Asia in the most positive way, especially in global quality system implementation and GMPs as well as implementation of Quality System in Japan....My attendance at Board Director Meeting and related PDA meeting (PDA/FDA and EMA/PDA Joint Regulatory Conferences etc.), has given me the bridge to cross over from Asian Countries to the US, EU and other regions, sharing information to bring about positive change and promote development in PDA for all to achieve success.



### Chris Smalley

It is an honor to be renominated by the Nominating Committee and approved for the ballot by the PDA Board of Directors. It has been an exciting journey during my first term on the Board of Directors....As Chairperson of the *2011 Annual Meeting* and continuing to work on the Planning Committee for the *2012 Annual Meeting*, changes are underway to make the meetings pertinent to you and your career. As chairman of one of the Paradigm Change in Manufacturing Operations (PCMO<sup>SM</sup>) teams responsible for driving the best practices for Knowledge Management, our team hopes to be able to shortly deliver to you tools necessary to maximize the value of your data, truly producing knowledge...

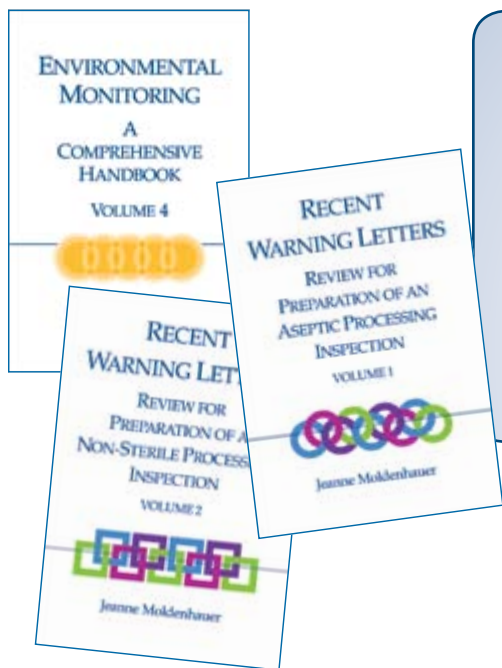


### Michael VanDerWerf

I am honored to be nominated to the PDA Board.... PDA has been an influential organization for me since I started my career in biotech because it offered valuable resources.... PDA meetings contained new insights and allowed networking with people facing similar challenges. I remain involved in PDA because I continue to learn and appreciate being part of an organization that values and encourages the contributions of its members to meet collective goals.... Charles Darwin observed "In the long history of humankind those who learned to collaborate and improvise most effectively have prevailed." I will work to support the collaborations of members so PDA can continue to provide the resources needed to thrive in the 21st Century. 🌈

## 2010 Honor Awards Recipients

The PDA Honor Awards are bestowed on members who provide exceptional leadership and service to the Association, and have been awarded at the Annual Meeting since 1958. The 2010 award winners were announced at the *2011 Annual Meeting* in April, and they will be highlighted in each *PDA Letter* until next year's event.



### Distinguished Editor/Author Award

This award is presented annually for the best editor/author of PDA-DHI co-published books as selected by PDA members. This year's author that received the honor was **Jeanne Moldenhauer** for the following books:

*Environmental Monitoring: A Comprehensive Handbook, Volume 4*

*Recent Warning Letters Review for Preparation of an Aseptic Processing Inspection, Volume 1*

*Recent Warning Letters Review for Preparation for a Non-Sterile Processing Inspection, Volume 2*

## Missouri Valley Chapter Holds Supply Chain Trends Meeting

Jeff Hargroves, ProPharma Group

On Monday, September 12, the PDA Missouri Valley Chapter hosted a fall meeting at the award winning Embassy Suites in St Charles, Missouri (St. Louis metro). The meeting topic was on *Supply Chain Trends*.

Following a networking/vendor reception and buffet dinner, the meeting included talks from two great speakers representing industry and the U.S. FDA.

**Cindy Buhse**, Director of Pharmaceutical Analysis, CDER/U.S. FDA (the only facility outside of the metro D.C. area) reviewed each of the laboratory's primary areas of responsibility, which include:

- Method Evaluation
- Rapid Response (Adverse Events, counterfeits)
- Research, including emerging technologies
- Surveillance (post-marketing safety)

She discussed examples for each area—including items such as their involvement in development of rapid screening methods that are then published and made available to the public. This presentation provided useful insights into the variety and depth of expertise in this laboratory/office and the many different ways they serve our industry and society.


**Martin VanTrieste**, Sr. VP, Quality, Amgen and founder of Rx360, shared insights about what we, our companies and our industry, can do to protect customers and stakeholders from the realities of diversion and substandard manufacturing controls associated with pharmaceutical ingredients. He also challenged the audience to:

- Apply common sense
- Embrace best practices
- Evaluate new technologies

- Expand collaboration between our companies

RX-360 continues to make progress with their collaborative initiatives, such as shared audit database efforts and other initiatives to strengthen and increase safety in our supply chains. We were reminded that "patient safety should never be a competitive advantage—share your information."

The event attracted a wide range of industry professionals, including many prospective PDA members and was supported by the following sponsors:

- cGMP Validation (annual sponsor)
- ACH Foam Technologies (annual sponsor)
- Accugenix
- Commissioning Agents
- BioVigilant
- ProPharma Group 



## Do You Qualify for One of PDA's New Membership Types?

To ensure that our membership is diversified and leave no member behind, PDA has made several important changes to its membership types by expanding the availability of membership to those in developing countries, individuals who have retired from the industry and those currently seeking employment.

For individuals in the developing world, the list of qualified countries where members can join under PDA's Emerg-

ing Economy membership has been expanded. Based on the World Bank's list of Developing Countries, we are now accepting people from 150 countries.

In addition, we have introduced a new membership type for retired members in recognition of the high-value PDA places on those members who are no longer actively working in the industry but still have knowledge and experience to contribute to the PDA community.

Finally, PDA is interested in helping our members who are not currently employed but who still want to remain active in our Association by creating a transitional member type.

If you fall into one of these categories or know of someone who does or would simply like to learn more about these membership changes, please visit [www.pda.org/membership](http://www.pda.org/membership) or contact the Membership Team directly at [info@pda.org](mailto:info@pda.org). 🌐

## UK and Taiwan Chapters Seek Opportunities to Cooperate

**PDA UK Chapter President Siegfried Schmitt, PAREXEL**

On August 1, I was welcomed to the PDA Taiwan chapter (TPDA) offices in Taipei. The key objective was to exchange information on the chapters and to explore opportunities for cooperation. Whereas the UK has seen much of the manufacturing pharmaceutical industry move their operations away (often to Asia or Central/South America), Taiwan has the good fortune to have a thriving industry.

The mix of Pharmaceuticals and Traditional Chinese Medicines makes it a very interesting regulatory environment—different to what we have in Europe. This varied membership and the fact that the local regulatory authorities actively support PDA in Taiwan makes this a most active chapter, with its own offices and full-time staff.

As expected, there are some areas that are of particular interest to the membership in both regions, such as stability testing and analytical methods validation. Other hot topics in Europe are freeze drying and pre-filled syringes. The possibility of guest speakers from Europe at the PDA Taiwan Annual Meeting was discussed.

The Taipei office team has a well-stocked library, and I had the honor to sign the office library copy of my latest book *QbD-Putting Theory into Practice*.

The meeting was very amicable and all agreed that such visits are helpful in creating and strengthening ties between the chapters. TPDA members may con-

tact me if they require any assistance from PDA's UK Chapter at [siegfried.schmitt@parexel.com](mailto:siegfried.schmitt@parexel.com).

**Minyoung Kim**, Manager, PAREXEL, joined me on the trip.

The TPDA team's hospitality is gratefully acknowledged. 🌐



(left to right) Yi-Yin Lu, Minyoung Kim, Siegfried Schmitt, John Lin and Shih-Yu Lee at the TPDA office

If you are interested in volunteering with PDA's United Kingdom Chapter, please contact Siegfried at [siegfried.schmitt@parexel.com](mailto:siegfried.schmitt@parexel.com)

## Advisory Board *Watch*

### The BioAB: A Productive and Influential First Six Years

Emily Hough, PDA

Between 2000 and 2004, there was a lot of industry excitement about the use of biological cells for the production of human therapeutics. Monoclonal antibodies entered the mainstream, and the manufacturing of these biological drugs became the subject of intensive debate and discussion. The success of PDA global events on biotechnology topics, such as the Process Validation Workshop and Viral Safety and Clearance, demonstrated the strong interest in these topics by PDA members.

**Gail Sofer** said, “Many people working in biotechnology felt that PDA needed a group to focus in this area. PDA task forces had addressed some relevant topics, but it was felt that an advisory board would be a more productive means to providing technical advice in biotechnology that also considered regulatory requirements.”

Teaming up with **John Geigert**, PhD, who was the quality leader for the first monoclonal antibody therapeutic approved in the United States in 1997, Gail lobbied PDA to form the Biotechnology Advisory Board (BioAB) to focus PDA task force efforts on viral and mycoplasma contamination, mycoplasma and viral filtration, chromatography and analytical development, and validation for biotech products and processes.

The Board of Directors sanctioned the BioAB in 2005. It was charged with focusing on areas and questions that were different than for traditional pharmaceuticals, such as why bulk sterility testing is necessary for biologics and not for drugs

**Barbara Potts**, PhD, the current co-chair of the BioAB, credited Gail and John’s partnership and styles for getting BioAB off to a successful start. “Gail and John’s respective expertise provided a synergy in leadership style that was needed for starting and leading the BioAB,” she said. “Both John and Gail continue to support BioAB activities and are always available for much appreciated advice and guidance.”

PDA Sr. VP, Scientific and Regulatory Affairs **Richard Levy**, PhD, who as a PDA Officer in 2005 voted for BioAB, said that the BioAB’s second set of leaders, **Norbert Hentschel** and **Jeff Baker**, marked a time of renewed focus on ensuring that task forces delivered technical reports in a timely fashion to ensure that the reports were relevant and impactful.

The current leaders, Barbara Potts and **E. J. Brandreth**, already have a great legacy at PDA. Potts, according to Levy “thinks strategically.” Currently, Potts leads the Mycoplasma Task Force on top of her duties as BioAB co-chair. She has been involved with other initiatives at PDA, including the Viral Safety Investigation Medical Products Task Force.

Brandreth has also been an active participant in a number of technical reports, including *PDA Technical Report No. 42, Process Validation of Protein Manufacturing*, and is currently participating in PDA’s Paradigm Change in Manufacturing Operations (PC-MO<sup>SM</sup>) task force on process validation and verification.

BioAB is very active and recently approved several new task forces to examine cell substrate related issues, as well one new task force which will be looking at gene and cell therapy biological products (referred to as Advanced Medicinal Therapeutic Products)—clearly keeping PDA on the cutting edge of biopharmaceutical science. 🇺🇸

A few events that started the advisory board as well as to ensure that the topic garnered enough interest within the PDA community were:

The U.S. FDA *Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use* document.

The publication of *PDA Technical Report No. 42: Process Validation of Protein Manufacturing* in 2007, that assured that biotechnology was a “hot topic.”

A collaboration between **Kurt Brorson**, PhD, and **Richard Levy**, PhD, during the PDA viral contamination meetings held in 2001, 2003 and 2005, which focused on biosafety.

The 2001 meeting in Berlin, Germany on Process Validation for the Manufacturing of Biologics and Biotechnology Products that helped lead to the formation of the BioAB.

**Vince Anicetti**, along with **Chris Joneckis**, co-organizing the *2000 FDA PDA/FDA Process Validation for Biologics Symposium*.

The European Medicines Agency establishing a biosimilar Task Force around 2004.

## Interest Group *Report*

### Biotech IG Focuses on Bioburden, Biofilm

Emily Hough, PDA

Earlier this year, **Vince Anicetti** became the leader of PDA's United States section of the Biotechnology Interest Group (IG). Anicetti, who recently joined the Keck Graduate Institute of Applied Life Sciences as an adjunct professor, has some important goals for the group. Chief among these are a focus on bioburden and biofilm management, continued efforts in the cellular and gene therapy arena, and the development of a coordinated agenda with the European section of the IG.

Anicetti said that a task force to work on biofilm and bioburden management has been approved by PDA, and an impressive group of experts has been organized to work together on this project. The task force had its first meeting at the *2011 PDA/FDA Joint Regulatory Conference*, where the project scope, goals and timeline were approved. An additional face-to-face meeting will occur during *PDA's 6th Annual Global Conference on Pharmaceutical Microbiology & TRI Courses* (Oct 17-19). A technical report is expected to be published in 2012, and a report of progress will be made at the Biotech interest group during the 2012 Annual meeting

He expects that both sections of the IG will soon have defined goals for a dedicated task force to work on gene and cell-based therapy issues and continuing close coordination in this field. The field of gene and cell-based therapies is very important for development of standards and best practices. "Both sections of the biotech IG have done important work in this regard and are committed to helping PDA contribute at the forefront in the development and education of best practices in this area."

Anicetti also said he would like to see more interaction between the US and European IG's as he feels most topics in the Biotechnology arena are not region specific: "I'm sure that there are more similarities and common needs than differences between the United States and Europe. Together with the ongoing global mandate for harmonization in all aspects of pharmaceutical manufacturing and control it's extremely important that we combine our efforts as much as possible."

#### About the Expert

**Vince Anicetti** is an Adjunct Professor with the Keck Graduate Institute of Applied Life Sciences teaching in the area of Biopharmaceutical Quality. During his 30-year professional career Vince has worked closely with regulatory agencies in the development and approval of new biotech products and application of cGMP (current Good Manufacturing Practices) for Biotech operations. Vince serves as an editor/reviewer for BioQuality, is a past chairman and member of the Executive Committee of the Parenteral Drug Association, the head of the PDA Biotech Interest group, a member of the *PDA Letter* Editorial Committee, and chairman of the 2012 Annual Meeting. 🍷



## Journal *Preview*

### U.S. FDA Analysis of Recalls Hones in on *B. Cepacia*

Issue 65(5) features a Review article from the U.S. FDA on *Burkholderia cepacia*, the result of an FDA initiative to analyze drug product recalls. Consultant, PDA faculty member and author **Lynn Torbeck** worked with FDA researchers on the project. FMEA for biopharmaceuticals is discussed in a Commentary by **Hartmut Zimmermann** and **Norbert Hentschel** (PDA BioAB). Journal Editor **Govind Rao** welcomes readers to the "iPDA."

#### *Editorial*

Govind Rao, "Welcome to the iPDA!"

#### *Research*

Ajay K. Banga, et al., "Iontophoretic Delivery of Acyclovir: Intradermal Drug Monitoring Using Microdialysis and Quantification by Skin Extraction"

Isobel A. Cook and Kevin R. Ward, "Headspace Moisture Mapping and the Information That Can Be Gained about Freeze-Dried Materials and Processes"

Yuh-Fun Maa, et al., "Root Cause Investigation of Rubber Seal Cracking in Pre-filled Cartridges: Ozone and Packaging Effects"

Nitin Rathore, et al., "Variability in Syringe Components and its Impact on Functionality of Delivery Systems"

Basavaraj K. Nanjwade, et al., "Pulmonary Drug Delivery: Novel Pharmaceutical Technologies Breathe New Life into the Lungs"

#### *Technology/Application*

Dana Morton Guazzo, et al., "Vacuum Decay Container Closure Integrity Leak Test Method Development and Validation for a Lyophilized Product-Package System"

Harald Stahl, U. Meissner, and D. Steinkellner "Detection of Silicone Oil Leakages in Freeze Dryers"

#### *Commentary*

Hartmut F. Zimmermann and Norbert Hentschel, "Proposal on How To Conduct a Biopharmaceutical Process Failure Mode and Effect Analysis (FMEA) as a Risk Assessment Tool"

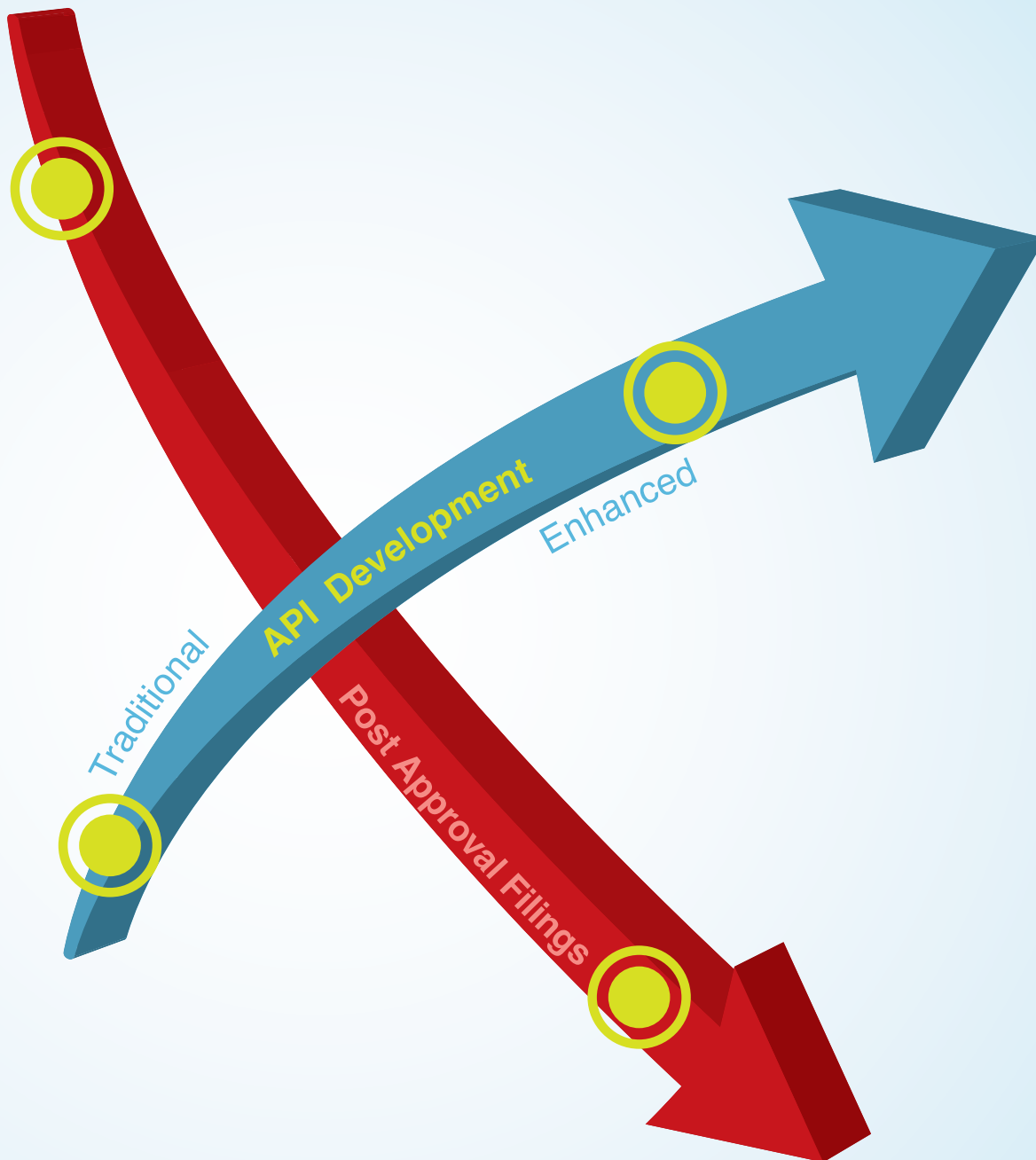
#### *Review*

Lynn Torbeck, Diane Raccasi, Dennis E. Guilfoyle, Richard L. Friedman, and David Hussong et al., "*Burkholderia cepacia*: This Decision Is Overdue" 🍷

# With ICH Q11, More Development Means Less Filings

Q11 Examples Offer Insight into Setting Design Space

Walter Morris, PDA



There are always benefits to going the extra mile or two in anything you do, and now pharmaceutical manufacturers who want to pursue the enhanced approach to licensing filings, including fully supported design space, will benefit from increased flexibility to enact post-approval changes.



That is the promise specifically made in ICH's Q11, *Development and Manufacture of Drug Substances*, lines 671-672, which read: *This includes movements within the Design Space, which do not require approval by regional regulatory authorities.* The guidance does emphasize that changes within the Design Space are subject to internal change management processes as part of the overall Quality System.

The language on manufacturing flexibility in Q11 is more direct than the statements made in ICH Q8(R2), which offers a great amount of detail explaining the concept of Design Space. Section 2 "Pharmaceutical Development" of Q8(R2) offers this seemingly more round about explanation of the regulatory relief proposition: *Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory post approval change process.* Other portions of the guidance refer to a "flexible regulatory approach" as a result of design space filings.

The stronger statement offered in the Q11 draft could reflect further evolution of the idea. But, whatever the reason, it should assure all manufacturers that the regulatory authorities in the United States, Europe and Japan are serious in their desire to shift the burden of accountability for post-approval changes onto a company's expanded process understanding and supporting quality systems.

#### Q11 Discussed at PDA/FDA Conference

Members of the ICH Q11 Expert Working Group discussed highlights of the draft guidance at the *2011 PDA/FDA Joint Regulatory Conference* on September 19. **Betsy Fritschel**, Director, Quality & Compliance Worldwide, Johnson & Johnson, was PhRMA's lead representative on the expert working group (EWG) and discussed important concepts in the Step 2 document during the session.

First, she advised that "Q11 should be read as a whole document, not taking discreet chapters out of context. You need to look at the whole thing, includ-

ing the examples—there is good information throughout the guidance."

Fritschel next addressed the two paths of drug substance development: traditional and enhanced (see definitions in box). The enhanced approach, she said, "is more inclusive of the principles of Q8, Q9 and Q10, including quality risk management, quality by design and pharmaceutical quality system."

#### Enhanced, Traditional, or a Bit of Both

From the regulators' perspective, the enhanced approach is one that offers many benefits to manufacturers, not the least of which is the possibility of manufacturing flexibility post-approval. However, drug substance manufacturers/developers are not required to pursue the enhanced approach nor must they follow one approach or the other.

The document offers flexibility and manufacturers can decide how best to generate their product and process development data. "One of the really important things to keep in mind is that Q11 does not say that we only follow one of these approaches," Fritschel said. "It recognizes that most of us in the drug substance manufacturing business are somewhere between the traditional approach and the enhanced approach."

Fritschel showed a slide with an arcing blue line representing a continuum between the traditional and enhanced approach (see Figures 1 and 2), an image she used to distinguish between the approaches for Manufacturing Process Development (Chapter 3) and the Control Strategy (Chapter 5).

"Most of us are somewhere on the continuum between traditional and enhanced approach, and even within one drug synthesis or, in the case of large molecules, even within one drug substance process, you may have some unit operations that are more traditional and others that are more enhanced," she explained.

An important aspect of the enhanced approach to both drug product and drug substance development is the identification of critical quality attributes (CQAs). ICH Q11 was a necessary

guidance, because ICH Q8(R2) links final drug product CQAs to those of the drug substance: "CQAs are generally associated with the drug substance, excipients, intermediates (in-process materials) and drug product."

Fritschel, speaking specifically about traditional small-molecule products, indicated that assignment of CQAs for the drug product and drug substance is interrelated, but generally flows from the drug product to the drug substance. "The drug product quality target product profile (QTPP) and the potential CQAs of the drug product lead to the development of the drug substance CQAs, and the drug substance CQAs are in turn very important to the drug product QTPP and potential CQAs" (see Figure 3).

For large-molecule (biotech) products, on the other hand, the guidance states, *most of the CQAs of the drug product are associated with the drug substance and thus are a direct result of the design of the drug substance or its manufacturing process.* This point was highlighted during the next talk by FDA's **Patrick Swann, PhD**, Deputy Director, Division of Monoclonal Antibodies/Office of Biotechnology Products/CDER, who was

#### Traditional Approach

- Defined set points and operating ranges for process parameters
- Drug Substance control strategy typically based on:
  - a. Demonstration of process reproducibility
  - b. Testing to meet established acceptance criteria

#### Enhanced Approach

- Risk management and more extensive scientific knowledge to select process parameters and unit operations
- Evaluation in studies to establish design space and control strategies applicable over the lifecycle of the drug substance

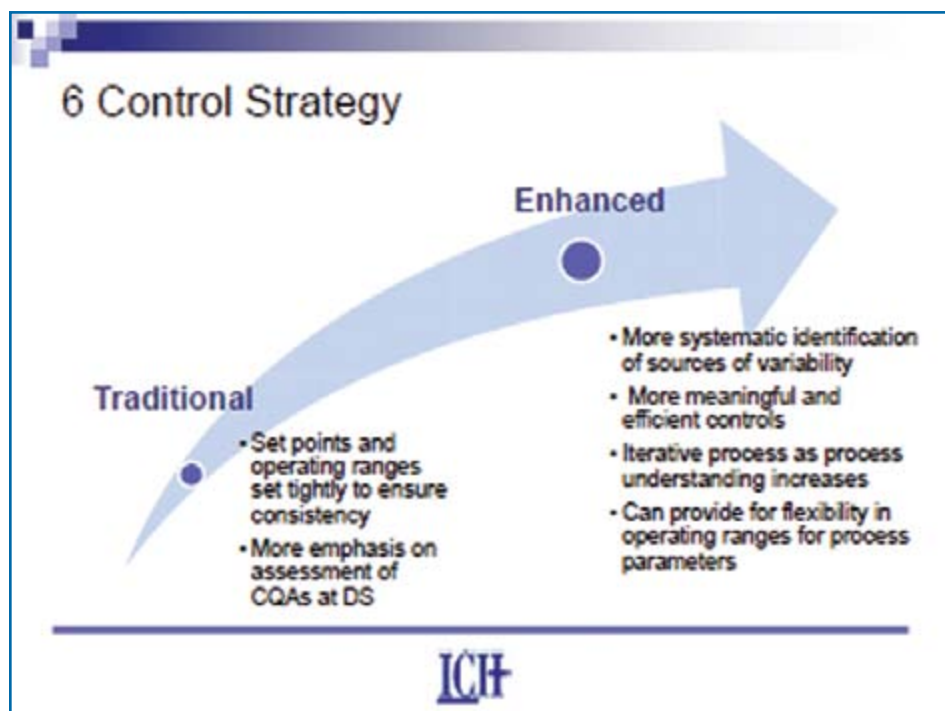
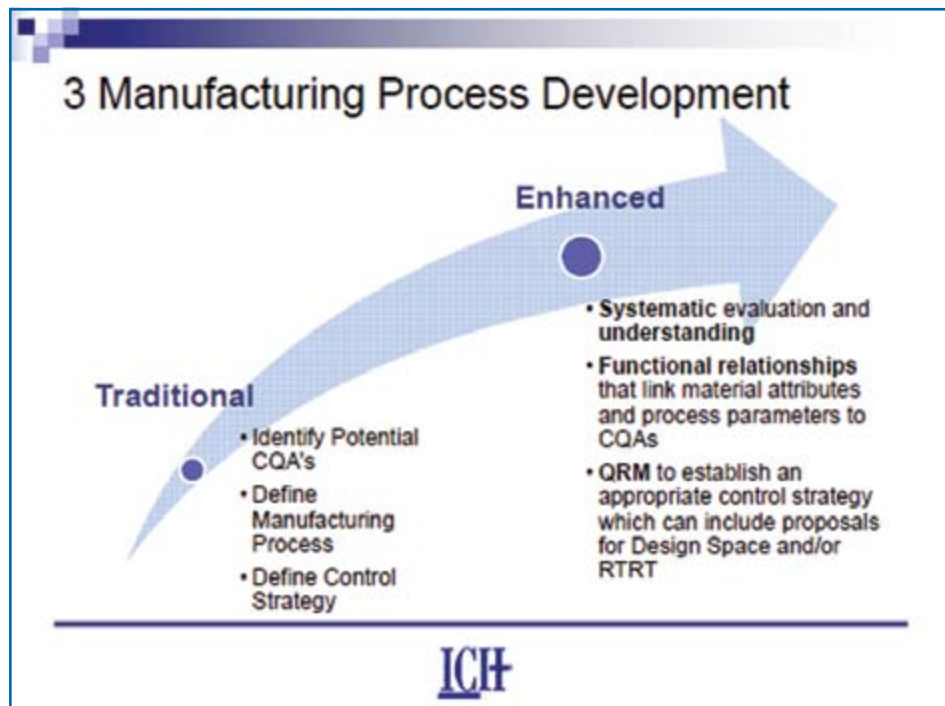
# Assignment of CQAs for the drug product and drug substance is interrelated, but generally flows from the drug product to the drug substance

one of FDA's representatives on the Q11 EWG.

The guidance includes five "illustrative examples" to help manufacturers con-

ceptualize key concepts. Example 1 handles the linkage of material attributes and process parameters to drug substance CQAs. Fritschel emphasized that it was a "simplified example."

Figures 1 and 2: Fritschel used the below graphs to demonstrate Traditional and Enhanced Approaches



These examples, the guidance states, *are provided for illustrative purposes and only suggest potential uses. In addition, they are not intended create any new expectations beyond the current regulatory requirements.*

Fritschel explained that Example 1 is a "simple" one and that "reality is a little bit more complicated." The purpose, however, is "to show an example of how you could take a traditional approach or an enhanced approach with the same unit operation and how that would impact the parameters that you develop. We went on to show the development of your design space using prior knowledge and also chemistry first principles. We adapted this particular example from the training workshops that the implementation working group did last year on Q8/9/10."

## Public Comments Like Q11, with Caveats

Overall, there seems to be a lot of support for the Step 2 draft as written. In the public docket for comments on the guidance in the United States (available at [www.regulations.gov](http://www.regulations.gov)), 21 companies, associations (including PDA), and trade groups issued comments on the document. The *PDA Letter* reviewed every comments document and found no major objections to the guidance in general and quite a bit of support for many of its tenants.

PDA's comments, devised by a task force of member volunteers representing a broad swath of the industry (see page 39 for the cover page and task force list), states the Association's position that Q11 "is an impressive effort to capture the latest thinking around modern pharmaceutical quality and development science." PDA offers kudos specifically for the emphasis on design space, risk management and the quality by design approach.

PDA does feel that the term "enhanced approach" is unique to Q11 and believes that it is synonymous with the term "quality by design" more commonly used in ICH Q8/Q9/Q10. PDA suggests, "The connections between these terms and concepts should be explicit" and requests that a formal definition of ►





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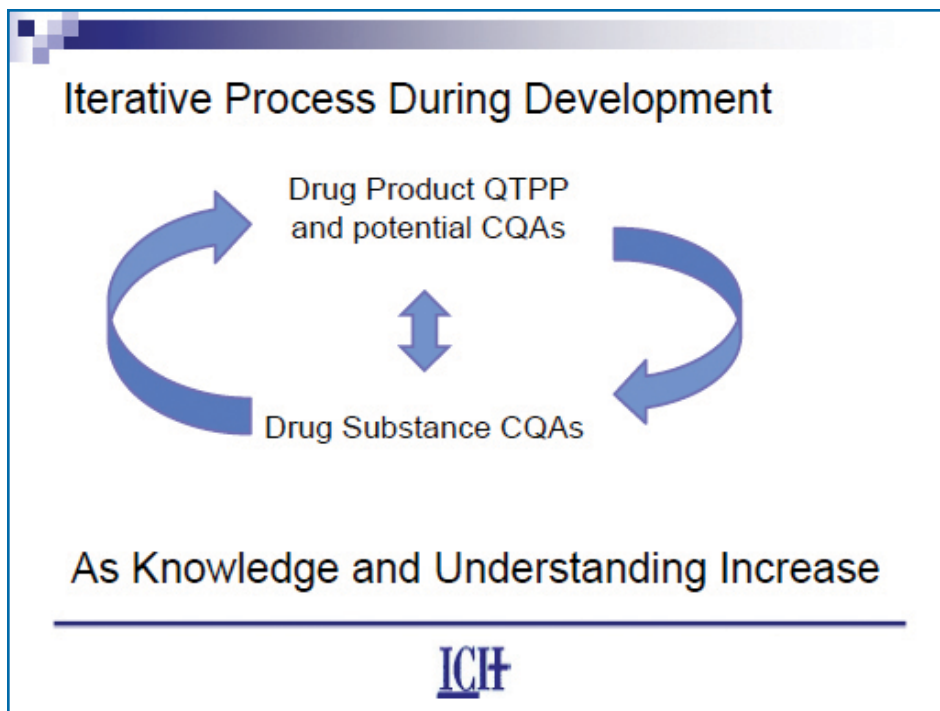
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Figure 3: Fritschel illustrated the interrelationship between drug substance and drug product CQAs



“enhanced approach” be included in the glossary. (The full comments grid developed by the PDA task force is available on the PDA website, at [www.pda.org/regulatorycomments](http://www.pda.org/regulatorycomments).)

## PhRMA’s believes that the Introduction to Q11 needs to “clarify why Q11 is needed in addition to Q8, Q9 and Q10”

The International Society for Pharmaceutical Engineers (ISPE) “warmly welcomed” the publication of draft Q11, noting that it “provide a wealth of helpful information to developers of both chemical and biotechnology drug substances.” The Society would like to see the EWG explicate “design space movement and its implications to the control strategy and quality system.”

The U.S. industry trade organization, Pharmaceutical Researchers and Manufacturers of America (PhRMA), offered the most incisive critiques of the draft

guidance. Recognizing and supporting Q11 as “an important document for international harmonization,” PhRMA states the document does much in achieving the vision set for it in a con-

cept paper several years ago. However, the trade group focused on four areas of Q11 which it believes “editing and compromise needed to reach Step 2 in the ICH process” has resulted in the “loss of important content.” These are: the Introduction, Design Space, Control Strategy and Lifecycle Management.

PhRMA believes that the Introduction to Q11 needs to “clarify why Q11 is needed in addition to Q8, Q9 and Q10.” The ability to control and remove impurities, in PhRMA’s view, “is an important difference between drug sub-

stance and drug product manufacturing in both the traditional and enhanced approach.” For this reason, PhRMA suggests the insertion of language into the Introduction to make this clear.

When it comes to the “enhanced approach,” PhRMA believes the continued use of the phrase “flexible regulatory approaches” (line 82 in the draft) continues to confuse a concept that “has never been clearly defined and is misunderstood in many cases to be regulatory flexibility or regulatory relief.” Instead, “the focus should be on enhanced process knowledge and a more flexible control strategy or manufacturing flexibility,” PhRMA says. To solve this, the group recommends striking the term “regulatory” from the paragraph.

PhRMA also offered a lengthy critique of Section 6, Control Strategy. The group’s belief is the section is too repetitive with language in Q8(R2) and “does not address or clarify the differences in drug product and drug substance.” In particular, PhRMA feels the term “real time release” does not properly reflect the long history of “assurance of removal of impurities at an earlier step rather than testing the final drug substance.” PhRMA recommends either restricting the use of the term to drug products or adding language (provided in PhRMA’s comments) that clarifies the differences between drug products and drug substances.

### Ambitious Goal

These and all the comments received in the United States, Europe and Japan will have to be considered by the EWG during Step 3 as they prepare the final guidance. The public comment period ended in September in all regions.

Fritschel stated that the group original planned to resolve the public comments at its next meeting in November, but now, based on the number of comments received, that timeline is “a stretch goal.” 🍷





# PDA Israel Chapter Calls for Additional Work on Q11

Karen Ginsbury, PCI Pharmaceutical Consulting Israel

On July 26, 2011, despite it being the height and heat of the summer, the PDA Israel Chapter attracted 120 people to a discussion meeting on the draft ICH guidance, *Q11: Development and Manufacture of Drug Substance*. Alex Weisman, PhD, VP R&D, Chemagis, gave a rapid overview of the guide and summarizing it as "Design Space" for "Drug Substance" (DS) whereby the outcome of the formula  $DS \times DS = DS^2$ !

Weisman emphasized that considerations for a company when deciding to adopt a traditional or an enhanced approach to development should focus on what works for the company culture. Additional factors that might be considered include: raw materials availability, scale up and engineering changes further down the line if anticipated. Using a case study, he shared with participants how his company had used DoE to leverage enhanced control over the interactions of critical process parameters resulting in a yield increase of API from 80% to 92% and enhanced purity of the product. Clearly the use of the enhanced approach paid both economic and quality dividends in this case.

A second presentation addressed current practices and regulatory expectations for APIs and DMFs. Ori Lerman, PhD, Chief Chemist, Ministry of Health, addressed issues related to DMF submissions and expectations for the type and format of data submitted to the Ministry when a company requests approval of a new API. Lerman's view was that the Q11 guidance did not substantially upgrade expectations from the type of submissions his group presently sees.

A lively discussion ensued and the main take home point was that the incorporation of expectations for biological drug substance alongside chemical APIs in the document had caused considerable confusion. It was generally felt that the document could be considerably enhanced by separation of the two areas since the processes for manufacture of biopharma-

ceuticals as opposed to traditional small molecules are completely different. Participants even went further with the discussion, pointing out that biologists and

chemists have little in common!

At the end of the discussion, it was generally felt that the document is of value, but requires substantial additional work  
*continued at bottom of page 28*

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# Personalized Medicines: The Next Big Thing in Healthcare

Emily Hough and Walter Morris, PDA



Since our genetic makeup is unique, shouldn't the medicines used to treat a disease be individualized to offer a greater degree of efficacy? As personalized medicines evolve, they will revolutionize the way people are diagnosed and treated, how and where drugs are made, and will potentially affect how the industry functions. Personalization, however, brings greater challenges to the manufacturer and industry at large.

The U.S. FDA approved two cancer-fighting drugs in August that are both considered milestones in the advancement of personalized medicines.

Genentech (a member of the Roche Group) announced in an August press release that one of the first milestones for personalized drugs was recorded this past summer when the U.S. FDA approved Zelboraf (vemurafenib) for the treatment of BRAF V600E mutation-positive, inoperable or metastatic melanoma. At the same time, FDA also approved the cobas 4800 BRAF V600 Mutation Test, a companion diagnostic test to the Zelboraf that was developed by Roche to identify patients who are eligible for Zelboraf.

The company claimed that Zelboraf is the first and only FDA-approved personalized medicine shown to improve survival in people with BRAF V600E mutation-positive metastatic melanoma, demonstrating the benefits of Roche's personalized healthcare approach. The product is designed to target and inhibit some mutated forms of the BRAF protein found in about half of all cases of melanoma, the deadliest and most aggressive form of skin cancer.

"The FDA approval of Zelboraf marks a major step forward in personalizing the treatment of metastatic melanoma, a devastating disease that until this year had limited approved treatment options," said **Hal Barron**, MD, chief medical officer and head, Global Product Development, Roche. "We will continue to study this medicine with a goal of further improving outcomes for people with melanoma and other cancers that are driven by BRAF mutations."

This announcement was quickly followed by the approval of Pfizer's XALKORI (crizotinib). According to the company's Aug. 26 press release, it is the "first and only therapy specifically for patients with locally advanced or metastatic alk-positive non-small cell lung cancer."

Like Zelboraf, approval of the Pfizer anti-cancer therapy was simultaneously accompanied by the approval of a diag-

nostic tool—one developed by Abbott Molecular. Aligned with FDA's latest guidance on targeted therapies and companion diagnostics, the company worked closely with FDA and partner{{d with Abbott Molecular's business in Pfizer's clinical studies to ensure the simultaneous review and approval of XALKORI along with a diagnostic test, Abbott Molecular's Vysis ALK Break Apart FISH Probe Kit, to identify presence of the ALK fusion gene. The simultaneous approval of XALKORI in parallel with Abbott Molecular's ALK FISH Test marks the first time a Pfizer oncology drug or any lung cancer medication was developed and approved in parallel with a diagnostic test."

In its own Aug. 26 press release, Abbott Molecular's **Stafford O'Kelly**, head of molecular diagnostics business, said: "The Abbott-Pfizer collaboration marks a breakthrough in the advancement of personalized medicine—and companion diagnostics specifically—that will help a subset of lung-cancer patients get treatment tailored to their unique genetic profile."

As defined by a 2008 report by the U.S. President's Council on Advisors on Science and Technology, "Personalized Medicine" refers to the tailoring of medical treatment to the individual characteristics of each patient...to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Preventative or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not."

Cell and gene therapies are common forms of personalized medicine.

### Cell Therapies

Personalized regenerative medicine, commonly considered a form of cell therapy, is a method used to grow and fix damaged tissue and promote healing. For example, researchers can use cartilage (chondrocyte) cells to repair cartilage in joints such as the knee.

Cell therapies are still in the research and early clinical trial stages. This research is an outgrowth of stem cell re-

search that has been performed mainly in government-regulated laboratories by traditionally trained scientists. Now, companies are beginning to acquire manufacturing licenses to produce cell therapy medicinal products in their laboratories.

An article in *Genetic Engineering & Biotechnology News* states that there are challenges with autologous cell-based therapies: "based on the collection, manipulation, and delivery of live cells including the timeline in which the cells must be collected, processed, and returned to the patient to ensure optimal viability and outcomes." (1)

One of these challenges is that of manufacturing a cell-based therapy on a commercial scale.

It is unlikely that a cell-based therapy could be produced at commercial scale cost-effectively using manual methods. Some of the concerns include the following:

- Mechanisms to ensure that multiple patient product streams are combined correctly and that the correct product is delivered to each patient
- The extraordinarily high number of individual batches being tested and released for commercialization needs
- The complexity of process scheduling, traceability, and release issues for autologous cellular therapies

According to another article published in the *Genetic Engineering & Biotechnology News*, a system designed to maintain the chain of custody and scalability of testing (minimizing the amount of product lost to testing and the time delay in product delivery) is needed. (2) Also, moving to large-scale manufacturing means potentially thousands to tens of thousands of

### Article's DNA

- U.S. FDA recently approved two new drugs under "personalized medicine" umbrella
- Several Types of personalized medicines are under development
- Regulators are setting standards

## It is unlikely that a cell-based therapy could be produced at commercial scale cost-effectively using manual methods

batches could be made every year for just one patient, and effective methods of control, such as a well-designed manufacturing execution system to manage those activities and enable electronic batch records with release by exception, need to be developed.

### Gene Therapies

Genetic therapies, or molecular profiling, offer a molecular analysis to better identify a patient's disease or predisposition to a disease.

Currently, oncological applications lead the field of personalized medicine research, although other applications are under development. Research is being done on cardiovascular diseases, central nervous system conditions, and immunology and is expanding into metabolic and respiratory therapies as well as virology, according to the Pharmaceutical Research and Manufacturing Association (PhRMA).

Specifically, according to a report by the Personalized Medicine Coalition, the use of genetic screening would allow physicians to select an appropriate, efficacious treatment from the start of treatment. (3) According to the same report, personalized therapies would also increase patient compliance to treatment as patients would be more likely to continue with treatment if they had fewer side effects to the medication or saw improvements in their conditions. Medical products that are administered by trial and error would also be safer if a patient's variation of genes was taken into consideration.

Once fully developed, gene therapy could allow a cancer patient and doctor to not only know the grade and stage of the tumor or malignancy, but also the relevant gene expression pattern. This information could become a tool for selecting the most promising drug regime, predicting the metastatic potential of the cancer, and

allowing patients and physicians to weigh the relative merits of aggressive treatment earlier in the course of disease.

One barrier for determining the molecular profile of a tumor is the cost of microarray technology, which takes an orderly arrangement of samples where matching of known and unknown DNA samples is done based on base pairing rules. An array experiment makes use of common assay systems such as microplates or standard blotting membranes.\*

"This technology is expensive, requires special handling procedures, and lacks standardization within the research community," according to a *Clinical Medicine & Research* article. (4) However, standardized microarrays, necessary for clinical application and interpretation of results, have not been created: "Efforts are underway to reduce the problems associated with molecular profiling in order to bring this technology from bench to bedside."

### Clinical Trials

Personalized medicines will help reduce time, cost and failure rate of clinical trials. According to the Personalized Medicine Coalition report, using patients' pharmacogenomic data responsiveness to a drug product would be determined to "reduce the time and cost of drug development in addition to reducing the rate of drug failures by allowing researchers to focus on sub-sets of patient populations." (3)

### Regulations

According to **Ilona Reischl**, PhD, Manager, AGES PharmMed, the area of personalized medicines is where the biologics industry was 10 years ago. She stated in an interview with the *PDA Letter* that while regulations on advanced therapy medical products\* in Europe have been issued for "almost a decade," this is generally a new field for regulators. Reischl cited inexperience and knowledge-gap as a prime reason why guidance and inno-

vation are limited in this area. (Nonetheless, the EMA has released several draft guidelines for consideration regarding the approval process for advanced therapy medicine products in Europe. See box on next page for EU regulatory documents released since 2001.)

FDA began addressing personalized medicine in earnest earlier this year with guidances and hiring experts. One such

**According to the National Human Genome Research Institute, microarray technology allows scientists to study which genes are active and inactive in different cell types. This helps scientists understand how these cells function normally and how they are affected when various genes do not perform properly.**

expert is **Steven Spielberg**, Director of the Center for Personalized Medicine and Therapeutic Innovation at Children's Mercy Hospital in Kansas City, who was assigned to FDA's newly created position of Deputy Commissioner for Medical Products and Tobacco. According to an article in the *Pharmacogenomics Reporter*: "Spielberg's hire comes during a time when the Agency has been working to align the efforts of its various centers to coordinate regulatory oversight of drugs and devices that ideally need to be reviewed, approved, and marketed together in order to deliver personalized care." (5)

In February 2011, the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiological Health published the draft guidance, *Clinical Pharmacogenomics: Premarketing* ►

**Advanced therapies include cell therapy, gene therapy and tissue engineering, and are a subset of personalized medicine.**



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**Some of the more commonly referred to regulations and guidance around personalized medicines are as follows:**

Directive 2001/20/EC of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

Directive 2006/17/EC implements Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells

Directive 2006/86/EC implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells

EMA/CHMP/410869/2006 Guideline on human cell-based medicinal products

Council Directive 90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices. This later was revised in 2007.

Regulation (EC) No 1394/2007 of the European Parliament and of the Council on advanced therapy medicinal products amending Directive 2001/83/EC and Regulation (EC) No 726/2004

Doc. Ref. EMA/149995/2008 Guideline on Safety and Efficacy Follow-up Risk Management of Advanced Therapy Medicinal Products Directive 2009/120/EC amended Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use as regards advanced therapy medicinal products

CAT/CPWP/568181/2009 Reflection paper on In-Vitro cultured chondrocyte containing products for cartilage repair of the knee

EMA/CAT/571134/2009 Reflection paper on stem cell-based medicinal products

EMA/CHMP/GTWP/671639/2010 Draft guideline on the quality, preclinical and clinical aspects of medicinal products containing genetically modified cells

*Evaluation in Early Phase Clinical Studies* in order to “assist the pharmaceutical industry and other investigators engaged in new drug development in evaluating how variations in the human genome could affect the clinical pharmacology and clinical responses of drugs.”

Published a few months later in July by FDA’s Center for Drug Evaluation and Research, the Center for Biologics Evalu-

ation and Research, and the Center for Devices and Radiological Health, a draft guidance was released on *In Vitro Companion Diagnostic Devices* to clarify relevant policies relevant to devices and products.

The draft guidance states that while FDA “encourages the development of therapeutic products that *depend on* the use of approved or cleared IVD companion diagnostic devices,” proper safe-

ty and effectiveness must be proven with an IVD Companion diagnostic device for health care professionals to rely on the results received from those devices.

While the Personalized Medicines Coalition’s blog, “The Age of Personalized Medicine,” found the draft guidance a step in the right direction, it criticizes the draft document for being too brief and not clarifying some of its positions. For example, the blog points out that the guidance says there is collaboration between the drug and device centers but doesn’t provide any detail beyond that. Also, FDA does not clarify what it means by “risk in the case of a diagnostic.”

On August 11, the *Federal Register* published a notice that the International Conference on Harmonisation issued a guidance on *E16 Biomarkers Related to Drug or Biotechnology Product Development Context, Structure, and Format of Qualification Submissions* available. This guidance describes recommendations regarding the context, structure, and format of qualification submissions for clinical and nonclinical genomic biomarkers related to development of drug or biotechnology products, including translational medicine approaches, pharmacokinetics, pharmacodynamics, and efficacy and safety aspects. The guidance is intended to create a harmonized recommended structure for biomarker qualification applications that will foster consistency of applications across regions and facilitate discussions with and among regulatory authorities.

**Industry Viewpoint**

PhRMA has been advocating for personalized medicine since 2005 when **Billy Tauzin** became president of the organization. In 2010, when Tauzin resigned, some were worried that PhRMA would stop championing personalized medicine. Tauzin’s successor, **John Castellani**, however, alleviated concern by pledging PhRMA’s ongoing efforts to promote personalized medicine, in June 2011, he delivered his first speech on personalized medicine at the Personalized Medicine Coalition’s Seventh Annual State of Personalized Medicine Luncheon.

Castellani discussed how personalized  
*continued at bottom of page 30*

**Companies that are involved in personalized medicine**

Abbott	Eli Lilly and Company	Merck
Amgen	Endo Pharmaceuticals	Millennium: The Takeda
Boehringer-Ingelheim	GE Healthcare	Oncology Company
bioMérieux	Genzyme	Novartis
BD	GlaxoSmithKline	Pfizer
Bristol-Myers Squibb	Johnson & Johnson	Sanofi Aventis

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# Evaluating the Use of RFID in the Pharmaceutical Industry

Ashley Goldberg, Baxter

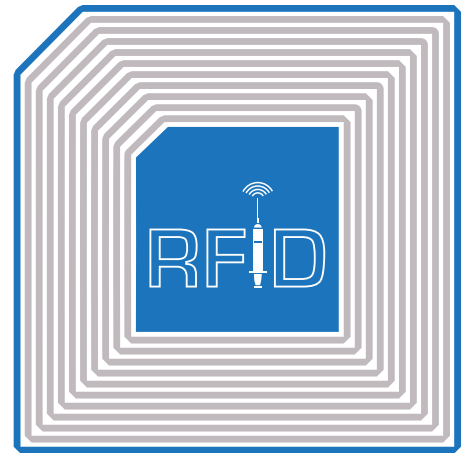
As an industry we need to evaluate RFID (radio-frequency identification) technology in our supply chains. Compelling arguments exist for the use of RFID as the pharmaceutical industry is increasingly a target for counterfeiting and cargo theft. A 60 Minutes episode that aired in March of 2011 included a raid in Lima, Peru that exposed counterfeit activities and found hundreds of thousands of counterfeit medicines manufactured in crude environments. The Pew Health Group recently published a white paper examining case studies on the risks of substandard and counterfeit drugs. (1) Examples include cough syrup distributed in Panama that contained diethylene glycol instead of glycerin and a bulk antibiotic supplier in Europe that falsified documentation to conceal the location of manufacturing sites from the U.S. FDA. (1) In the case of the antibiotic supplier, the successor company pled guilty to conspiracy and distribution of adulterated drugs and was ordered to pay a fine in excess of \$23 million (USD) plus forfeiture of \$10 million (USD) in proceeds to the U.S. government. (1)

Following these events, our industry has seen an increased focus on supply chain security. In 2010, FDA published its final guidance on Standards for Securing the Drug Supply Chain—*Standardized Numerical Identification for Prescription Drug Packages* as one step in setting standards for securing the drug supply chain. (2) The FDA guidance aligns with the GS1 Healthcare Standards. (3) The regulatory guidance and pharmaceutical company movement toward implementation of systems such as RFID for product traceability and supply chain visibility are responses to the vulnerabilities highlighted in the recent contamination events. While the likelihood of supply chain contamination and detection are low, the risk to patient health is potentially high. As a result, we should approach this risk with the same

risk management methodology we apply to the other facets of our business.

The most widely accepted numbering system used in RFID (radio-frequency identification) is the Electronic Product Code (EPC). (4) EPC generation 2 tags are currently the highest-performing technical protocol for passive RFID tags, the most likely choice for drug identification. These tags are approved by EPC-global, an organization that sets international RFID standards and comply with the GS1 standard. (5) RFID technology links the EPC stored on a tag's tiny computer chip to information stored in a database that provides unique, positive identification and can house additional information associated with the object. This technology is an additional measure of supply chain security that may detect potentially counterfeit material and deter criminal activity. The cost for implementation of RFID on counterfeit material is substantially higher than mimicking existing packaging material and shipping documents.

RFID has been implemented in many industries including government, retail and healthcare. Its use and preference stem from the reduction in direct labor costs and errors associated with other product identification solutions. One of the largest proponents of RFID is the United States Department of Defense whose requirements for RFID tags on packages are prescribed in the Defense Federal Acquisition Regulations Supplements 252.211-7006 following the EPC global standards. In 2003, Wal-Mart announced that by 2006 it would require RFID EPC tags on all pallets and cases from all suppliers. (6) Wal-Mart, which owns Sam's Club, sent letters to their suppliers (dated January 7, 2008) that outlined requirements and timelines for application of EPC generation 2 RFID tags on single product pallets and cases on mixed product pallets with penalty fees for non-compliance. (7) The retail giant's requirements also branched into



the pharmaceutical industry. In 2004, Purdue Pharma started applying RFID tags to OxyContin bound for Wal-Mart. (8) In February 2007, Purdue Pharma announced plans to rollout a full-scale implementation by tagging every bottle and case of the drug that it produced. The serialized EPC tags were encoded into the product label by Purdue's label manufacturer and affixed to the bottles as part of Purdue's packaging process. (9)

Challenges implementing RFID in our industry are synonymous with the challenges we face implementing Track and Trace. Barriers include a lack of consistent global regulation, potential impact of the tags on product, and the high cost of the infrastructure in our manufacturing, distribution and pharmacy locations. Adding RFID tags to a drug product may require additional extractable/leachable testing depending on its proximity to the primary container. The use of RFID tags could introduce additional interference factors that may not have established test methodologies.

The infrastructure needed for implementation of RFID in the pharmaceutical supply chain is highly dependent upon development of global regulation or standardization. The cost associated with infrastructure implementation varies based on the method of technology used. Boeing implemented an RFID system to facilitate both receipt of ►



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# 2011 PDA UPCOMING EVENTS

OCTOBER 2011

**3-6**

## 2011 PDA Visual Inspection Forum & TRI Course

Bethesda, Maryland

[www.pda.org/visualinspection2011](http://www.pda.org/visualinspection2011)

**4-6**

## Pharmaceutical Quality System (ICH Q10) Conference

Arlington, Virginia

[www.pda.org/Q10](http://www.pda.org/Q10)

**10-14**

## Aseptic Processing Training Program – Session 5 Week 1 (Week 2: November 14-18)

Bethesda, Maryland **SOLD OUT**

[www.pda.org/2011aseptic](http://www.pda.org/2011aseptic)

**17-21**

## PDA's 6th Annual Global Conference on Pharmaceutical Microbiology & TRI Courses

Bethesda, Maryland

[www.pda.org/2011microbiology](http://www.pda.org/2011microbiology)

**24-28**

## PDA TRI Filtration Week

Bethesda, Maryland

- Filters and Filtration in the Biopharmaceutical Industry – Basics Course (October 24-25)
- Filters and Filtration in the Biopharmaceutical Industry – Advanced Course (October 26-28)

[www.pda.org/filtrationweek](http://www.pda.org/filtrationweek)

**25-28**

## Pharmaceutical Freeze Drying Technology

Barcelona, Spain

<https://europe.pda.org/FreezeDrying2011>

**27**

## ICH Q9: Application of a Risk-based Approach to Freeze Drying Processes

Barcelona, Spain

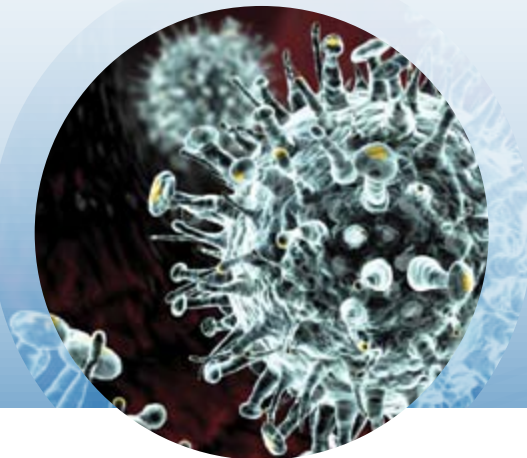
<https://europe.pda.org/WSFreezeDrying2011>

**27-28**

## Development of a Freeze Drying Process – From Formulation to a Robust Process

Barcelona, Spain

<https://europe.pda.org/TCFreezeDrying2011>



[www.pda.org](http://www.pda.org)

For an updated PDA calendar of events please visit  
[www.pda.org/calendar](http://www.pda.org/calendar).



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## NOVEMBER 2011

**1-2**

**Quality and Compliance Management for Virtual Companies – *New Course***  
Bethesda, Maryland  
[www.pda.org/virtualcompanies](http://www.pda.org/virtualcompanies)

**2-4**

**PDA/FDA Adventitious Agents and Novel Cell Substrates: Emerging Technologies and New Challenges**  
Rockville, Maryland  
[www.pda.org/adventitious2011](http://www.pda.org/adventitious2011)

**3**

**Process Validation for Pharmaceuticals – Current and Future Trends**  
Bethesda, Maryland  
[www.pda.org/processvalidation](http://www.pda.org/processvalidation)

**7**

**The Future of Glass as Parenteral Primary Packaging: Issues and Challenges**  
Basel, Switzerland  
<https://europe.pda.org/WSPrefilled2011>

**7-8**

**Preparation of Virus Spikes Used for Virus Clearance Studies – *New Course***  
Bethesda, Maryland  
[www.pda.org/viruspikes](http://www.pda.org/viruspikes)

**7-11**

**The Universe of Pre-filled Syringes and Injection Devices**  
Basel, Switzerland  
<https://europe.pda.org/Prefilled2011>

**8-10**

**Validation of Biotechnology-related Cleaning Processes – *New Course***  
Bethesda, Maryland  
[www.pda.org/validationbiotech](http://www.pda.org/validationbiotech)

**10**

**Quality of Glass Containers**  
Basel, Switzerland  
<https://europe.pda.org/TCPrefilled2011>

**10-11**

**Development of a Pre-filled Syringe – Hands-On Training Course**  
Basel, Switzerland  
<https://europe.pda.org/TCPrefilled2Days2011>

**29-30**

**Single-Use-Systems for Pharmaceutical Applications**  
Uppsala, Sweden  
<https://europe.pda.org/SingleUse2011>

## DECEMBER 2011

**5-9**

**Quality Systems for Aseptic Processing – *New Course***  
Bethesda, Maryland  
[www.pda.org/qualitysystems](http://www.pda.org/qualitysystems)

**6-7**

**Modern Biopharmaceutical Manufacturing**  
Bordeaux, France  
<https://europe.pda.org/Biopharma2011>

**8**

**PDA Technical Report: Single-Use-Technologies**  
Bordeaux, France  
<https://europe.pda.org/TCSingleUse2011>

**8**

**PDA Technical Report: Cleaning Validation**  
Bordeaux, France  
<https://europe.pda.org/CleaningValid2011>



materials and payment to suppliers at the cost of \$16,000 which saved over \$29,000 in six months. (10)

The benefit of RFID technology is clear. It enables product identification without line of sight. This increases throughput, efficiency and accuracy at each step of the supply chain. Analysis of hospital supply chains completed by the University of Cincinnati demonstrates an opportunity for RFID to make supply and re-supply within the hospital leaner and more cost effective. (11) An additional study conducted by the RFID Research Center at the University of Arkansas at JCPenny demonstrates that areas that already have high inventory accuracy can be significantly improved with RFID. (12)

In order to be successful, we need a harmonized legislative environment; regional and global coordinated approaches rather than national or regional initiatives. Stakeholder involvement in design of legislation that includes clear timeframes for implementation with a transition period and risk-based approach is critical. Industry adoption of global standards such as GS1 Healthcare and EPCglobal as well a centralized registration database will ease implementation for each of the stakeholders within the supply chain (suppliers, manufacturers, distributors, pharmacies, etc.).

Advancing technology has continued to drive cost reductions in RFID tags and nanotechnology continues to advance with developments in microsupercapacitors that demonstrate remarkable properties for energy storage in increasingly smaller units. The volume derived from a global standard in RFID application and reading within the pharmaceutical

industry would drive increased demand for the technology's infrastructure and the opportunity for standardization and cost reduction of implementation.

Is RFID the solution to identification, security and visibility in the pharmaceutical supply chain? It can be, but we must work together as a global industry with our regulators to make it happen.

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#### About the Author

**Ashley Goldberg** joined Baxter Healthcare in 2009 having held previous roles in sterile large and small volume parenteral manufacturing quality and product development specializing in advanced aseptic processes in Blow Fill Seal Technology. Today, Ms. Goldberg is responsible for Global Supply Chain quality strategy and compliance. If you would like to contact the author for more information, she can be reached at [ashley\\_goldberg@baxter.com](mailto:ashley_goldberg@baxter.com). ☺



#### PDA Israel Chapter Calls for Additional Work on Q11 continued from page 17

in order for it to be a useful guidance that can be applied to the relevant development process.

The discussion group was organized by and facilitated by **Raphy Bar**, PhD, Pharmaceutical Consultant, BR Consulting, and the high level of industry

participation was a good indicator of the importance of the topic to both API manufacturers and finished product manufacturers alike. ☺



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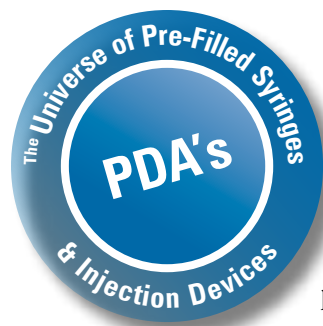
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# Device Usability: Getting It Right from the Start

Andy Fry, Team Consulting

Recently there has been a huge increase in interest within the pharmaceutical and drug delivery community around “human factors” (HF), or usability. Interest is not being driven by new regulations; instead, it is a change in the behavior of regulators.

Regulators increasingly are concerned about inadequate device safety and are placing greater emphasis on seeing proof that misuse of devices will not impact patient safety. As a result, devices are being rejected at the point of approval and either require in-depth user analysis studies to prove their safety or, in the worst case, expensive redesigns to actually address issues.

As far as the regulators are concerned, “usability” is primarily focused on user safety: The patient must be able to use the device correctly and without risk, and the company must be able to prove that this is the case.

To reduce the risk of a product being rejected by the regulator (at least on the basis of safety), companies should strive

to integrate human factors engineering from the outset and throughout product development. At each stage of the process—concept generation, prototyping and final embodiment—the device must be placed in the hands of users, then they must be watched and their actions analyzed.


It is worth highlighting at this point that usability research is not only about statistical data, the U.S. FDA places a great deal of importance on observational analysis that has been unpicked, challenged and discussed qualitatively; after all, the causes of misuse might be down to a range of factors such as the user’s psychology, the design of the device or the instructions.

Observing patients or caregivers using prototypes or the final product can provide some invaluable insight especially when successfully combined with analytical and empirical HF techniques. By doing this at all stages you can adapt the design and functionality of the device as it evolves and in the end help achieve the objective of safe and appealing devices that minimise the core physical and cognitive

burden of delivering a dose. This process should also be satisfactory from the regulatory point of view as you can demonstrate that patient usability has been central to the development and that it has been correctly and thoroughly assessed.

As well as the focus on observation at the beginning, middle and end of development, the best advice is to follow the usability engineering process with passion and creativity, which involves understanding the FDA guidance, ISO/IEC 62366 and ASNI/AAMI HE75:2009 documentation from cover to cover. Yes, they are regulatory necessity, but they also offer exceptionally useful best practice guides for integrating human factors principles throughout development and greatly increasing your chances of getting your therapy and device through the regulators and into the market.

## About the Author

**Andy Fry** is a member of the PDA and is the founder of Team Consulting Ltd, a UK-based medical device developer. Andy will be speaking at the forthcoming PDA Universe of Pre-filled Syringes and Injection Devices Conference (see p. 46) on the topic of trends in parenteral drug delivery. 

## Personalized Medicines continued from page 22

medicine has the potential to improve health outcomes and bend the cost curve by making the health system more efficient. According to a Personalized Medicine Coalition press release, Castellani’s speech “emphasized the biopharmaceutical sector’s commitment to personalized medicine amid the complexities of applying insights from recent discoveries in genetics and molecular biology to research and development.”

### Future of Success or of Failure for Industry?

As more personalized medicines reach commercial scale, pharma companies will need to find innovative ways to raise funds, since they will be relying on a smaller market of drugs in their product port-

folio as opposed to a major blockbuster drug, according to an article in *Bloomberg Businessweek*. (7) The author says, “There’s no certainty ... as the markets for specific drugs shrink, that drug companies will be able to make up for the size of their lost blockbusters by developing enough new products to treat the same population their drugs previously treated.” However, the same article states: “The hope is that increased safety and quality assurance—and the possibility of moving drugs up into earlier phases of treatment—could bolster sales and help make up for narrower markets for each drug.” (7)

A paradigm shift is beginning in the world of medicines based on this better way to

treat disease and cure patients through the promise of highly efficacious medicines as well as regenerative options. Targeted with the greater goal of more effective disease treatment tailored to specific patient needs, this effort appears to allow better ways of improving quality of life for patients.

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*continued at bottom of page 52*

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## Task Force *Corner*

### QRM “Hot Topic” for PCMO<sup>SM</sup> Initiative

Emily Hough

**Ghada Haddad** is the Task Force leader for the Paradigm Change in Manufacturing (PCMO<sup>SM</sup>) PCMO Initiative R05, “Quality Risk Management (QRM) Packaging and Labeling,” an annex to the parent Task Force R01, “Implementation of Quality Risk Management for Commercial Pharmaceutical and Biotech Manufacturing Operations.”

The *PDA Letter* recently conducted an interview with Ghada about how her task force is addressing the hot topics specific to the application of QRM.

**PDA Letter:** What are some of the hot topics plaguing the Task Force?

**Haddad:** The application of QRM in general is a hot topic. QRM should enable proactive identification and management of potential risks that may impact supplying safe, high quality products to patients by embedding QRM into routine operations and decision making through consistent application, training and education.

Per ICHQ9, “appropriate use of quality risk management can facilitate but does not obviate industry’s obligation to comply with regulatory requirements.” In order to implement a harmonized Quality Risk Management program that focuses on risks to product quality and patient safety, there needs to be a robust infrastructure to integrate QRM into Pharmaceutical Quality Systems (PQS) and quality processes and a standard risk management decision making and communication process. Along with that, the industry currently struggles with understanding the concept of QRM as the pool of QRM experts in the industry is still low.

The biggest challenges are with QRM being:

- A systematic process
- Objective and transparent
- Data-driven
- Multidisciplinary
- Focused on product quality and patient safety
- Applicable throughout product lifecycles

Currently, QRM is used as it can hide risks, justify a predetermined conclusion, help employees get out of required GMP activities and, sometimes, even be a “box-checking exercise.”

On another note, in all higher risk manufacturing processes like packaging/labeling and sterilization, there is an expectation by the industry and the regulatory agencies to see examples of QRM application from using risk management tools to possibly a standardized risk scoring criteria to risk control and risk review.

**PDA Letter:** How is your TF addressing those issues?

**Haddad:** As part of a supplement to *PDA Technical Report No. 44 volume II, How to Implement Details for Application of QRM to Manufacturing Processes*, our Packaging and Labeling task force worked on developing five examples of case studies under Annex D, *Case Studies Examples for Packaging and Labeling*, for performing risk assessments on packaging and labeling operations and provides detailed guidance for application and implementation of quality risk management principles throughout the product lifecycle as well as guidance for integrating quality risk management into the pharmaceutical quality systems.

Each case study provides a specific example based on subject matter experts’ opinions and experiences of how to apply quality risk management tools to the packaging and labeling of products. The goal of the case studies examples was to outline the scope and details needed to adequately perform an analysis of risks associated with the packaging and labeling processes and provide sufficient information to launch a risk assessment of a similar operation from analyzing risks, managing risks to acceptable levels by communicating risks to effectively monitoring risks.

**PDA Letter:** What are some upcoming major projects that your TF is working on right now?

**Haddad:** Currently, our five case studies examples are undergoing technical editing by a PDA member. Prior to review and balloting for publication by the PDA Advisory Boards and the PDA Board of Directors and after technical editing, the draft documents will go out for peer review and PDA members will be invited to volunteer to participate in these reviews with clear deadlines for such participation. Once all the feedback has been received the Task Force plans on a face-to-face meeting to adjudicate the comments and finalize the document. The Annex should be ready for publishing by the end of this year.

*continued at middle of page 40*

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## EMA/FDA Joint Inspections to Continue Following Pilot

Emily Hough, PDA

The European Medicines Agency (EMA) says that it had successfully completed joint inspection pilot programs for Good Clinical Practices and APIs with its international partners, the U.S. FDA and Australia's Therapeutic Goods Administration (TGA), according to an August 2 press release.

The impetus of the Good Clinical Practices (GCP) Inspection Pilot Program with the FDA was the success of recent collaborative efforts and the success of the 2008 FDA-European Medicines Agency GMP inspection pilot, globalization of clinical trials, barriers to product development, and duplication of inspections among regulatory bodies, according to the joint *EMA and FDA Good Clinical Practice Initiatives Frequently Asked Questions and Answers* document.

Under the 18-month (concluding March 2011) joint good clinical practice inspection pilot program, the EMA and the U.S. FDA exchanged more than 250 documents relating to 54 different medicines and, in conjunction with the GCP inspectors of the EU Member States, organized 13 collaborative inspections of clinical trials. This laid the foundation for a more efficient use of limited resources, improved inspectional cover-

age and better understanding of each agency's inspection procedures.

Products included for joint inspection under the pilot program were those submitted as new drug applications and biologics license applications to the U.S. FDA and the same products submitted as marketing authorization applications to the EMA.

Future inspection collaboration can be improved, according to the EMA, if the parties involved:

- Harmonize predefined metrics to assess GCP compliance and data reliability
- Strengthen training/understanding of each region's inspection procedures in terms of preparation, conduct and reporting of inspection
- Identify opportunities for joint training activities
- Develop a common system for tracking information
- Establish procedures for handling the large amount of information exchanged.

The pilot, according to the press release, helped "lay the foundation for a more efficient use of limited resources, improved inspectional coverage and better understanding of each agency's inspection procedures." Based on its

success, the initiative will expand to sites outside the United States and European Union. In addition, bioequivalence trials in generic applications will be considered and the initiative clinical trials under FDA's center for biologics will be included.

The API pilot, according to the *Final Report on the International API Inspection Pilot Programme*, fostered cooperation and mutual confidence between participating regulators through communication and exchange of information on inspection planning. The final report states, "New tools for work sharing and exchange of information were developed and used by the participants to share inspection reports and to organize joint inspections of API manufacturers located outside the participating regions. Increased transparency and visibility of inspections performed by participating authorities allowed a successful collaboration between authorities on sites of common interest and increased the number of inspections performed of value to more than one authority."

Over a period of 24 months, participating authorities (EMA, France, Germany, Ireland, Italy, United Kingdom, EDQM, FDA and Australia's TGA), shared their surveillance lists and found 97 sites com-

*continued at top of page 40*

## USP General Chapter <1224> Official November 2011

At the 2011 PDA Analytical Methods Development and Validation Workshop, **Gregory Martin**, President, Complectors Consulting, reviewed new USP general chapter <1224>, *Transfer of Analytical Procedures*.

The <1224> is based off of the "Stimuli" paper, "Transfer of Analytical Procedures: A Proposal for a New General Information Chapter." which was published in

the Pharmacopeial Forum 35(6). The General Chapters-Physical Analysis Expert Committee to form <1224> then published a draft of the chapter in the Forum 37(1). The general chapter will become official with USP 35, which will publish in November 2011, and will officially be effective on May 1, 2012.

According to <1224>, when setting the

transfer rationale it is important to demonstrate the procedure is suitable for its intended use in the receiving laboratory utilizing the personnel, equipment and reagents available. According to **Horacio Pappa**, Principal Scientific Liaison, USP, the chapter is intended to explain the basic steps of analytical method transfer and more details such as which tools to use will be "left for the future." ☞





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# PDA Wants Biotech Guide to be Consistent with Existing Guides

*For the comments grid, visit [www.pda.org/regulatorycomments](http://www.pda.org/regulatorycomments)*



31 August 2011  
 Secretariat, Biologics Working Party (BWP)  
 European Medicines Agency  
 7 Westferry Circus  
 Canary Wharf  
 London E14 4HB  
 United Kingdom  
 BWPSecretariat@ema.europa.eu

## Reference:

*Concept paper on the need for a guideline on process validation of medicinal products containing biotechnology derived proteins as active substance*

(EMA/CHMP/BWP/25360/2011, 19 May 2011)

To: Secretariat, EMA/Biologics Working Party (BWP)

PDA is pleased to have the opportunity to comment on the referenced concept paper proposing a guideline on process validation for protein biotech medicinal products. We have three general comments regarding such a guideline.

1. Value to stakeholders: We support preparation of an appropriate process validation guideline to the extent that it facilitates the quality, manufacture and registration of such medicinal products.
2. Modern quality principles: The guideline should incorporate, and be consistent with, the validation principles and terminology found in ICH Q5, Q6 and Q7, and also the quality concepts embraced by Q8, Q9, Q10 and (when finalized) Q11.
3. Prior knowledge: To the extent useful, the guideline should consider and be consistent with existing industry guidance, 'points to consider,' and consensus-based technical information relating to process validation for medicinal products.

Consistent with point No. 3, PDA is including in our comment matrix a listing of our published Technical Reports which should be helpful for the BWP drafting group. Copies of these Technical Reports will be forwarded to the BWP Secretariat under separate cover.

Thank you again for the opportunity to support the consultation process. Please contact me, or James Lyda of the PDA staff (lyda@pda.org), if you have questions.

With very best regards,

Georg Roessling, Ph.D.  
 Senior Vice President, PDA Europe  
 Roessling@pda.org

cc: S. Rönninger, S. Schniepp, J. Lyda, R. Levy, R. Dana

## PDA Commenting Task Force

**Michael VanDerWerf**, GlaxoSmithKline (Task Force Chair)

**James C. Lyda**, PDA

**Robert L. Dana**, PDA

**Steven Mendivil**, Amgen

**Amy Giertych**, Baxter Healthcare Corporation

**Barbara J. Potts**, PhD, Potts and Nelson Consulting

**Norbert Hentschel**, Boehringer Ingelheim Pharma GmbH & Co

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Some of the highlights will be:

- **From Genomic Platform to Bio Industry**  
Dominique Rollin, *Directeur Scientifique Centre Génomique Fonctionnelle Bordeaux (CGFB)*
- **ICH Q11: Impact on Biopharmaceuticals**  
Pierrette Zorzi, *Former Head of Biological Evaluation of AFSSAPS*
- **Industry Perspective on Partnership with Authorities and the Status of the Paradigm Change (Quality by Design)**  
Georges France, *Pfizer*
- **Single-Use-Systems: Implementation and Supplier Qualification**  
Steven Brown, *Vivalis*

- **Compatibilities, Extractable & Leachable Strategies, SFSTP Commission**  
Natacha Sehnal, *SFSTP/Sanofi*
- **Extractable and Leachable Studies for Stoppers and Elastomers: How to Set-up the Right Testing Strategy?**  
Piet Christiaens, *Toxikon*
- **Application of QbD Principles for Innovation and Compliance**  
Irwin Hirsh, *NovoNordisk*
- **From Process Validation to Continuous Verification, Following the EMA Guideline**  
Véronique Davoust, *Pfizer*
- **Cleaning Validation: Case Study in the Vaccine Industry**  
Anne Rigoulot, *Sanofi Pasteur*

*Please view the agenda on our web site for the other presentations!*

**6-8 December 2011**  
**ENSTBB-IPB**  
**Bordeaux, France**

Additionally, we are offering 2 one day Training Courses:  
**PDA Technical Report: Single-Use-Technologies**  
**PDA Technical Report: Cleaning Validation**

CONFERENCE 6-7 Dec | TOUR OF ENSTBB 7 Dec | EXHIBITION 6-7 Dec | TRAINING COURSES 8 Dec

<https://europe.pda.org/BioPharma2011>



## PDA Calls ICH Q11 Impressive Effort

*For the comments grid, visit [www.pda.org/regulatorycomments](http://www.pda.org/regulatorycomments)*

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

### Reference:

Draft Guidance entitled “Q11 Development and Manufacture of Drug Substances”; Docket No. FDA-2011-D-0436

Dear Sir/Madam:

PDA is pleased to offer comments on the ICH draft guidance entitled “Q11 Development and Manufacture of Drug Substances”. 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 drug substance and drug product development, CMC and GMP regulations, including members representing our Biotechnology, Regulatory Affairs and Quality, and Science Advisory Boards. PDA appreciates the opportunity to offer comments and wishes to thank FDA for the opportunity to do so. These same comments are also being submitted to the European Medicines Agency as part of their consultation process.

PDA commends this continuing initiative to develop global consensus guidance. In General, we find this guidance an impressive effort to capture the latest thinking around modern pharmaceutical quality and development science. We are especially pleased to note the guidance’s emphasis on design space, risk management and the use of a Quality by Design approach.

**Enhanced approach:** The guidance makes frequent references to what is described as “the enhanced approach”. Since there is no consensus in the industry over what this really means, it would be helpful if the term were defined in the Glossary or a reference for the definition were provided. It appears the enhanced approach referred to is the same as (or very much aligned with) the Quality by Design concept discussed in Q8 and referred to in the documents supporting the implementation of Q8/Q9/Q10 and the ICH Quality IWG Points to Consider Guide for ICH Q8/Q9/Q10 Guidelines. The connections between these terms and concepts should be explicit.

In addition, our reviewers found the dual focus on both the traditional and enhanced approaches to development, as presented in the draft guidance, somewhat confusing. We recognize the need to provide a continuum of approaches, as allowed by regulations and historical precedent, as appropriate for each case and company business decision. However, it might have been preferable to acknowledge that the two approaches are not mutually exclusive and that either approach or a combination could be used (as described in the concluding paragraph of the Introduction section) and then focus on providing guidance on the execution of the enhanced approach only. Perhaps an acceptable solution would be to refer to existing guidelines that address the traditional approaches and use Q11 to promote and describe only the “enhanced” approach.

**Existing ICH guidance:** There are several areas where Q11 adds language that is already contained in existing ICH guidance. Q11 could be made briefer by just making reference to these guidances rather than re-stating them. This would also avoid divergent or conflicting interpretations by users of the various guidelines.

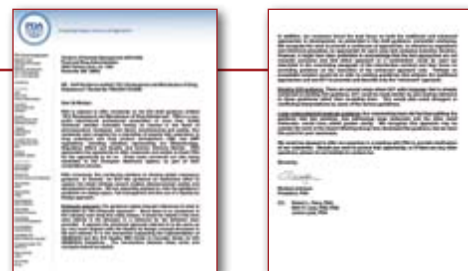
**Large molecule/small molecule guidance:** Our commenting team did feel that splitting the guidance into two sections, one addressing large molecules and the other small molecules, would have added greater clarity. We recognize this approach may be outside the remit of the Expert Working Group who developed the guidance, but we raise this point for your awareness.

We would be pleased to offer our expertise in a meeting with FDA to provide clarification of our comments. Should you wish to pursue that opportunity, or if there are any other questions, please do not hesitate to contact me.

Sincerely,

Richard Johnson  
President, PDA

cc: Robert L. Dana, PDA, Rich V. Levy, PhD, PDA, James Lyda, PDA



# "The Gold Sheet"

PHARMACEUTICAL & BIOTECHNOLOGY QUALITY CONTROL

## Bulletproof guidance for the QA/QC professional.

### In 2010, were you...

- Ready for every single new development in FDA and other regulatory enforcement?
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It's easy to deliver headlines and soundbites. **"The Gold Sheet"** goes above and beyond that to uncover the trends and big picture guidance that help you be pro-active in keeping your operations fully compliant.

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With the global economy making mincemeat of supply chains, many a formerly clean operation has fallen drastically foul of FDA standards. Make sure it doesn't happen to you by reading **"The Gold Sheet's"** detailed reports on these issues and guidance in avoiding disaster.

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Micro issues such as sterility, microbial controls, validation, laboratory data integrity, cross-contamination, out-of-spec (OOS) results and stability testing can be create macro problems. Let **"The Gold Sheet"** drill into the data and on-the-ground realities to keep these details from escaping you.

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Count on **"The Gold Sheet"** to deliver exactly what QA/QC professionals need to know, not just general news reports aimed at executives with no quality responsibilities.

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Thanks to **"The Gold Sheet's"** global contacts, you get bulletproof guidance from the most experienced QA/QC pros in the business, making you look like a hero to your supervisor and shareholders.



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<http://pages.ElsevierBI.net/GS021D>

*EMA/FDA Joint Inspections to Continue Following Pilot continued from page 34*

mon to all three regions, resulting in the exchange of nearly 100 inspection reports and in nine joint inspections.

During the pilot, a master list was made that included initial information of API manufacturing sites provided by each participant. This list was regularly amended by additional information provided regularly by the participants: new sites, new inspection dates, planned inspection dates and APIs manufactured. This list helped increase transparency and visibility of inspection activities.

A final report on the international API inspection pilot program stated that “efforts to reduce the number of duplicate inspections should be continued as it allows saving costly inspectional resources and it also reduces the number of repeated often similar inspections to which the API manufactures are subjected.” A total number of 137 sites were shared between two participants. Also, the exchange of inspection-related information included

in the master list allowed participants to know about inspections performed by other participants and their outcome. This information increased the number of inspections performed of value to more than one authority. This list was found to be a “rich source” of information.

Following the conclusion of the pilot, all partners agreed to extend the participation of the pilot to other European authorities.

Based on the positive experience in the two pilots, the agencies have agreed to continue with their collaboration on inspections taking into account the experiences and lessons learned during the pilot phases. In the short term, collaboration will continue within the existing format and will be extended to all EEA Member States. However, a long term goal will be to extend the program to more comparable regulatory authorities and possibly the World Health Organization.

According to **Vladimira Yalmanova** from

the EMA press office, “with the increasing number of interactions at an international level, increasing benefits of international collaboration are being identified. It is very possible that new pilot programs will be embarked upon in one of the current areas of cooperation, but it is very difficult to be more specific at this stage.”

In March, the EMA and the U.S. FDA published a report that discussed how the EMA and FDA will process the parallel review of Quality by Design applications in a new pilot program. The pilot, initiated in April, will provide a forum for harmonizing FDA and EMA approaches such as emerging regional practices or guidance. At the conclusion of the pilot phase, in three years, a joint assessment on the outcomes of the pilot will be made by the EMA and FDA. Applicants willing to participate to the pilot should notify both agencies of their interest in the pilot at least three months prior to the anticipated submission date. 🇺🇸

*Task Force Corner continued from page 32*

**PDA Letter:** What do you hope that your Task Force accomplishes by the end of this year?

**Haddad:** We hope to provide the industry with an official approved robust guidance and relevant examples of case studies for application and implementation of QRM principles and integration into the PQS in the area of Packaging and Labeling.

**About the Expert**

**Ghada Haddad** is a Senior Technical Manager in the Global Quality Risk Management for Genentech/Roche. She is a Chemist and holds an MBA with over 12 years experience in the Biotech industry, including research, management (people and projects), process development, auditing, regulatory



agency inspection, Change Control and Validation (Equipment, Systems, Processes, Facilities, Packaging and Labeling). Her experience in Quality Risk Management includes integration of Quality Risk Management principles into Change Control, CAPAs, Discrepancies and Validation. She currently trains people on Quality Risk Management tools (Failure Mode Effects Analysis, preliminary hazard analysis, fault tree analysis) and principles. Haddad is a member of PDA's Drug Products Liquids and Solids Task Force. 🇺🇸

*PDA Calls ICH Q11 Impressive Effort continued from page 38***PDA Commenting Task Force for ICH Q11**

**Michael VanDerWerf**, GlaxosmithKline (Task Force Chair)

**James C. Lyda**, PDA

**Earl S. Dye**, PhD, Genentech

**Jacqueline Veivia-Panter**, Abbott Laboratories

**Jeffrey R. Broadfoot**, Cangene Corporation

**John Geigert**, PhD, Biopharmaceutical Quality Solutions

**Joyce E. Bloomsfield**, Merck, Sharp and Dhome Corporation

**Michael A. Long**, PhD, ConcordiaValSource

**Paul J. Larocque**, Acerna Incorporated

**Siegfried Schmitt**, PhD, PAREXEL Consulting





## PARENTERAL DRUG ASSOCIATION TRAINING AND RESEARCH INSTITUTE (PDA TRI)

# Aseptic Processing Training Program

### 2012 Schedule:

#### Session 1:

Week 1: January 9-13  
Week 2: February 6-10

#### Session 2:

Week 1: March 5-9  
Week 2: March 26-30

#### Session 3:

Week 1: May 14-18  
Week 2: June 4-8

#### Session 4:

Week 1: August 20-24  
Week 2: September 10-14

#### Session 5:

Week 1: October 15-19  
Week 2: November 5-9

## The most comprehensive program in the preparation of sterile parenteral products

This two week comprehensive training program, taught by 20 industry leading experts in their fields, with over 300 years of combined experience, will give you and your personnel the training and information needed to properly evaluate and improve your aseptic processes to ensure sterile products. This program provides the perfect balance of hands-on laboratory and lecture training, equipping you with tools and actual experience you can bring home and apply immediately on the job.

#### For more information contact:

James Wamsley, Senior Manager, Laboratory Education  
Tel: +1 (301) 656-5900 ext. 137 | E-mail: wamsley@pda.org

#### Location:

PDA Training and Research Institute  
4350 East West Highway, Suite 150, Bethesda, MD 20814  
Tel: +1 (301) 656-5900 | Fax: +1 (301) 986-1093

### Benefits of Attending

- Learn to relate and incorporate each component of aseptic processing into one operation for an overall improved process and finished product
- Understand the theory and practice behind personnel gowning and aseptic technique qualification to minimize risk of product contamination by personnel
- Use proper environmental monitoring techniques combined with a good cleaning and disinfection program to avoid common sources of contamination in your facility
- Learn to incorporate proper documentation practices into your aseptic processing program to facilitate regulatory compliance

### Learning Objectives

Upon completion of this course, you will be able to:

- Demonstrate an increased proficiency of techniques and skills relating to aseptic processing
- Evaluate and improve current aseptic processing procedures at your facility
- Limit risk for manual product contamination with airflow visualization studies
- Evaluate your environmental monitoring program to collect appropriate data, identify and interpret trends
- Incorporate proper gowning principles into a complete personnel qualification program
- Describe the importance of filter integrity testing when filtering water, gases, or proteinaceous solutions

**SPACE IS LIMITED - REGISTER NOW:**  
[www.pda.org/2012aseptic](http://www.pda.org/2012aseptic)



# Annual Meeting to Foster Interaction Between Speakers, Audience

Phoenix, Ariz. • April 16 – 20, 2012 • [www.pda.org/annual2012](http://www.pda.org/annual2012)

Marsha Hardiman, Dendreon

It's October, and as we reflect on the great presentations and PDA's Training and Research Institute's (TRI) courses at the 2011 PDA/FDA Joint Regulatory Conference, I want to let you know that the planning committee has been very busy at work planning and preparing for the 2012 PDA Annual Meeting. The conference portion of the meeting will be held on April 16–18 and the post conference PDA TRI courses will occur on April 19–20.

The program planning committee is using a different approach this year in regards to putting the meeting together. I know that I speak for the entire committee when I say that we are very excited about the way it is coming together. We are carefully selecting topics and speakers that represent current industry hot topics and innovative technology advancements. The sessions are designed to allow for interaction between the speakers and the audience.

## The Theme

The theme of the 2012 Annual Meeting is *Manufacturing Innovation: Achieving Excellence in Sterile and Emerging Biopharmaceutical Technology*. Our program will feature a one day track on Monday on personalized medicine that will focus on challenges in manufacturing and quality assurance/quality control of these types of products. The program will also feature sterile biopharmaceutical manufacturing with a focus on manufacturing innovations and new technologies as well as regulatory perspectives on biopharmaceuticals. Properly planned and performed process design, development, validation, sourcing, process control, contamination control, testing, handling, product and supply chain security, distribution, and manufacturing all drive product quality and essentially positive business results. Use of innovation and new technologies helps to ensure success of these processes.

## The Keynote Speakers

We are excited to present industry leaders to talk about the future of personalized

medicine and the future of the biopharmaceutical industry. **David Shanahan**, President, Mary Crowley Research Center and President, CEO and Founder, Gradalis will be one of the opening keynote presenters along with **Ted Love**, Executive Vice President, Head of R & D, Onyx Pharmaceuticals. In addition, the U.S. FDA will discuss emerging regulatory expectations.

## The Sessions

The meeting will include 15 sessions broken out over three tracks. There will be two speakers-per-session. We have allowed adequate time at the end of each session for question and answer interaction so we can all share information and broaden our knowledge together. Current presentation topics include:

- Microbial Control in Advanced Aseptic Technology
- Challenges in Manufacturing and Quality for Personalized Medicines
- Current Practices and Opportunities in Biopharmaceuticals
- Contamination Control
- Biofilm Management
- Disposable Manufacturing Systems
- Risk-based Method Lifecycle Strategies
- Combination Product Challenges
- Process Control
- Manufacturing Innovation
- Container Closure Integrity
- Supply Chain Control
- Evolving Regulatory Expectations

Updates on current PDA technical reports will also be presented. In addition, there will be 14 interest group meetings to discuss the most current industry developments and trends. The interest group meetings are always very informative sessions that harbor camaraderie and networking.

## Learning Objectives

The meeting will cover:

- The latest technical advances in personalized medicine, cellular therapies and sterile biopharmaceutical manufacturing

- Challenges in manufacturing and quality assurance/quality control of sterile products
- Keynote lectures on the future of personalized medicine and biopharmaceuticals
- Current regulatory expectations, philosophies and challenges for manufacturing processes and emerging technologies
- Microbiological control in the manufacturing environment for biopharmaceuticals and advanced aseptic technologies
- Case studies highlighting techniques to plan and implement biopharmaceutical process development, manufacturing, testing and distribution procedures using risk and science based approaches, LEAN manufacturing approaches, statistical process control, PAT, etc.
- Newly released PDA Technical Reports and use of PDA training programs to improve process development, manufacturing, testing and distribution of sterile products

## TRI Courses

Immediately following the Conference on Thursday and Friday, PDA TRI will be offering several courses designed to complement what you've learned at the Conference. These courses will focus on Biotechnology and Bioprocessing; Sterile Dosage Forms and Operation; and Design of Cleanrooms.

## The Venue

The meeting will be held in Phoenix, Ariz. at the JW Marriott Desert Ridge Resort. The resort is less than 20 miles from the Phoenix Sky Harbor International Airport. The meeting space allows for easy access to the exhibit area from the conference session and breakout rooms. This beautiful resort features championship golf, luxury spa, expansive pool facilities and elegant event venues in a gorgeous desert setting. Four acres of fun-filled pools, lazy river, waterslides and serpentine shaped pools will entertain your family as you enjoy the conference sessions.

*continued at bottom of page 45*



*The Parenteral Drug Association presents...*

# 2012 PDA ANNUAL MEETING

*Manufacturing Innovation: Achieving Excellence in Sterile  
and Emerging Biopharmaceutical Technology*

**April 16-18, 2012**

JW MARRIOTT DESERT RIDGE RESORT • PHOENIX, ARIZONA

**Website Now Live for the 2012 PDA Annual Meeting!  
View at [www.pda.org/annual2012](http://www.pda.org/annual2012)**

This year's meeting will focus on the keystone of our industry: the manufacturing of quality products. Experts from academia, industry and regulatory agencies from around the world will discuss current practices and opportunities in sterile and emerging biopharmaceutical manufacturing.

Take the opportunity to participate in presentations, case studies and initiate discussions on:

- Manufacturing innovation
- Productivity in large scale sterile manufacturing and contract manufacturing
- Automation
- New technologies, such as personalized medicine and cellular therapeutics

Immediately following the conference, PDA will be hosting a post conference workshop on Single Use Systems on April 18-19 and the PDA Training and Research Institute (PDA TRI) will be offering stand-alone courses on April 19-20.

**For details and to register, visit  
[www.pda.org/annual2012](http://www.pda.org/annual2012)**

**EXHIBITION:** April 16-17 | **WORKSHOP:** April 18-19 | **COURSES:** April 19-20

## ADVANCED NOTIFICATION -

Sign up to receive an email when more information is available about this conference! Visit [www.pda.org/annualnotice](http://www.pda.org/annualnotice).



# New Challenges Discussed at Adventitious Workshop

Rockville, Md. • November 2–4 • [www.pda.org/adventitious2011](http://www.pda.org/adventitious2011)

James Gilbert, PhD, Biogen Idec

The goal of the 2011 PDA/FDA *Adventitious Agents and Novel Cell Substrates: Emerging Technologies and New Challenges Workshop* is to bring together scientists from industry, academia and regulatory agencies to present data and information on the benefits and potential applications of emerging broad virus detection technologies for safety testing and characterization of biological products. In order to facilitate safety testing of novel cell substrates, including plant and insect systems.

This workshop will provide an open and engaging forum for the participants and the audience to discuss and integrate current and emerging technologies and strategies for detection of virus contamination, assessment and control of raw materials and enhancement of product safety.

## Day 1—November 2

The first day session keynote address will be given by **Johannes Löwer**, MD. The talk will focus on safety concerns regarding different types of cell substrates and the key issues related to use of novel cell substrates. He will also discuss the development of new adventitious virus detection assays to meet the challenges of using novel cell substrates for product development.

The Plenary Sessions on Day 1 target emerging technologies for adventitious virus detection and the application of such technologies to the evaluation of biological materials.

Session speakers include:

**Michael Wiebe**, PhD, who will discuss conventional assays and the need for new technologies

**David Munroe**, PhD, who will give a general presentation on next generation sequencing platforms

**John Kolman**, PhD, who will speak about HTS – 454 MPS

**Matthew Friedenber**, PhD, who will hold a discussion on single molecule real-time HTS using the PacBio system

**Ranga Sampath**, PhD, who will talk about long range PCR and mass spectrometry (PLEX-ID)

**Houman Dehghani**, PhD, who will also present data on the use of PLEX ID

**Tom Slezak**, PhD, and **Charles Chiu**, MD, who will give presentations on virus microarrays

**Marc Salit**, PhD, who will discuss standards and standardization as applied to new technologies

**Paul Duncan**, PhD, who will discuss viral risk assessment of a positive signal from random application/deep sequencing strategy

Rounding out the day's presentations will be a presentation from **Arifa Khan**, PhD, who will give a talk about the different emerging technologies.

## Day 2—November 3

The Day 2 sessions keynote address on retroelements will be given by **Marcie McClure**, PhD, an expert on molecular evolution of retroid agents and complexities of genome analysis. Day 2 sessions are devoted to novel cell substrates, including insect, plant and avian cell systems. Presentations center on potential risks associated with these systems and quality issues arising from their use.

Presenters scheduled to speak include:

**Vivadi Yusibov**, PhD, who will address issues associated with plant cell substrates

**Jonathan Stoye**, PhD, who will discuss the risks associated with retroelements and lessons from mammalian cell substrates

**Celine Breda**, PhD, will hold a presentation on the characterization and sanitary status of the avian cell substrate EB66

**George Rohrmann**, PhD, who will speak about baculoviruses, retroviruses and insect cell lines

**Glyn Stacey**, PhD, who will outline the suitability of insect cells for use in manufacture of biological products

**Rosemarie Hammond**, PhD, who will

give a presentation on the risks associated with plant viruses and viroids

## Day 3—November 4

Closing out the workshop will be the topic of raw materials, their sourcing, treatment, analysis and strategies for viral risk mitigation.

Speakers for this session include:

**Tara Tagmyer**, PhD, who will speak about evaluating safety of source materials by vendors

**Ivar Kljavin**, PhD, who will identify source materials of reagents

**Rosemary Versteegen**, PhD, who will talk about appropriate strategy for raw materials used for cell banking/seed production versus routine batch-to-batch use

**Mark Plavsic**, PhD, who will discuss treatment methods and analytical considerations

**Steven Lang**, PhD, who will talk about raw materials and reagents

The format of the 2011 PDA/FDA *Adventitious Agents and Novel Cell Substrates Workshop: Emerging Technologies and New Challenges Workshop* includes panel discussions with audience participation at the end of each day, poster sessions, networking opportunities and an atmosphere promoting stimulating information exchange on this important and rapidly advancing area in biopharmaceutical development.

The PDA/FDA *Adventitious Agents and Novel Cell Substrates: Emerging Technologies and New Challenges Workshop* Program Planning Committee has planned an information-packed workshop and all participants from industry, testing labs, suppliers, regulatory agencies and academia should find the discussions engaging and relevant to current events.

For more information, visit [www.pda.org/adventitious2011](http://www.pda.org/adventitious2011).

## PDA's Who's Who

**Celine Breda**, PhD, Quality Director/Dir. Pharma Operations, Vivalis





## Upcoming PDA Web Seminars – Interactive Online Learning

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

### November 2011



November 3, 2011, 1:00 p.m. – 2:30 p.m. ET

**Cleaning and Cleaning Validation – Principles, Development, Performance and Maintenance**

**Paul L. Pluta**, PhD, Adjunct Associate Professor and Editor-in-Chief, *University of Illinois-Chicago* and *Institute of Validation Technology/Advanstar Communications*



November 10, 2011, 1:00 p.m. – 2:30 p.m. ET

**Cleaning and Cleaning Validation – Problems and Misunderstandings**

**Paul L. Pluta**, PhD, Adjunct Associate Professor and Editor-in-Chief, *University of Illinois-Chicago* and *Institute of Validation Technology/Advanstar Communications*



November 17, 2011, 1:00 – 2:30 p.m. ET

**GMP Compliance and the Bacterial Endotoxins Test – Workshop Two: Routine Testing**

**Karen Z. McCullough**, Principal Consultant, *MMI Associates*

### December 2011



December 8, 2011, 1:00 – 2:30 p.m. ET

**GMP Compliance and the Bacterial Endotoxins Test – Workshop Three: GMP Applications of BET**

**Karen Z. McCullough**, Principal Consultant, *MMI Associates*

### Presentations with Voice Over Commentary Are Now Available for Purchase for the Following PDA USA Events:

#### 2011 PDA/FDA Pharmaceutical Supply Chain Conference

Below are the sessions now available:

- Supply Chain Security – Global Initiative
- Solutions That You Can Use Today
- Ensuring Secure Distribution of Finished Products
- Risk Model: Materials

The recordings are available for \$199 each. To purchase please visit [www.pda.org/supplychainaudio](http://www.pda.org/supplychainaudio)

#### PDA Single Use Systems Workshop

Below are the sessions now available:

- Technology Showcase
- Section 4 – Technologies and System Integration
- Section 5 – Business Drivers
- Section 6 Part 2 – Goals of Implementing Single Use Systems (SUS)
- Section 6 Part 1 – Qualification
- Technical Report (TR) Overview
- Single Use Systems Knowledge Management
- Implementation

The recordings are available for \$199 each. To purchase please visit: [www.pda.org/singleuseaudio](http://www.pda.org/singleuseaudio)

For more information on PDA Web Seminars please visit [www.pda.org/webseminars](http://www.pda.org/webseminars)

**Charles Chiu**, MD, Director, Viral Diagnostics and Discovery Center, UCSF-Abbott

**Houman Dehghani**, PhD, Director, Amgen

**Paul Duncan**, PhD, Senior Investigator, Bioprocess Research and Development, Merck

**Matthew Friedenberg**, PhD, Senior Director, Product Development, Gen-Probe

**Rosemarie Hammond**, PhD, Research Plant Pathologist, USDA Agricultural Research Service

**Arifa Khan**, PhD Senior Investigator, CBER/FDA

**Ivar Kljavin**, PhD, Sr. Manager, Genentech

**John Kolman**, PhD, Senior Director, BioReliance

**Steven Lang**, PhD, Senior Manager, Johnson and Johnson

**Johannes Löwer**, MD, President, International Alliance for Biological Standardization (IABS) and past president of the Paul-Ehrlich-Institut

**Marcie McClure**, PhD, Professor, Department of Microbiology, Montana State University

**David Munroe**, PhD, Director, Technology Development, SAIC-Frederick

**Mark Plavsic**, PhD, Senior Director and Corporate Biosafety Advisor, Genzyme (Sanofi Aventis)

**George Rohrmann**, PhD, Professor, Microbiology, Oregon State University

**Ranga Sampath**, PhD, Director, Science and Technology, IBIS/Abbott

**Marc Salit**, PhD, Group Leader, Biochemical Science, National Institute of Standards and Testing

**Tom Slezak**, PhD, Associate Program Leader for Informatics, Lawrence Livermore National Laboratories

**Glyn Stacey**, PhD, Director, Stem Cell Bank, MRC National Institute for Biological Standards and Control

**Jonathan Stoye**, PhD, Head of the Division of Virology, National Institute for Medical Research

**Tara Tagmyer**, PhD, Process Scientist, Viral Vaccine Technology and Engineering, Merck

**Rosemary Versteegen**, PhD, Chief Executive Officer, International Serum Industry Association

**Michael Wiebe**, PhD, President, Quantum Consulting

**Vivadi Yusibov**, PhD, Executive Director, Fraunhofer USA CMB 🇺🇸

*Annual Meeting to Foster Interaction Between Speakers, Audience continued from page 42*

On behalf of the entire planning committee, I want to invite you to attend the *2012 PDA Annual Meeting*. We are very excited about the conference and we are certain you will be too. Come join your colleagues and industry leaders from around the world in the pharmaceutical and biopharmaceutical industry. For more information or to register, visit [www.pda.org/annual2012](http://www.pda.org/annual2012). 🇺🇸

# Universe of Pre-Filled Syringes Expands to 500 Participants

Basel, Switzerland • Nov. 7-11 • [europe.pda.org/prefilled2011](http://europe.pda.org/prefilled2011)

Conference chair Joerg Sielemann, F. Hoffmann-La Roche

As project manager for combination products at Roche, I have to deal with biotech requirements as well as with technical challenges of medical devices which end in high-value products.

This year's PDA *Universe of Pre-Filled Syringes and Injection Devices* focuses on device usability and compliance. The conference covers a broad range of topics including overviews and focus sessions.

Topics covered are on application systems; marketing, business development; new technologies; materials; usability and convenience of application

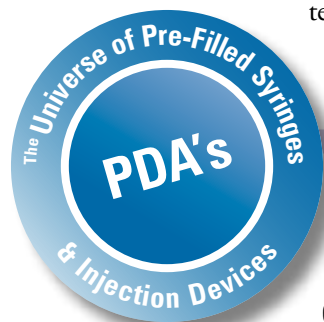
systems; safety aspects of syringes; and development and manufacturing, testing of syringes and devices. Case studies from pharmaceutical companies and suppliers will also be presented.

Please note this is the biggest conference on this topic, with about 500 participants and 80 exhibitors. It is a communication platform for experts from the pharmaceutical industries and related supplier companies dealing with development and manufacturing of application systems. In addition, there will be a pre-conference workshop dealing with the latest issues on glass containers, like defects, breakage and delamination. Test methods and new pro-

cess handlings will be discussed between suppliers and representatives from the pharmaceutical industry.

Following the main conference several training courses are offered, including one offering hands-on lessons regarding syringe processing, e.g., to siliconize syringes, fill and set stoppers. In addition there are many opportunities to network like the welcome party and the gala event in a museum.

Please join this ideal opportunity to get an update on current developments. I am looking forward to welcoming you in Basel. ☺



## Future of Pharma Glass Topic of 1-day Workshop

Basel, Switzerland • Nov. 7 • [europe.pda.org/prefilled2011](http://europe.pda.org/prefilled2011)

Conference chair Thomas Schoenknecht, Schott

On November 7, the PDA is hosting a special workshop focusing on current trends and issues associated with glass as container material for parenteral's and drug delivery systems.

Glass is the dominant container material in modern parenteral packing offerings, however over the last years increasing drug and drug delivery system requirements challenged the existing standards and common market offerings for Ampoules, vials, cartridges and especially syringes. Glass container quality issues resulting in product recalls have further sensitized the regulatory agencies and drives significant quality improvements in the glass industry.

The workshop will address by short

presentations from industry leaders followed by a panel discussion how the industry is addressing the concerns on glass stability and glass container drug compatibility by case studies addressing the following topics:

- Cosmetic quality improvements by improvements in glass handling during container production and fill&finish
- Chemical durability of Glass: Delamination and other Quality aspects, methods for characterization
- Mechanical properties, scratches, breakability and test methods
- Adaptation of containers to the design space of modern and future drug delivery systems
- Drug product/container compatibil-

ity issues related to extractables and leachables, siliconization, and physical requirements of drug delivery systems

This workshop should prepare the groundwork for the "Universe of Prefilled Syringes and injection Devices" conference, where industrial experts will discuss the latest trends in modern drug delivery.

More than 80 exhibitors will show their services and products related to the parenteral drug delivery universe, from contract manufacturing over containers, closures, accessories, labels and devices. With these experts at place, the trends for the future of glass as primary container material can be clearly explored.

I look forward to welcoming you at the workshop and the conference in Basel. ☺



*PDA Welcoming Party*

## The Universe of Pre-filled Syringes and Injection Devices



# Join us at the Top of Basel

**7 November 2011, 19:00-23:00 Bar Rouge, Messeplatz 10, 4058 Basel, 31st Floor of Switzerland's Highest Building.** Prior to the start of the "2011 PDA Europe Conference The Universe of Pre-filled Syringes and Injection Devices".

Please let us know if you are joining us for the music, drinks, a first class swiss food and a chance to chat and relax. **Please register easily online or by email by 28 October.**

<https://europe.pda.org/Prefilled2011>

7 November 2011  
from 19:00-23:00  
at the Bar Rouge,  
Messeturm Basel

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CONFERENCE 8-9 Nov | EXHIBITION 7-11 Nov | WORKSHOP 7 Nov | TRAINING COURSES 10-11 Nov

7-11 November 2011 | Congress Center Basel | Switzerland



# SUS Workshop Investigates the Importance of Pharma Apps

Uppsala, Sweden • November 29-30 • [europe.pda.org/singleuse2011](http://europe.pda.org/singleuse2011)

Stephen Brown, Vivalis

From their beginnings more than 25 years ago, single-use systems (SUS) have evolved to become a hot topic within the biopharmaceutical industry. The technology has its roots in filtration technology and blood containers, moving through simple, small scale culture systems such as roller bottles and the use of mobile storage systems. The growth in interest in SUS has been phenomenal during the last 10 years, and this technology can be seen as a major innovative growth area for the start of the 21<sup>st</sup> century. The technology has developed rapidly, and it's now feasible to exploit single-use technology for many pharmaceutical processes for drug substance and drug product manufacturing with biologics and small molecules. Suppliers have responded to the market and end-user demand, improving their capabilities, technology offering and technical support to end-users.

Advantages frequently attributed to the deployment of SUS over classical stainless steel systems (called multiple-use systems or MUS) include improved flexibility, cost reduction and accelerated operations i.e., faster time to market. But how does this work in practice? As for all new manufacturing innovations, the early phases of their developmental lifecycle can be more or less difficult and it frequently takes a consensus position between industry enablers—suppliers, end users and regulators in order to help consolidate a new technology's position. Over the last three years there have been a number of initiatives from organizations with interests in the field, such as PDA, ISPE, BPSA, ASME and ASTM, to construct guidance accommodating the practical needs around today's regulatory paradigm, GMP, QbD and QRM.

PDA's Single Use Systems Task Force is in the final stages of preparing a technical report on this subject. At a June workshop in Bethesda, Md., PDA gave

participants an opportunity to meet with the task force in order to review the technical report, with publication planned for the end of 2011. Chaired by **Robert Repetto**, Director, Strategy and External Affairs, Pfizer, and **Morten Munk**, Vice President, CMC Biologics, PDA's Single Use Systems Task Force members include a representative panel of industry enablers who have helped to provide a balanced, well-vetted and consensus driven viewpoint. The philosophical basis of approach is based on QbD principles with a detailed science and technology driven look at manufacturing strategies, technologies and system integration, business drivers, qualification and implementation.

Guided by the technical report, PDA is hosting a two day workshop on *Single Use Systems for Pharmaceutical Applications* in downtown Uppsala, Sweden on November 29-30.

On day one, the workshop will provide an overview of the technical report followed by **Tor Gråberg**, Chairman, PIC/S and Chief Pharmaceutical Inspector, Medical Products Agency, who will give a regulator's perspective. These sessions will prepare the ground for a Q&A session at the end of the day. To round off day one, delegates will benefit from a series of case studies covering the manufacture and supplier qualification of SUS and end user perspectives on development, scale-up and manufacturing with SUS.


Day two will be held at the GE Healthcare facility in Uppsala where delegates will benefit from a site visit and an overview of important issues such as Leachables & Extractables biocompatibility and other SUS in-process controls such as bioburden, particulates and leak testing. A CMO perspective on the ready to process system and an environmental study will equally be reviewed (more

on this below). The day will be finalized with practical hands-on sessions in small groups with single use bioprocessing equipment and a look at the economic considerations for SUS.

The environmental study at the facility may be of particular interest. The presentation (1) will describe a recently completed cradle-to-grave study comparing SUS and MUS for the production of monoclonal antibodies. The study considers the full process train required to produce monoclonal antibodies at 100L, 500L and 2000L scales. The scales were chosen to reflect the clinical phase, the scale-up phase and the final production phase. The two process approaches were compared using environmental lifecycle assessment, a systematic methodology for evaluating environmental impacts across the entire lifecycle of a product or process from raw material extraction and refining through manufacturing, distribution, use, and ultimate disposal or recycling. Process data were derived in collaboration with BioPharm Services. The study results show that, for the conditions explored in this study, the single-use process technology exhibits lower environmental impact in 10 of the 11 environmental impact categories studied at the 500L and 2000L production scales, and in all 11 environmental impact categories at the 100L scale.

If you are already working with SUS or are considering investing in this technology, then this workshop is a must for you!

## References

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*The Parenteral Drug Association presents...*



# 2011 PDA Europe Workshop on Single-Use-Systems for Pharmaceutical Applications

The workshop addresses the vital role that Single-Use-Systems play in pharmaceutical development and manufacturing. Guided by the PDA Technical Report learn the advantages, disadvantages and when to use Single-Use-Systems. Benefit from applicable case studies, discussions with regulators and a tour of the GE Healthcare manufacturing facility for Single-Use-Systems.



**29-30 November 2011**  
Uppsala, Sweden



WORKSHOP 29-30 November | EXHIBITION 29-30 November

<https://europe.pda.org/SingleUse2011>

The Parenteral Drug Association presents...



# 2011 | 2012 PDA Europe Upcoming Activities and Events

29-30 November	PDA Europe Workshop on Single Use-Systems	Workshop, Exhibition	Uppsala, Sweden
6-7 December	Modern Biopharmaceutical Manufacturing	Conference, Exhibition, Training Courses	Bordeaux, France
7-8 February	Clinical Trial Materials	Conference, Exhibition	Basel, Switzerland
28 -29 February	Microbiology/Endotoxins/RMM	Conference, Exhibition, Training Course	Berlin, Germany
6-7 March	QbD: Impact on Analytics	Workshop, Exhibition	Liverpool, UK
13-16 March	Parenteral Packaging	Conference, Exhibition, Training Course	Berlin, Germany
8-9 May	PDA/EMA Joint Conference	Conference, Exhibition, Workshop, Training Course	Munich/Frankfurt, Germany
5-6 June	Advanced Therapy Medicinal Products	Workshop, Exhibition	Lisbon, Portugal
12-13 June	Monoclonal Antibodies	Workshop, Exhibition	Basel, Switzerland
25-26 September	Pharmaceutical Cold Chain Management & Good Distribution Practice	Conference, Exhibition, Training Course	Berlin, Germany
9-10 October	Visual Inspection	Conference, Exhibition, Training Course	Berlin, Germany
30-31 October	Pharmaceutical Freeze Drying Technology	Conference, Exhibition, Training Course	to be announced
6-7 November	Parenterals 2012 Integrating Process, Technology and Regulation	Conference, Exhibition, Training Course	Berlin, Germany
20-21 November	Outsourcing/Supply Chain	Conference, Exhibition	Amsterdam, The Netherlands
4-5 December	Modern Biopharmaceutical Manufacturing	Conference, Exhibition, Training Course	Lyon, France

For latest info: <https://europe.pda.org>

Subject to change

Shortlist 2011-08-29

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<https://europe.pda.org>

## Cheryl Custard, Sanofi Pasteur

As a TRI Instructor for the past 10 years, **Cheryl Custard** has developed course material for the Aseptic Technique and Qualification segment taught as part of the PDA's two-week Aseptic Processing Training Program. She makes sure the course covers global as well as local regulatory requirements. She also ensures the content of the course includes method, concept, regulatory and hands-on training to challenge the trainee's aseptic processing skills in a controlled/training area.

**Course that you teach for PDA:** Aseptic Processing Training Program

**How long have you been an instructor for PDA?** 10 years

**What are the challenges that this course identifies and offers solutions to?** Other training companies can tell you the regulatory rules, but few can tell you how to apply them. We [the PDA] teach you how to apply them.

**What makes this course different than others which may be out there?** This is a hands-on-application course. Also, it is offered by PDA. PDA is recognized by reputable companies in the industry as a training institute that provides quality training by reputable instructors.

**Why should people attend this course over others?** It is a PDA course which provides a hands-on-approach. You just can't get the same quality elsewhere.

**What would you say to people considering taking a PDA course?** Take them. You are in contact with industry leaders who understand and evolve policies and try to implement them. Other companies preach policies, PDA both influences and interprets policies and standards. 🍷



## TRI Offers Courses Based on Technical Reports

**James Wamsley, PDA**

PDA's Training and Research Institute (PDA TRI) has been offering and running courses for almost 15 years, and we continue to introduce new courses to help you advance your career and help your company. This fall, TRI will be taking things to another level when we introduce training courses on recently published technical reports.

PDA was founded with the mission to develop scientifically sound, practical technical information and resources to advance science and regulation for the pharmaceutical and biopharmaceutical industry through the expertise of our global membership. One of the primary ways PDA has accomplished this mission over the past 65 years is to develop technical reports. PDA's technical reports cover a wide variety of subjects relating to pharmaceutical production, validation and quality assurance. These global consensus documents are prepared by member-

driven task forces comprised of content experts including industry, regulatory and academic scientists and engineers.

Once the task force responsible for developing and writing a technical report has finished the document, they will now also develop a training course for PDA TRI.

These courses will allow students to get hands-on training directly from the experts who developed the Technical Report! These documents have been widely used by the pharmaceutical and biopharmaceutical industries for decades to help ensure the quality of products being produced. In the past, when a technical report was released you were left to decipher the information contained in the report for yourself. Now you can come to a class to learn how to implement these reports into your processes.

TRI will be offering the first two of these courses in November. The first, "Prepara-

tion of Virus Spikes Used for Virus Clearance Studies" will be offered November 7-8 in Bethesda, Md. This lecture- and lab-based class will provide an overview of *PDA's Technical Report No. 47: Preparation of Virus Spikes Used for Virus Clearance Studies*. This document is the first to provide practical advice and recommendations regarding preparation and quality control of these critical validation tools. In addition to a lecture component covering the entire technical report, the course has a lab-based component where participants will learn basic techniques for virus sample characterization. The objective is to understand quality attributes that need to be tested and controlled in virus spikes so that they can be used in representative scale down validation studies.

This class will teach participants principles and practical applications for preparation and testing of high quality virus spikes. Scale down unit operations need to be



representative of large scale when validating an industrial bioprocess. It is critical to understand and control virus spike quality attributes to ensure that they do not perturb unit operation performance during these validation studies, otherwise the study won't be representative of large scale.

The class will be taught by two instructors. The first instructor, **Kurt Brorson**, PhD, is a staff scientist in CDER's Division of Monoclonal Antibodies, Office of Biotech Products, U. S. Food and Drug Administration. In addition to review, inspection, training and policy activities, he conducts research on viral safety issues associated with biotechnology products. He has won numerous internal awards from FDA, CBER and CDER and is the author of more than 55 scientific journal articles and book chapters. Kurt was also a member of the task force that produced the technical report this course is based on.

viral assay development, and virus filter performance studies. Lute was an active participant of the PDA Virus Filter Task Force responsible for standardizing the nomenclature of both large and small pore size virus filters, performing much of the lab based development work. He also has won several internal awards from the FDA and is an author on more than 20 scientific articles and book chapters.

TRI will be offering a second course, "Validation of Biotechnology-related Cleaning Processes" November 8-10 in Bethesda, Md. This course is a biotechnology-focused modification of the general laboratory cleaning validation course. It includes the lab elements of the standard course modified to focus specifically on issues for biotechnology manufacture. The lecture elements of the course will review all sections of *PDA Technical Report No. 49: Points to Consider for Biotechnology Cleaning Validation*.

These labs demonstrate the application of current cleaning principles to modern pharmaceutical equipment. The different elements of the hands-on aspect of the course include: spray ball coverage testing (riboflavin), visual detection, swab recovery, cycle development – cleaning agent concentration determination, cycle development – CIP cycle exposure time determination, cycle development – CIP cycle rinse time determination, manual cleaning process validation and CIP process validation.

The instructor, **Destin LeBlanc**, is a Consultant for Cleaning Validation Technologies. He recently retired as Vice President of Technical Support for STERIS Corporation. He had been with STERIS for over 20 years, primarily in product development and technical service for cleaning and antimicrobial applications. LeBlanc has lectured on issues related to contamination control internationally, and has written widely on cleaning validation issues. He is the author of the recent book *Validated Cleaning Technologies for Pharmaceutical Manufacturing*. He is a member of the faculty at the PDA Training and Research Institute.

For more information on the above courses and to register, please visit [www.pda.org/courses](http://www.pda.org/courses).

Be on the lookout in 2012 for more TRI courses based on PDA Technical Reports. TRI will develop new courses based on technical reports in the coming years. 🌐

## *Be on the lookout in 2012 for more TRI courses based on PDA Technical Reports*

The second instructor, **Scott Lute**, has been with the FDA since 2002 in the Bioprocessing laboratory run by Kurt Brorson. Over the past 9 years he has extensively studied the viral safety of downstream processing associated with monoclonal antibody manufacturing, including: column resin lifetime studies, virus characterization studies, Q-PCR

This course is ideal for anyone involved in cleaning validation for biotechnology manufacture. This course provides attendees with a complete, hands-on cleaning validation education program covering both automated (CIP) and manual cleaning for biotech manufacture.

Extensive use of wet labs will help to emphasize the principles learned in the lec-

### *Personalized Medicines continued from page 30*

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# Parenteral Drug Association Training and Research Institute (PDA TRI)

## Upcoming Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

### October 2011



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2011 PDA Visual Inspection Forum & TRI Course

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October 5-6, 2011 | Bethesda, Maryland | [www.pda.org/visualinspection2011](http://www.pda.org/visualinspection2011)

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Course Series:

- Environmental Control and Monitoring for Regulatory Compliance - *New Course* (October 20)
- Rapid Microbiological Methods: Overview of Technologies, Validation Strategies, Regulatory Opportunities and Return on Investment (October 20)
- Auditing for Microbiological Aspects of Pharmaceutical and Biopharmaceutical Manufacturing (October 21)
- Microbiological Issues in Non-Sterile Manufacturing (October 21)

#### PDA TRI Filtration Week

October 24-28, 2011 | Bethesda, Maryland | [www.pda.org/filtrationweek](http://www.pda.org/filtrationweek)

- Filters and Filtration in the Biopharmaceutical Industry - Basics Course (October 24-25)
-  Filters and Filtration in the Biopharmaceutical Industry - Advanced Course (October 26-28)

Save 10% when you register for both courses!

### November 2011

#### Quality and Compliance Management for Virtual Companies - *New Course*

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#### Process Validation for Pharmaceuticals - Current and Future Trends

November 3, 2011 | Bethesda, Maryland | [www.pda.org/processvalidation](http://www.pda.org/processvalidation)



#### Preparation of Virus Spikes Used for Virus Clearance Studies - *New Course*

November 7-8, 2011 | Bethesda, Maryland | [www.pda.org/viruspikes](http://www.pda.org/viruspikes)



#### Validation of Biotechnology-related Cleaning Processes - *New Course*

November 8-10, 2011 | Bethesda, Maryland | [www.pda.org/validationbiotech](http://www.pda.org/validationbiotech)

### December 2011



#### Quality Systems for Aseptic Processing - *New Course*

December 5-9, 2011 | Bethesda, Maryland | [www.pda.org/qualitysystems](http://www.pda.org/qualitysystems)



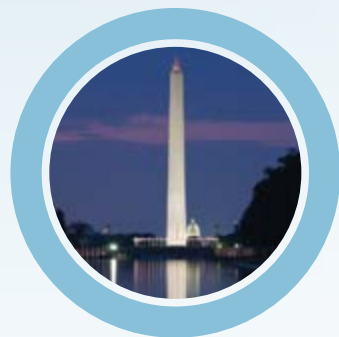
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The PDA Training and Research Institute is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education.

All 2011 Aseptic Processing Training Program Sessions are sold out.  
The 2012 schedule is available now! Visit [www.pda.org/2012aseptic](http://www.pda.org/2012aseptic).

For more information on these and other upcoming PDA TRI courses please visit [www.pda.org/courses](http://www.pda.org/courses)



## Editor's Message

### The Tough Decisions of an Editor!


Part of the demands of working in the pharmaceutical industry is the need to make extremely tough decisions that impact both the health of patients and the bottom line of companies. When should a batch be recalled? Destroyed? Reprocessed (can it be)? These kinds of decisions are made on a routine basis. PDA members are the best when it comes to making these decisions!

Contrast that with the life of an editor. We routinely face many tough decisions, though they hardly ever rise—well, never, ever rise to the level of life and death, though they can impact our company's bottom line. What kind of decisions do we make? Any attentive reader will see that the last few issues have been larger than usual. Well, with interest in publishing and advertising in the Letter sharply rising in recent years, we frequently must decide between publishing all the great content we get or sticking to our page count criteria (52 pages for regular issues and up to 72 pages for our two double issues). We haven't had a 52-page issue in quite a while, and the July/August issue topped out at 80 pages. Clearly, we've decided that good content and increased advertising is too hard to pass up.

However, in both this and the last issue, we have attempted to restrict the page counts to more manageable and readable levels. As a result, readers might have noticed some of our regular content—Chapter Contacts, Volunteer Spotlights, New Members, Tools for Success, Regulatory Briefs—has been missing. Are these the right decisions? Is the content we are publishing in place of those regular pieces more impactful/interesting? We think so, and thus the decisions made.

Another challenge we face is when to blend common terms into one word (called a “portmanteau”). For example, several years ago, the *PDA Letter* stopped hyphenating “email.” We also joined “web” and “site.” Usually, we like to wait until the Merriam-Webster Dictionary, the Associated Press or the New York Times says it is okay (makes the same decision), but in those cases, our impatience was too great and we took the plunge early. Other phrases are harder. Is it “clean room” or “cleanroom”? How about “health care” versus “healthcare”? Another sticky wicket is “life cycle” as opposed to “lifecycle.”

I'm happy to announce that we've made an internal decision on each. From now on, if you see a space in “cleanroom,” “healthcare” and “lifecycle,” it is an error. We are now choosing to close these words permanently, at least in the *PDA Letter*. We are very confident in our decision to close “cleanroom,” as a quick search of the *PDA Journal of Pharmaceutical Science and Technology* revealed that the closed version is a term of art in the pharmaceutical industry, thus our ability to eschew the guidance of the Dictionary, the AP and the snooty NY Times (which has the nerve to even use quotes around “clean”: “...a future Dow ‘clean’ room...”). Our decision on “lifecycle” was trickier, as it is not a portmanteau yet in the three aforementioned guides, but is now officially closed in the ICH guidelines Q8, Q9, Q10 and Q11. Writing about Q11 in this issue raised my awareness and led to our decision to once and for all close the phrase.

“Healthcare” is much trickier, as the Dictionary, AP and NYT keeps “health” and “care” decidedly separate, and it is general, not technical phrase. Deferring to those sources' style would be the easy thing to do. But, is it the right thing? The U.S. government cannot even decide! Searching the portmanteau version, you will find it all over the U.S. FDA's website. However, you will find the opened phrase as well. Same with other government websites and such venerable industry sources as the Pink Sheet, Gray Sheet, etc. However, based on our “Google” test—480 million hits when searching “healthcare” versus only 99.6 million for “health care”—we feel that the time has come for joining the phrase, at least in the *PDA Letter!* 

# PDA Letter

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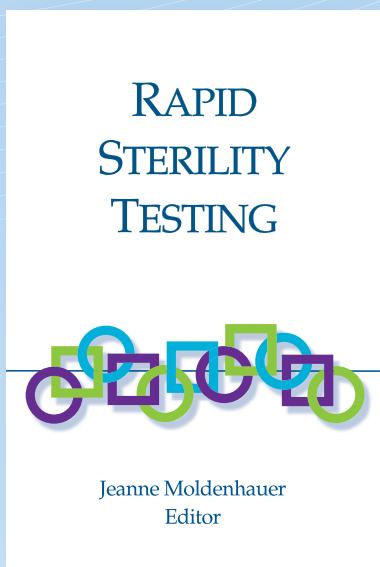
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# New Release at the PDA Bookstore



## Rapid Sterility Testing

*Edited by Jeanne Moldenhauer*

To date, regulatory approval has not been gained to support programs of parametric release for aseptically filled products. As a result, many companies are looking towards rapid sterility testing methods to reduce the release time for aseptically-filled products.

Editor Jeanne Moldenhauer explores the history, regulatory requirements and allowances for gaining approval of rapid sterility test methods. Compendial requirements for validation and implementation of these methods in the United States and Europe are also discussed. In addition, subject matter experts provide information on the types of methods that can be considered for aseptic sterility testing and discuss issues such as the statistical methods used to validate these methods, especially since many of the new technologies are superior to the conventional methods. There are a substantial number of case studies describing how various companies have approached selecting, validating and implementing new methodologies for sterility testing at their site.

Section chapters include:

- Regulatory Expectations for Rapid Sterility Tests
- Compendial Expectations
- General Information
- User Case Studies

For more information please visit [www.pda.org/rapidsterilitytesting](http://www.pda.org/rapidsterilitytesting)

### The PDA Bookstore's September Top 5 Best Sellers



**1** GMP in Practice:  
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**3** Thermal  
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Sterilization  
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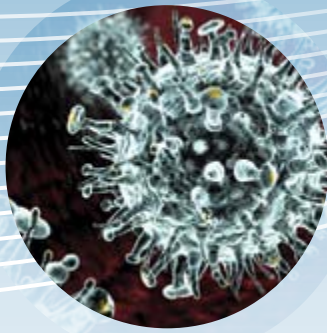
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Handbook, Volume V  
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**5** PDA Technical  
Report No. 49,  
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*The Parenteral Drug Association Presents...*

# PDA/FDA Adventitious Agents and Novel Cell Substrates: Emerging Technologies and New Challenges

**November 2-4, 2011**

EXHIBITION: November 2-3

Hilton Hotel Rockville | Rockville, Maryland

This event is being organized in response to the need to evaluate the benefits and potential applications of emerging broad virus detection technologies for safety testing, characterization of biological products and to facilitate safety testing of novel cell substrates.

The *PDA/FDA Adventitious Agents and Novel Cell Substrates: Emerging Technologies and New Challenges* event will provide an engaging forum for all participants to discuss and integrate current strategies for controlling virus contamination and enhancing product safety.

Plenary sessions at this year's conference include:

- Keynote Presentation: Risks Associated with Cell Substrates and Other Biological Materials and Product Safety
- Adventitious Agent Testing and Emerging Methods Part I and Part II
- Technologies and Application for Evaluation of Biological Materials Part I and Part II
- Panel Discussion – Technical Challenges of New Methods
- Keynote Presentation: Evolution of Mutualism Between Retrotransposons and Retroviruses, and the Cell
- Insect, Avian and Mammalian Cell Substrates Part I and Part II
- Potential Safety and Quality Issues Related to Plants and Plant-based Products
- Adventitious Agents and Raw Materials Part I and Part II
- Two Panel Discussions

**Register By October 17 -**  
The Last Registration Savings Deadline!

**For details and to register, visit**  
[www.pda.org/adventitious2011](http://www.pda.org/adventitious2011)

*"This workshop was very useful...I highly appreciated the quality of the talks and speakers. Sharing experience and views from manufacturers and regulators is major."*  
Past Attendee from  
Sanofi Pasteur