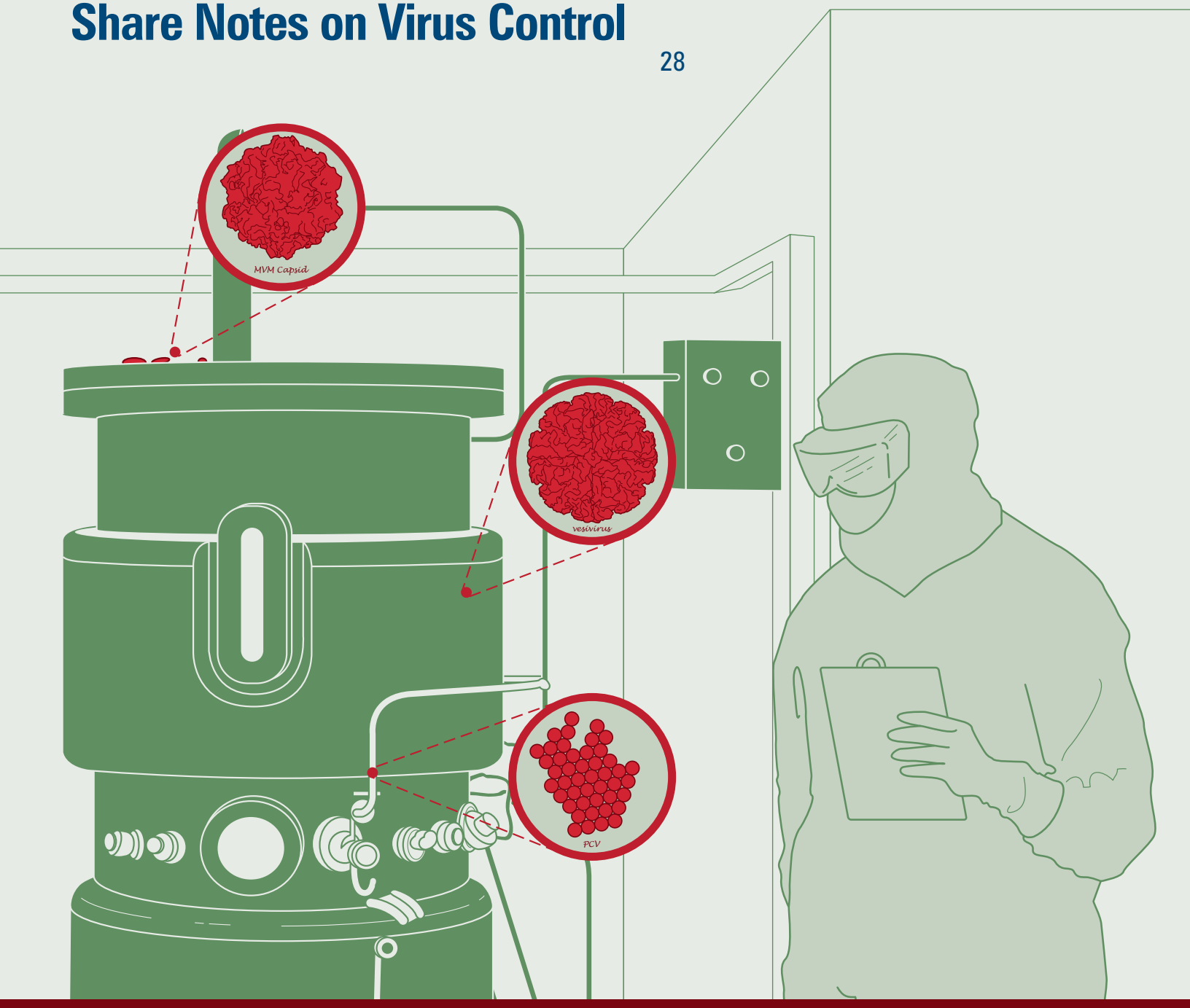
People • Science • Regulation

PDA Letter

Volume XLVII • Issue #2 www.pda.org/pdaletter February 2011

U.S. FDA, Industry Meet to Share Notes on Virus Control

28



2011 PDA Europe
Conference, Exhibition,
Training Courses

Parenteral Packaging

21-23 March 2011
Berlin, Germany

Glass has been the traditional container material for pharmaceuticals and the expansion of proteins and other biotech products is giving continued life to this material and its ancillary parts like stoppers, caps and other container closure system components. Recent action by regulatory bodies has highlighted the importance of securing quality of container closure systems. This conference will discuss key topics including:

- Quality of components
- Manufacturing issues
- Container Closure System quality
- Critical Quality Attributes and testing
- Safety evaluation
- Change Management
- Extractables/Leachables
- Regulatory expectations

Meet regulators, industry experts and suppliers to find out what challenges you will face.

CONFERENCE, EXHIBITION TRAINING COURSES

https://europe.pda.org/Parenteral2011

PDA's 6th Annual Global Conference on Pharmaceutical Microbiology

October 17-19, 2011 | Bethesda, Maryland

Call for Abstracts/Case Studies

The Program Planning Committee for this conference invites you to submit a scientific abstract for presentation at *PDA's 6th Annual Global Conference on Pharmaceutical Microbiology*. The theme of this year's conference is: **Challenges Facing Pharmaceutical Microbiology in the 21st Century**. Suggested topics include, but are not limited to:

Case studies, such as:

- Satisfying Global Regulatory Requirements
- Meeting Pharmacopeial Expectations
- Quality Risk Assessment/Quality by Design (Microbial Control)
- Application of Modern Microbial Methods in Manufacturing Settings

- Trends in Environmental Monitoring
  - Sampling, Detection and Data Analysis Methods
  - Scientific Principles on Recovery Efficiency
  - Viable but Non-culturable Organisms
- Setting Alert/Action Limits
- Advancements and New Technologies
  - Bio-Sensors, Bio Chips and Micro Arrays
  - Nanotechnology
  - Metagenomics
  - Alternative Microbiological Methods
  - Use of Statistics in Qualification of New Methods
- Microbial Identification in the Pharmaceutical Industry
- Advances in Aseptic Processing
- Microbial Control Environments
  - Biofilms
  - Microbiological Aspects of Cleaning Validation
  - Sterilization, Disinfection and Preservation
  - Biological Indicators
- Biotechnology Manufacturing
  - Upstream (Culture Control Issues)
  - Downstream (Purification Processes)
  - Regulatory Expectations
- Recent Regulatory Issues in Non-pending Cases (FDA Enforcement Officers/Auditors)
  - Compliance
  - Review
  - Inspection
  - Global
  - Guidelines for Improving a Sterility Assurance Submission
- Sterile and Non-sterile Products
  - Viable and Non-viable Monitoring
  - Microbial Challenges
  - Objectionable Organisms
  - Quality of Product Intermediate Steps
  - Predictive Stability
  - Parametric Release
- Supply Chain Issues
  - Raw Materials
  - Active Ingredients
  - Transportation/Shipping
- Medical Devices/Combination Products
  - Container Closure Systems
- Media Fill Design
- Product and/or Labeling Attributes Potentially Impacting Sterility Assurance
- Investigation on Microbial Data Deviations
- Globalization and Harmonization
  - Challenges and Lessons Learned
- Lean Labs/Future Labs

Abstracts must be received by March 4, 2011 for consideration.

Visit **www.pda.org/2011microbiologycfp** to submit an abstract.

Case studies are particularly desired. Commercial abstracts featuring promotion of products and services will not be considered. After June 1, 2011, you will be advised in writing of the status of your abstract. PDA will provide one complimentary registration per podium presentation. Additional presenters and poster presenters are required to pay appropriate conference registration fees. All presenters are responsible for their own travel and lodging, with the exception of health authority speakers.

QUESTIONS?

Contact PDA:
Leon D. Lewis, Assistant Manager, Programs and Web Seminars
Tel: +1 (301) 656-5900 ext. 149
Fax: +1 (301) 986-0296
E-mail: lewis@pda.org

ALL ABSTRACTS WILL BE REVIEWED

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

ATTENTION EXHIBITORS

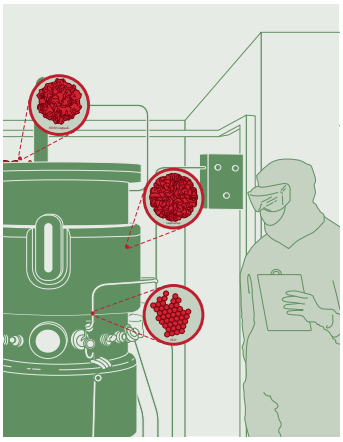
PDA is seeking vendors who provide excellent products/services in support of this conference. Space is limited and is on a first-come, first-serve basis. To reserve your space, please contact David Hall at hall@pda.org or +1 (301) 656-5900 ext.160

www.pda.org/2011microbiology

PDA Letter

Volume XLVII • Issue #2 www.pda.org/pdaletter

Cover



Cover Art Illustrated by Katja Yount

Departments

News & Notes

People

Science

Regulation

Programs & Meetings — North America

Programs & Meetings — Europe

TRI — Education

Contents

Contribute to Upcoming *PDA Letters*

We are always looking for articles on the latest regulatory developments, science and technology trends, and other topics important to our community. For the May issue, we are looking for articles on supply chain, for June, internal investigations, and for the July/August issue, aseptic processing. If you want to contribute, contact **Emily Hough** at hough@pda.org.

PDA Initiates Rapid Response to Tribromanisole Contamination

New Task Force Seeks to Define Mitigation Strategies

Tribromanisole (TBA) contamination has already affected multiple firms. As acknowledged by the U.S. FDA's **Rick Friedman**, issues related to firms' management of their supply chains, including pallets, continue to emerge as a threat to quality and consistency of both prescription and OTC products.

In direct response to this emerging threat, PDA has formed a Task Force of experts to develop a comprehensive technical report that will address the following areas:

- Benchmarking: TBA in the Food and Beverage Industry and Knowledge Gap Analysis
- Supply Chain: Pharmaceutical Manufacturing and Distribution Process Flow Considerations
- Analytical and Standards: Analytical methods and standards for TBA testing
- Toxicology and Safety of TBA
- Risk Analysis
- Mitigation of TBA

Currently, the following experts are on the Task Force:

Brad Barker, GlaxoSmithKline
William Beierschmitt, Pfizer
Jeff Burris, Rexam Healthcare
William Callahan, Depomed
John Clark, Risk Benefits
Anthony Cundell, Merck
James Egan, GlaxoSmithKline
Jonine Greyling, Johnson & Johnson
Nick Grisham, Schering Ploug
Warren Horton, Patheon
Rachel Humphreys, Perrigo
Nirdosh Jagota, Genentech
Robert Johnson, GlaxoSmithKline
William "Al" Kentrup, Sandoz
Marc Lemieux, Amcor
Rich Levy, PDA
Janet Lim, Johnson & Johnson
Mark Paviglianiti, Merck
William Powers, Johnson & Johnson
Rachael Roehrig, CHPA Consumer Healthcare
Douglas Ross, Pfizer
Anil Sawant, Johnson & Johnson Consumer Companies
Megan Sewell, Merck
Edward Smith, Packaging Science Resources
Kathy Stetson, GlaxoSmithKline
Dirk Stevens, Covidien
James Strickland, Pfizer
Eric Thostesen, GPSG (Johnson & Johnson)
Christine Vietri, AstraZeneca
Gary Wilson, West Pharma

The following is an interview the *PDA Letter* conducted with the Task Force.

PDA Letter: The issue of tribromoanisole (TBA) is a relatively new one to pharmaceuticals, but the wine and food industry has dealt with this for a while. Why is this issue just starting to crop up in pharmaceuticals? Can't we just borrow the solutions that the food and wine industry have taken by barring pallets treated with TBA used with their products?

Task Force Members: Although the issue of TBA taints is relatively new to the pharmaceutical industry, an organohalogen taint, trichloroanisole, was reported in associattion with compressed tablets by Upjohn in the early 1990's. Organohalogen taints were first reported in Dutch boiler chickens exposed to trichlorophenol-treated wood chips used as bedding materials 45 years ago. Numerous reports can be found in literature about tainted food and beverages. Perhaps the most well-known is the so-called corking of fine wines mainly due to organohalogen contamination of corks and wooden barrels.

Numerous risk mitigations have been implemented in the food and beverage industry and we can certainly learn from these industries. The pharmaceutical industry may need to customize some solutions to fit our supply chain and product differences. Banning the use of TBP-treated pallets would be helpful but may be ineffective then there are in excess of 1.5 trillion pallets in the supply chain and lumber companies, wholesalers and pallet manufacturers may be unaware of the consequences of TBP treatment or have economic reasons to not restraint from using TBP treatment

PDA Letter: Do we know exactly what is causing this problem?

Task Force Members: The task force members believe that a number of factors occurred in the pharmaceutical supply chain to cause product recalls for TBA taints by three pharmaceutical companies. Apparently green lumber in Latin America was treated with tribromophenol (TBP) to prevent pest infestation and mold discoloration of the wood. Wooden pallets were constructed from this lumber and the pallets where used to transport packaging components to pharmaceutical plants in Puerto Rico. Fungal growth on the wooden pallets resulted in the biomethylation of TBP to TBA. The moisture content of wood must exceed 13% to support fungal growth so insufficiently dried lumber or pallets exposed to relative humidity exceeding 70% will be susceptible to fungal growth. Poor ventilation of warehouses may have contributed to the fungal growth. TBA, a highly volatile chemical, is detected at part per trillion concentrations as a moldy, musty odor, was absorbed into the walls of high density polyethylene containers and nauseated people when they open containers of consumer healthcare products.

PDA Letter: Why and how are pallets treated?

Task Force Members: Due to the International Plant Protection Convention, most pallets shipped across national borders must be made of materials that are incapable of being a carrier of invasive insects and plant diseases. The voluntary standards for pallets used in international trade are specified in the International

Standards for Phytosanitary Measures 15 *Guidelines for Regulating Wood Packaging Material in International Trade*. Pallets used in international commerce are heat treated at 56ºC for at least 30 minutes and fumigated with methyl bromide as specified in the ISPM 15 Guidelines. The wooden pallets that comply with the standard are stamped HT for heat treated or MB for methyl bromide fumigated near the IPPC logo. Many food companies are specifying the use of heat-treated pallets.

PDA Letter: Is the musty odor, which has stood as the number one complaint of TBA contamination, the only symptom of contamination or are their more serious concerns?

Task Force Members: The detection of musty, moldy odors may be subjective and not consistent given the wide range of sensory perception of TBA taints, i.e., there is a 2000–fold difference between individuals' sensory perceptions and products may be tainted unevenly, as well as a dispersal of odor when containers are opened. In fact, the initial investigations of customer complaints because of the odor characterization as musty, moldy appeared to have been focused on the usual suspects, namely fungal contamination of the tablets, which if stored properly would not support microbial growth on tablets due to their low moisture content.

A search of toxicology literature fails to reveal information on the safety of TBA. The material safety data sheets for TBA sold by fine chemical manufacturers address the general safety of the handling of the chemical with standard exposure limits far exceeding that of concentrations associated with TBA taints. No current evidence supports the belief that TBA taints constitute a serious health risk.

PDA Letter: Studies are ongoing to determine to see if there are additional side effect/dangers of TBA. Is TBA a relatively new chemical used to treat pallets? If no, why is more not know about it?

Task Force Members: No, TBP treatment is not new, but the chemical TBP is not registered as a pesticide by the U.S Environmental Protection Agency. Hence, it is illegal to use it to treat pallets in the United States. This is not the case in some Latin American and Asian countries. Lumber and/or pallets from these areas may be TBP treated and pharmaceutical products manufactured in Puerto Rico may be more vulnerable due to proximity to Latin America and the high temperature and humidity of their climate. Although there is very limited information in the public domain about TBA toxicity and safety, there may be data available that is not in the public domain that the task force would like to solicit and evaluate.

PDA Letter: What are the goals of the PDA task force?

Task Force Members: The primary goal of the task force is to issue a PDA Technical Report, an article for the *PDA Journal of Pharmaceutical Science and Technology*, and /or other related documents that addresse the following:

a. Industry benchmarking
b. Analytical method(s) and standard TBA testing
c. A threshold of acceptable TBA level
d. Controls to mitigate TBA buildup and taint

PDA Letter: How will the task force be collecting supportive information and data and how long do you think they will take before a paper/TR is issued?

Task Force Members: If information and data is readily available from companies participating in the task force, it is possible that it can be pooled and analyzed. However, it is likely that further investigation may be required before the task force publishes a comprehensive technical report. If data is not readily available, the task force will conduct benchmarking surveys. The target is to publish a report(s) in May 2011. The target is aggressive, but the nature of the problem, especially, the fact that there may be a latent period between exposure to TBP and manifestation of taint, requires the industry act quickly. Even if we find a perfect solution to the problem, it might be a while before the risk of tainted product moves out of the pharmaceutical supply chain.

PDA Letter: This task force, led by **Anil Sawant**, is set up in five different sections with five different leaders:

Background and Benchmarking led by Section Leader **Tony Cundell**

GDP/Supply Chain led by Section Leader **Jeffrey Burris**

Analytical and Standards led by Section Leader **Robert Alan Johnson**

Toxicology and Safety led by Section Leader **William Powers**

Risk Assessment led by Section Leaders **Jeff Burris, Tony Cundell,** and **William Powers**

How will each of these different sections work together to contribute to the overall cause? Will the section output coalesce into one report or bulletin?

Task Force Members: The sub-teams are meeting weekly to report on their progress. The entire team meets bi-weekly to collaborate on the technical report. It is hoped that using this concurrent approach we will be able to meet the aggressive timeline.

PDA Letter: What can PDA members do to be involved?

Task Force Members: Members can get their company to participate in a bench marketing survey that will be sent out in the middle of February. The recipients of the survey should work within their company to provide a representative response to the task force. When we are close to completion of the working draft, PDA will be asking for additional reviewers to read and comment on the draft. Potential reviewers are welcome to contact PDA to volunteer at this time.

[Editor's Note: To volunteer as a reviewer or to learn more about the task force, contact **Iris Rice**, rice@pda.org.**]**

PARENTERAL DRUG ASSOCIATION TRAINING AND RESEARCH INSTITUTE (PDA TRI)

2011 Aseptic Processing Training Program

2011 Schedule:

Session 2:
Week 1: March 7-11
Week 2: April 4-8

Session 3:
Week 1: May 9-13
Week 2: June 6-10

Session 4:
Week 1: August 22-26
Week 2: September 12-16

Session 5:
Week 1: October 10-14
Week 2: November 14-18

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: (301) 656-5900 | Fax: (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 certification program
- Describe the importance of filter integrity testing when filtering water, gases, or proteinaceous solutions

SPACE IS LIMITED - REGISTER NOW:
www.pdatraining.org/aseptic

Dinner Event Focuses on 21 CFR Part 11

PDA's Southern California Chapter Educates Local Industry Members About U.S. FDA's Motivations

Saeed Tafreshi, Intelitec Corporation

On November 11, the PDA Southern California Chapter held a very successful dinner event on the topic of "FDA's Renewed Scrutiny toward 21 CFR Part 11 Compliance" and discussed what we should all know about upcoming inspections. This topic was chosen by PDA's Southern California Chapter board based on feedback from its members indicating that 21 CFR Part 11 was a hot topic as the U.S. FDA's Center for Drug Evaluation and Research has a new initiative to conduct "tag-along" inspections for compliance with the requirements for electronic records and electronic signatures. It is believed that these inspections will be used to assess our industry's level of understanding and compliance with Part 11 and determine how it can impact the approach in interpretation and enforcement of the related regulation.

The presentation focused on what has motivated FDA's renewed attention on Part 11 and how companies can effectively prepare for inspections. This session included a review of what could be learned from FDA warning letters both before and after the 2003 scope and application guidance. This review identified some common industry misconceptions and vulnerabilities related to the topic, and was followed by discussions on how to apply a common sense, risked-based approach to ensure practical compliance with FDA's core expectations.

Our chosen speaker was **Gordon Richman**, Vice President of Strategic Compliance Consulting and General Counsel of EduQuest. Gordon has a unique background of over 20 years of regulatory, legal and corporate management experience within our industry. This event was sponsored by US Data Management and the exhibitors were Xnergy and Technical Safety Services.

Attendees included more than fifty of our local senior industry management, compliance managers, quality assurance personnel, validation specialists, engineers and independent consultants. PDA's **Hassana Howe**, Manager, Membership Services & Chapters, was our special guest and travelled across the country just for the event. She was a great help in executing the event and in greeting our members. Hassana's presence at the local event was another statement on PDA's commitment to its members through the chapters and also provided an opportunity for helpful discussions about the workings of PDA and its chapters.

The Southern California Chapter was happy after its successful dinner event. (l-r) Saeed Tafreshi, Intelitec Corporation; Bill Nichols (Ret.); Ruchika Raval, Global Biopharmaceutical Regulations; John Holmgren, Allergan; Bonnie Ward, Quality Compliance Partners; Tony Steinberg, Quality Compliance Company; Hassana Howe, PDA; Brian Underhill, BioSPEQ

PDA Tools For Success

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

How to Get the Job You Want

Jean Kelley

Whether you've been out of the employment market for a long time due to child rearing or have been recently laid off, you already know how tough it is to find a job in today's economy. For every job posting there are hundreds of resumes submitted and as many as 30-40 qualified candidates vying for the same position as you. Needless to say, you have to stand out if you want to get your foot in the door.

But standing out will only take you so far these days. You also have to sell yourself—something few people are good at. Sure, they may be able to sell a product or service, but when it comes to selling themselves, many people clam up.

Perhaps it stems from childhood when our parents told us, "It's not nice to brag." Today, you may even hear yourself echoing those same words to your own kids. No wonder so many competent men and women alike sell themselves short on job interviews.

Regardless of your desired industry or position, you simply must promote yourself if you want to get a job. Promoting does not mean exaggerating the facts. It simply means talking about your strengths, competencies and attituds as well as what you can do for the company. Remember, the person interviewing you has something you want…and there is a lot of competition. The more prepared you are for any interview and the more you sell yourself, the better your chances of getting the job.

As you continue to embark on your job search quest, keep the following guidelines in mind so you can promote yourself in the best way possible.

Know What You Want

If you don't know what you want, how can you find it? The floundering that job seekers do in terms of not knowing what they really want to do in life takes them off on some time-consuming tangents. If you don't know what you're good at or what you want to do "when you grow up," then get tested. Many state unemployment offices and colleges offer career testing so you can know what fields might be a good match for you.

If you're one of those people who apply to any job you can find, you're never really going to find what you want. Rather, you have to go with a clear-cut goal of what you're looking for. Think of it like digging for oil. If you know the oil is there and you dig five wells that are shallow, you're probably not going to get to your goal no matter how many holes you dig. But if you take that same energy and dig one really deep well, then you're going to hit black gold.

Fluttering around dilutes your energy. And energy management is so important when looking for a job because job hunting is depleting of your psychic and your physical energy, particularly if you have a family and you're depending on that income.

Build A Resume That Stands Out

No matter what kind of position you're applying for–from entry level to executive level–the resume is important. These days a resume can be either hard copy or electronic. Which you send depends on what the company has asked for in their employment ad. Whether they say to email or mail a resume or to apply online, do exactly as they say. And when you do apply online, be sure you fill out every box and complete every field. Do every single thing the prospective employer asks for. If you don't, you'll get automatically disqualified because the potential employer will think you can't follow directions. In fact, that's the number one first test of many employers–"Do they follow instructions?"

If you're mailing in a resume, pick a white or off-white paper. Unless you're in the arts, don't do anything wild with your resume. Make sure your font choice is readable both on and off screen. Font that is too tiny or too elaborate will not get read. Finally, there is never any excuse for an error on your resume. So if you're not good at proofing, find someone who is… and then find someone else who'll proof it again. You just can't be too cautious.

Know What To Say And What Not Say During an Interview

Being gracious, warm and cordial to the interviewer is great, but being chatty is not acceptable. So when someone asks you a question, answer the question with a brief example of what you're describing, but don't give the person a novela. They

don't want to hear your entire history–just the highlights of your work history. Remember that it's a job interview, not an afternoon tea party.

Whatever you do, never say anything negative about a past employer. It's a kiss of death for an interview. Even if you were fired from a past job and the incident comes up, don't say, "My boss was a jerk and fired me because he didn't know what he was doing. He couldn't lead his way out of a paper bag." Instead, stay as positive and likeable as possible. You could say, "Yes, I got fired. Here's why and here's what I've learned from it."

Realize that in some cases, being likable is more important than qualification. Companies want people who are likable, who get along well with others, who are creative and who can learn fast. Show them that you're that person in everything you say and do.

Don't Take Salary Advice From Family Members And Well-Meaning Friends

Never say to a potential employer, "My husband said I'm worth this much money," or "My mother said I should be making this level of salary." Truth be told, the people who are telling you what you should be paid don't know the market. The bottom line is that you're going to get paid what you're worth in the current marketplace. Unless someone purposefully takes advantage of you (which is not common), then you're going to get paid fairly.

The key is that you need to do some real research on what you're worth. As you do so, take into account your education level, years of experience, industry, size of the company you're interviewing with and even your geographic location. After all, a job for a small company in Yulee, Florida will pay a lot less than that same job for large company in Manhattan.

You can find realistic salary information from local temporary services, job posting boards and even websites like salary.com. Use the information you find out as a starting guide and adjust the figure up or down based on your specific circumstances.

Use The Four Magic Words During The Interview

The four magic words are: "I want the job."

If you've done all your research on the company and you like the person interviewing you and you know you want to work there, then you have to speak up and say so. Don't end the interview by saying, "I think this would be a great place to work. Thanks for the wonderful interview." That's too weak. You have come right out and say, "Thank you for the interview. I want the job. What are the next steps?"

As you do so, leave the door open so you can follow up with them rather than them having to follow up with you. You could say, "I'll follow up with you in a week." Chances are that because they're interviewing many people and are overwhelmed, they'll tell you not to follow up–that they'll take care of it. But follow up anyway. You'll never know what's happening on a job's status unless you follow up with the person.

You're Hired

No one ever said getting job in today's marketplace was easy. But it is doable if you have the right attitude, the right resume and the right goal in mind. So get clear on what you want and take control of your job search. With some patience and a proactive approach, you can find the job of your dreams.

About the Author

Jean Kelley, president and founder of Jean Kelley Leadership Consulting, is the author of Get A Job; Keep A Job. As the sole owner of Jean Kelley Personnel for 25 years, she personally helped more than 20,000 clients enhance their careers. Coupled with her other book, Dear Jean: What They Don't Teach You at the Water Cooler, Jean has positioned herself as America's workplace coach. For more information, please visit www.jeankelley.com.

New Jobs Posted Daily to PDA's Career Center

For a complete list of all job postings please visit www.pda.org/careers.

Latest Hot Job Postings

Perrigo Company, Allegan, Mich.
Procurement Sourcing Manager – Packaging

Merck, West Point, Pa.
Principle Development Engineer

Interested in posting a job? Take advantage of all our career job postings and packages.

Faces and Places: PDA/FDA Adventitious Virus Workshop

Current Regulatory Approaches for Control of Viral Contamination

(l-r) Anthony Lubiniecki, Centocor; Amy Rosenberg, U.S. FDA; Philip Krause, U.S. FDA; Johannes Blümel, Paul-Ehrlich-Institut; Chris Joneckis, U.S. FDA

Review of Viral Contamination and Case Studies

(l-r) Barry Cherney, U.S. FDA; Isabelle Pierard, GlaxoSmithKline; Michael Wiebe, Quantum Consulting; Colette Ranucci, Merck; Nathan Jones, Genzyme

Facility Control and GMP Expectations

(l-r) Patricia Hughes, U.S. FDA; Norbert Hentschel, Boehringer Ingelheim; Jay Eltermann, U.S. FDA; Rick Friedman, U.S. FDA; Ron Taticek, Genentech

Review of Viral Contamination and Case Studies

(l-r) Dominick Vacante, Janssen; Michael Wiebe, Quantum Consulting; Barry Cherney, U.S. FDA; Jim Skrine, Amgen; Mark Moody, Merrimack Pharmaceuticals

Viral Testing: Existing Assays and Emerging Technologies

(l-r) Rangarajan Sampath, Abbott Molecular; Arifa Khan, U.S. FDA; Jens- Peter Gregersen, Novartis Vaccines; Ivar Kljavin, F. Hoffmann-La Roche; David Onions, BioReliance Corporation

Process Design Strategies for Prevention of Viral Contaminations

(l-r) Patrick Swann, U.S. FDA; Robert Kozak, Bayer; Mahmood Farshid, U.S. FDA; Sridhar Pennathur, MedImmune; Robert Kiss, Genentech

Poster Exhibit

Faces and Places: Aseptic Processing Workshop

Innovative Approaches to Sterility Assurance

(l-r) Kristen Evans, Amgen; Neera Jain, Synta Pharmaceuticals; James Agalloco, Agalloco and Associates

Quality Systems

(l-r) Douglas Campbell, U.S. FDA; Randy Hutt, Lachman Consultant Services; Bryan Liptzin, Amgen

Intervention Control

(l-r) Ken Muhvich, Micro-Reliance; Kristen Evans, Amgen; Olivia Henderson, Biogen Idec

Technology

Hal Baseman, ValSource

Process Simulation

Randy Hutt, Lachman Consultant Services

Monitoring/Testing

Ken Muhvich, Micro-Reliance

Please Welcome the Following Industry

Shahid Abdullah, Genvion

Ande Abercrombie, Particle Measuring Systems

Miki Amin, Amin Solutions

Pascal Anger, Sanofi Chimie

Laurent Artaud, Stallergenes

Anne-Lise Bache, Novo Nordisk

Lisa Bahr

Mario Becker, Sartorius Stedim

Kathleen Bellorado, Pfizer

Aditya Bengali, Bristol Myers Squibb

Lisa Blankenheim, Celgene

Luc Boschung, UCB Farchim

Stefan Bracht, Bayer Schering

Christopher Brend, Abbott Labs

Christian Bruell, F. Hoffmann - La Roche

Ian Buckley, Friedrich Sanner

Bernhard Buehler, Optima Group

Charles Calderaro, Genentech

Mark Caswell, Genzyme

Ranela Ceci, National Centre of Drug Control Albania

Fabien Chaussade, Transgene

Ivy Chen, Pfizer

Bao-Lu Chen, Sangamo BioSciences

John D`Antonio, Merial

Chris Daugherty, Bristol-Myers Squibb

Misty Davis, Merial

Massimo De Carlo, F. Hoffmann-La Roche

Terri DeAngelo, Pfizer

Barry DeDominicis, Bracco Diagnostics

Vincent Delmotte, GlaxoSmithKline

Xavier Despinoy, Piramal Healthcare

Yair Dishon, Teva

Viola Draheim, Bayer Schering

Nils Engel, Boehringer Ingelheim

Tristram Evans, Biotec Services International

Renaud Faniel, GlaxoSmithKline

Timothy Farmer, Charles River Laboratories

Birgitte Find Madsen, Novo Nordisk

Jane-Ann Fitzgerald, Centocor Biologics

Alain Francon, Sanofi Pasteur

Arnaud Garbe, Merck Sharp & Dohme

Noel Gaule, Ann McGee Consulting

Brigitte Gayet Donnot, Guerbet

Pierre Geens, Glaxosmithkline

Eric Gounant, Assystem

Frank Guethlein, Roche Diagnostics

Dan Habtesion, United Therapeutics

Susanne Hahn, Baxter

Cyril Hardit, Sanofi Aventis

Roland Hecht, CMC Biologics

Magnus Hedfors, AstraZeneca

Jennifer Hoffrage, Meridian Life Science

Catherine Hogg, Eden Biodesign

Susan Hummel-Iversen, Statens Serum Institut

Brian Jackson, W. L. Gore & Associates

Kristien Janssen, Pfizer

Adrienne Janssen, Abbott

Kieran Joyce Allergan Pharmaceuticals

Alex Kersten, Abbott

Bernhard Kiefl, Wasserburger Arzneimittelwerk

Michael Kleinehanding, CSL Behring

Valerie Kowal, Boston Scientific

Haim Kreynin, D-Pharm

Stefan Krippendorff

Martin Christ Gefriertrocknungsanlagen

Gitte Vejmand Kuhre, Novo Nordisk

Erin Lanham, Covidien

John Levesley, PM Group

Hank Liu, Sanofi Pasteur

Stephen Mahoney, Genentech

Frank Matos, Genzyme

Lori McDonald, Bayer Schering

Heinrich Meintrup, GEA Lyophil

Petra Merker, Bayer Schering

Marjorie Monnet, Sanofi Chimie

Victoria Morgan, West Pharmaceutical Services

Perumal Munusamy, Vinkem Labs

Stephanie Myers, Eli Lilly

Manikandan Namasivayam, Genzyme

Hong Chau Nguyen, SUT

Vera Ott, Biotest

Francoise Perier-Baptee, Sanofi Chimie

Miloslav Pesl, Wasserburger Arzneimittelwerk

Lene Petersen-Cletus, Novo Nordisk

Bernhard Pichler, F. Hoffmann - La Roche

Aude Pons, Novartis

Oriol Prat Magrans, Grifols

Pirkko Puranen, Finnish Medicines Agency

Guy Ravanat, Millipore

Annamaria Reiter, Sandoz

Roland Reu, Inova Pharma Systems

Kia Bang Rottlaender, Novo Nordisk

Jean-Pierre Rouzes, Renolit

Williams Rufus, Gilead Sciences

Nicolas Salavin, Sanofi Chimie

Pedro Sanz, F. Hoffmann-La Roche

Raffaella Sartorio, Kuros Biosurgery

Gioval Scalzo, Pfizer

Harald Schoenfeld, Friedrich Sanner

Michael Sparozic, Biovail Technologies

Richard Steib, Intervet International

Werner Stilmant, Amgen

Arnold Stoker, Sanquin Plasma Products

Maria Stoop, Progress Project Management & Engineering

Sonja Stoyantshova, IDT Biologika

Markus Stuebchen, F. Hoffmann - La Roche

Mia Tagansky, Evogene

Mary Taylor, Micronova

Kathleen Testaverde, Pfizer

Carsten Thiemt, Arvato Distribution

Willis Thomas, Pfizer

Lisa Thompson, AstraZeneca

Tammy Thompson-Madsen, BioConvergence

Thomas Tipton, Sanofi Pasteur

Daniele Tonello, Nordtest

Carmen Torres-rodriguez, Merck

Yazaki Toshikazu, Kissei Pharmaceutical

Michael Triplett, Battelle

Justyna Troczynska, Centre for Probe Development and Commercialization

Melisa Troshani, National Centre of Drug Control Albania

David Truong, Allergan

Gilbert Tumambac, Pall Corporation

Iris Alexandra Unterrieder, Baxter Healthcare

Richard Urban, Pfizer

Leaders to the PDA Community

Teodoro Urbayan, GAR Laboratories
Erick Vallejo, GlaxoSmithKline
Aad Van Der Putten, Teva
Paul Van Hoever, Novartis
Sylvie Vanderstocken, Baxter Healthcare
Steven Vandewinkel, Helvoet
Francesco Vargas, Zambon
Koen Verhaert, Helvoet
Lina Vieraitis, MedImmune
Nikolett Vincze, Teva
Marga Vines, Grifols
Maaike Vinkenburg, OctoPlus
Alwinus Voetman, Progress Project Management & Engineering
Nikolaus Vogl, Verfahrenstechnische Anlagen
Christian von Falkenhausen, Transcoject
Herwig Vossius, Pfizer
Ingrid Wachtel, Baxter Healthcare
Mandy Wagner, EMD
Kevin Wallace, Sanofi-Aventis
Elaine Walsh, Pfizer
Bonnie Ward, Quality Compliance Partners
Kathleen Waters, Genentech
Lisa Weatherholt, ZymoGenetics
Ian Weir, Pfizer
Rudolf Weiss, Groninger
Simone Weissfloch, Trion
Uffe Bendfeldt Westergaard, Statens Serum Institut
Patrick Weverberg, Pfizer
Susan Wilder, IPM
Denise Williams, New England Student Chapter
Gareth Williams, Novartis
John Wilmot, Meridian Medical
Anette Winston, CSL Behring
Arend Winter, Transgene
Claudia Wirtz, West Pharmaceutical
Philip Wunderle, Zogenix
Rina Yamin, Rina Yamin Pharmaceutical Consulting
Deiter Yang, Sci Pharmtech
Hagit Yariv, Dexxon
Effat Zaboli, Novo Nordisk
Davide Zacchia, Institut Biochemique
Avi Zak, Teva Pharmaceutical
José Zapata, Cytochroma
Hans-Dieter Zeller, Wacker Biotech
Vesna Zerjav, Farmal
Regina Ziegler, Boehringer-Ingelheim
Maris Zivtins, Eli Lilly
Stephen Zoeller, Genentech
Mike Zsolt, Teva Pharmaceuticals
Andreas Zunt, Baxter Healthcare

Volunteer

Junko Sasaki, Quality Assurance Principal, Dainippon Sumitomo Pharma Co.

PDA Join Date: 2002

Areas of PDA Volunteerism: PDA Japan Chapter QAQC committee (2002- present); Development QA committee (2005-present); PDA Japan Chapter Board member (2007-present);Speaker at PDA conferences in Japan; RAQC member; PDA Board member (2009-present)

Interesting Fact about Yourself: When I am not working, I enjoy watching musicals, reading books and drinking wine as well as traveling to various countries to meet and learn about different people and cultures.

Why did you join PDA and start to volunteer? I was invited to join the PDA Japan Chapter Quality Assurance Quality Control (QAQC) committee by a PDA colleague when the committee was just forming. I found out quickly that I enjoyed talking and interacting with other committee members.

Of your PDA volunteer experiences, which stands out the most? In 2009, when I was elected to be a PDA Board member, I thought this was the culmination of all my hard work. It was a great experience when I spoke about the PDA Japan Chapter's activities at the PDA Annual meeting on Development QA. In Japan, I enjoy doing presentations that update trends from a global view.

How has volunteering through PDA benefitted you professionally? Since joining, I have benefitted greatly. For example, I have learned tremendously from other professionals in my field, and I have shared experiences that have given me greater insight into the field of Quality Assurance. Also, the inspiration to excel from my colleagues (especially from my mentors) in my field has been of enormous help to me.

Which PDA event/training course is your favorite? The events that I attend the most are the PDA/FDA and PDA/EMA joint conferences, because I can learn about FDA/EMA regulatory expectations and industry practices at the same time. In Japan, the annual chapter meeting, conferences with QAQC members or Development QA members are also favorite events to network.

What would you say to somebody considering PDA membership? I would add that membership enables someone to form support alliances with other members from other countries and allow discussions to take place on a global level. Please join and enjoy with us!

Meet and Eat at the 2011 PDA Annual Meeting

New Members Invited to the New Member Breakfast on April 11

Hassana Howe, PDA

Welcome new PDA members! If you joined PDA on or after March 1, 2010 you are invited to kick-start your PDA membership by attending the New Member Breakfast hosted on site at the *2011 PDA Annual Meeting* on Monday, April 11 from 8-9 a.m.

This is a wonderful opportunity to learn more about PDA and to meet other new members, board members and staff.

Only conference attendees are permitted to attend.

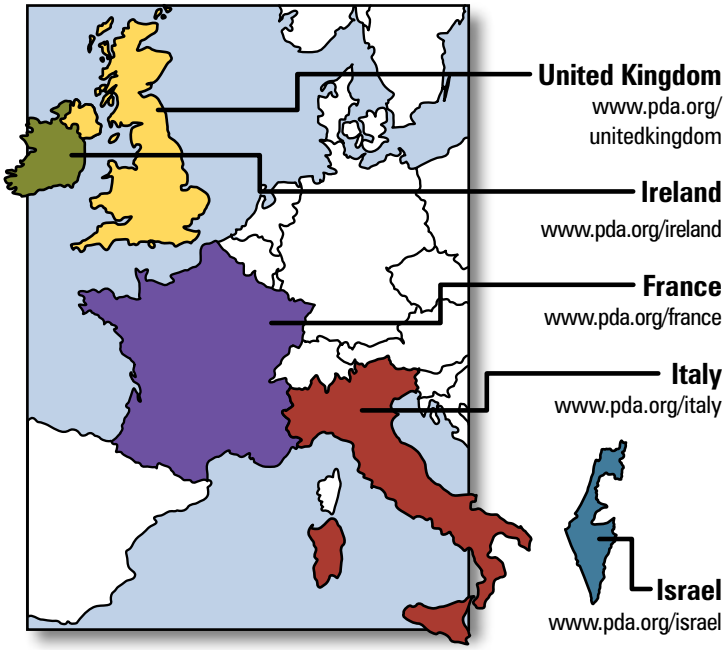
For more information and to RSVP by March 15, please contact **Hassana Howe** at +1 (301) 656-5900 ext. 119 or howe@pda.org.

New Members meet at the New Members Breakfast at the PDA Annual

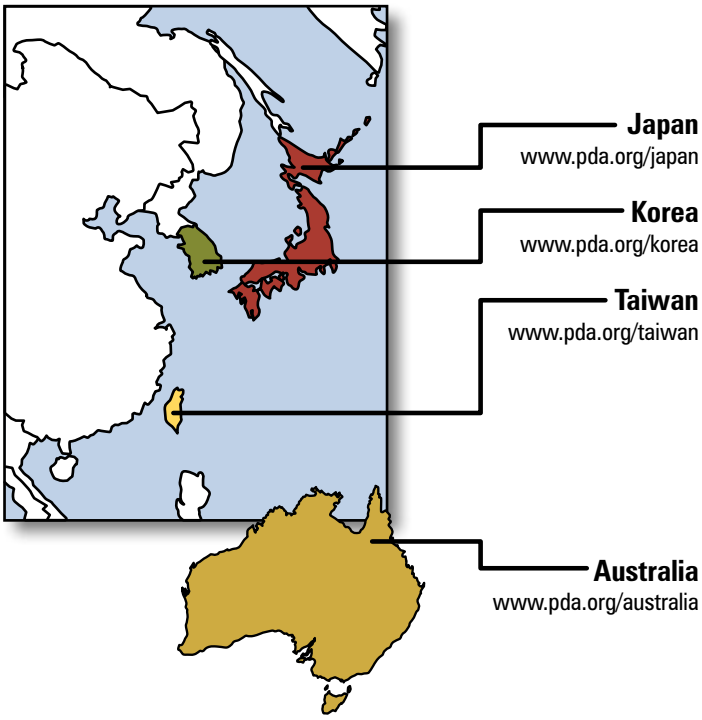
Chapter Contacts

The following are PDA's Chapters, organized by the regions of the world in which they are located. For more information on the Chapters, including their leaders and upcoming events, go to their websites which are listed below.

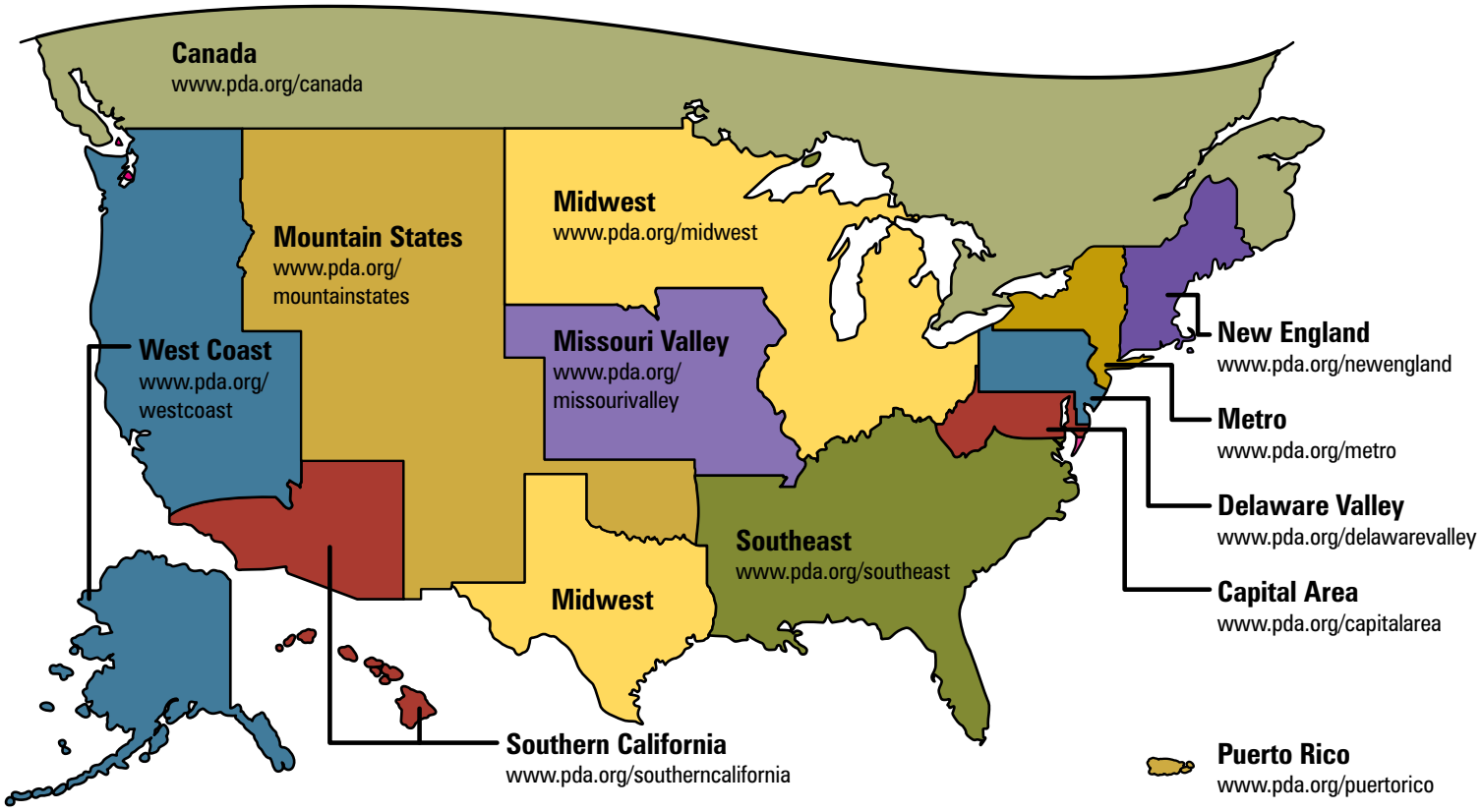
EUROPE



ASIA-PACIFIC



NORTH AMERICA



snapshot

Task Force *Corner*

Survey Results on Method Development and Qualification

Melissa Smith, MJ Quality Solutions

A survey was designed and administered by the Analytical Method Development and Qualification (AMD) Task Force to gain insight concerning key principles in connection with the upcoming Task Force report on Method Development and Qualification.

The following is a brief review of the survey answers and potential insights into current industry practices and perceived issues within the Method Development and Qualification arena.

One of the goals of the survey was to receive a high number of participants (at least 50) to obtain a more complete picture of the issues. Another goal was to minimize the time it took to complete the survey and to word questions to encourage open-ended comments.

The sixteen-question survey was sent to approximately 650 members who specified their area of expertise in analytical labs/stability. They represented a broad spectrum of company sizes and product types.

The survey had a 14.4% response rate with a total of 94 participants. Questions were considered successful if at least 80% of the participants answered the question, with the exception of the last question **(16)** which was an open-ended question. Question 8, 10 and 16 generated the most open-ended comments from the participants. The response rate for question 16 was considered successful with 42 comments.

Baseline Industry Practice

Questions 1 and **5** were designed to determine the baseline for current industry practices.

It was encouraging that 100% of the respondents answered the question and that none of them disagreed with the statement, although 6.5% were neutral. Examining the comments for more information, we saw varied responses, including respondents using unqualified methods, those using qualified methods, and others calling qualified methods "phase appropriate methods" instead. From a review of these comments, it is clear that a unambiguous definition of terms is required along with a phase appropriate understanding of method requirements.

The intent for companion question 5 was to ascertain what the respondent means when using the term method qualification. It appears that for a majority of the respondents, qualification is an identified activity in the organization. For 30.4% of the respondents, this is an activity that is part of development and not identified as a separate activity.

Therefore, the AMD Qualification Models should represent the current and best practices of the industry that are commensurate with the intended purpose of method qualification.

Method Qualification Life Cycle

The intended use of the qualified method and the ultimate goal for the method used were the intent for developing questions 2 and 3. 85% of the respondents agreed with the statement found in question 2.

Question 1: Qualified methods are used during Phase 1 and 2 as a minimum requirement for release and stability work. Do you agree with this statement?

Answer Options	Response Percent	Response Count
Strongly Agree	36.2%	34
Agree	50.0%	47
Neutral	6.4%	6
Agree	7.4%	7
Strongly Disagree	0.0%	0
Other (please specify)		11
answered question		***94***
skipped question		***0***

Question 2: "Phase 2b and 3 are when methods transition from Qualification to Validation, with the timeline and priority based on regulatory requirements and risk analysis. Do you agree with this?"

It was surprising that 5.5% disagreed with the statement, so we looked at the comments to try to determine what the reason could be.

One of the responses indicated that it could be difficult at times to discern a model for qualification depending on the company organization. The Task Force will consider various models which all describe the same end-goal of method qualification.

continued on page 20

Technology *Trend*

The Move from Stainless Steel to Single-Use Systems

Emily Hough, PDA

In the next ten years, more firms will be utilizing single-use systems. Citing significant reductions in environmental impact, as well as in time and cost, **Jerry Martin**, Sr. VP, Global Scientific Affairs, Pall Life Sciences and Chairman of the BioProcess Systems Alliance, said he expected to see the move from traditional systems to single-use systems take place by manufacturers of clinical batches, smaller scale and vaccine manufacturers.

According to Martin, when people think about the environmental impact of disposal of plastic systems, they mistakenly think that there will be a significant increase in solid waste relative to what they are currently disposing. But, they are not considering the waste in context of all of the plastics that a pharmaceutical facility disposes of, which would include packaging waste, maintenance, materials, laboratory and cafeteria plastics. "On a weight and volume basis, the additional waste in single-use manufacturing is a small increment compared to the total waste of what they are already disposing of."

Because the bags contain more than one polymer, traditional recycling is out of the question, but a few communities in the United States, and many communities in Europe, have started to build waste-to-energy facilities. These facilities incinerate combustible solid waste materials, take the energy that is derived from that incineration and create hot water and electricity. In that situation, the plastics used from single-use manufacturing are ideal for waste-to-energy conversion because they are clean burning (they typically don't include PVC which has chlorine and is associated with dioxins from incineration). They are converted to carbon dioxide and water, but they have as much energy content as gasoline, which makes them an ideal fuel for a waste-to-energy conversion facility. By doing this, the primary value (the energy) of the materials is being recycled, which greatly reduces the environmental impact. "The total amount of the carbon that is generated by incinerating [the bags] is still there, but it is actually less generated by a stainless steel facility that burns carbon sources to heat water to make steam and water for injection for cleaning."

Manufactures are finding creative solutions for the energy value of single-use solid waste. One vaccine manufacturer has partnered with a cement manufacturer and ships all of its single-use manufacturing and plastic waste to the cement plant. The cement plant uses it to fuel its cement making instead of burning coal or used tires, which are not clean burning. "Finding creative solutions like that can benefit the environment and greatly reduce the environmental impact of single-use [systems]."

Most people don't take into the account the waste generated in

continued on the bottom of page 25

Journal *POV*

Implementation of Quality by Design (QbD) for Biopharmaceutical Products

Anurag Rathore, Department of Chemical Engineering Indian Institute of Technology Delhi

[Editor's Note: The following is the editorial from the November/December issue of the *PDA Journal of Pharmaceutical Science and Technology*.**]**

Implementation of Quality by Design (QbD) has gained significant momentum lately in the biotech industry with both the regulators and the industry investing significant amount of resources to elucidate the path that would lead to successful adoption of QbD.

The fundamental elements of QbD can be found embedded in the FDA's *PAT—A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance* as well as the International Conference on Harmonization (ICH) guidelines: ICH Q8 *Pharmaceutical Development,* ICH Q9 *Quality Risk Management* and ICH Q10 *Pharmaceutical Quality System*. The traditional approach towards biotech production has been for the manufacturers to run the process within very tightly defined ranges so as to make the product with consistent quality. This approach has invited criticism from regulators and industry for its inefficiencies and rigidity. In contrast, the QbD approach is based on utilization of risk assessment and process and product understanding for successful development and commercialization of a biotech product.

Key steps for implementation of QbD include:

- Identification of the product attributes that are of significant importance to the product's safety and/or efficacy (Quality Target Product Profile and Critical Quality Attributes)
- Design of the process to deliver these attributes
- A robust control strategy to ensure consistent process performance
- Validation and filing of the process demonstrating the effectiveness of the control strategy
- Ongoing monitoring to ensure robust process performance over the life cycle of the product

Implementation of QbD in the biopharma industry continues to be impeded by several challenges, some of them uniquely associated with the complexity of biotech products and processes:

- A lack of standardization by which process and clinical data are collected, analyzed and reported
- Accessibility of data across molecules and sponsors
- Complexity of protein products with respect to the numerous quality attributes, structural heterogeneities and molecule-to-molecule variations in behavior
- Limitations associated with the ability of non-clinical tools

continued on the bottom of page 26

Task Force Corner, continued from page 18

Question 5: How would you describe Method Qualification in your organization?

Answer Options	Response Percent	Response Count
Identified activity	66.3%	61
Not done as a separate activity but is part of development	30.4%	28
Not done	3.3%	3
answered question		***92***
skipped question		***1***

This model would presumably represent, for example, when a method is qualified within the development phase and is not identified as a separate activity. Knowing the potential use for this type of method model can strengthen the task force report, as it is based on an understanding of current practices. These practices can define the activity and requirements and also represent industry best practice(s), which may not stand for a singular model in the case of method qualification. In addition, the comments will serve to give strong support for the definition of both Method Qualification and Phase Appropriate Validation within this Task Force Report.

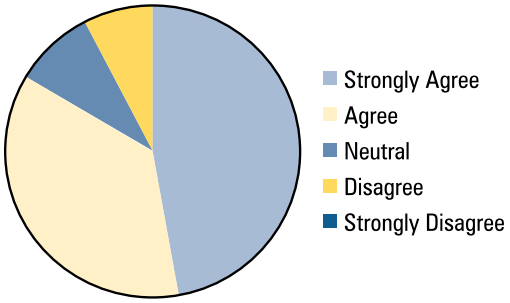
Some of the other comments received about question 2 include:

- We prefer to validate the methods once we know that the process is closer to validation. The methods used for Phase 2b and Phase 3 are reliable and scientifically sound
- It should be done case-by-case depending on how using, the method may need formal validation, e.g. potency assays
- I would want method validation to be initiated in late phase 2 and completed during phase 3. This is somewhat subjective to the type of method and the status of the process and/or formulation
- It is our experience that FDA expectations are for method validation when the drug is administered to humans, so leaving this to phase 2b or later would not meet this expectation
- The method validations evolve through Phases 2B and Phase 3. The key determinant for when final validation occurs is before the release and stability start for the drug substance and drug product ICH registration batches
- Registration stability studies should employ validated methods
- Validated methods are not required until conformance lots, which is typically after Phase 3 starts. The qualified methods are acceptable to support Phase 3 release

Of the 7.7% who disagreed with the question 3 statement regarding method status for process validation, it was not clear in the specific comments as to if they disagreed what their practice is. One of the answers may contain the information, in that "release methods usually only strictly apply to final API or DP, but if used to support upstream samples during PV, then those sample types should be qualified."

Question 3 Method Status for Process Validation

Process Validation always uses validated release methods and qualified characterization methods. Do you agree with this statement?



The Use of Statistical Tools for Method Qualification

Question 4 was designed to see what type of statistical information, if any, was desired by the respondents when it came to method development, transfer and qualification. Half of respondents just wanted examples, while the remaining 50% were evenly split over what was needed.

This represents a major area for the AMD report to address appropriately for our members.

The fact that 97% of respondents gave a specific response indicates to us that it is important to include statistical technique content in the task force report or in a supporting article. It appears ➤

Question 4: Guidance (within the AMD report) on the use of statistical tools for method qualification is needed.

Answer Options	Response Percent	Response Count
Use of a statistical reference is sufficient	12.1%	11
Examples of the use/interpretation of tools such as ANOVA and DOE would be helpful	15.4%	14
Use of statistical analysis for method transfer confirmation	11.0%	10
Use of statistical analysis for method equivalence (changing methods)	12.1%	11
Use of examples for all sections of method qualification is needed	49.5%	45
answered question		***91***
skipped question		***3***

Your Product is Unique, so is our Sterile Collection.

Custom Sterile Solutions

At Texwipe, we understand what you have invested in your product. We protect your investment by helping you produce the safest medicines for your patients.

Have a specific size, solvent or packaging in mind for your dry or prewet sterile wipers? Need additional testing for your IPA?

Call us - Texwipe is here to serve your needs.

North America
336 996 7046
info@texwipe.com

Europe
+45 87 400 220
info@itw-cc.com

Asia
+65 6468 9433
asia@texwipe.com

ITW Texwipe®

The Next Level of Clean™

www.texwipe.com

Veltek Associates, Inc.

One Wipe, MULTIPLE SOLUTIONS



For more than 30 years, VAI has pioneered the design and manufacture of hundreds of clean room solutions.

- **Cleanest wipe in the industry**
- **Asepti-Fill® closed filling system**
- **Laundered in Class 1**
- **Saturated wipes are made with WFI**
- **Lot Specific Documention for all wipers**
- **Laser cut sealed edges**

Quadruple Bagged using the ABCD Introduction System®

No other company offers this broad a range of wipers…

WIPEDOWN	PROCESS 2 WIPE	STERI-PEROX® WIPE	HYPO-CHLOR® Wipe	DECON-Clean® Wipe	ALCOH-Wipe®	STEEL-BRIGHT® Wipe	DAS-Wipe®
Dry cleaning wipe	70% USP IPA in Water for Injection saturated wipe	Saturated Hydrogen Peroxide Wipe	Saturated Sodium Hypochlorite Wipe	Removes residue from disinfecting agents	Saturated with DECON-AHOL® WFI 70% USP Isopropyl Alcohol	Stainless Steel Cleaning wipe	Stainless Steel cleaning and lubricant wipe

www.sterile.com

1-888-4-STERILE

Question 12: Please indicate which of these tools/areas would benefit from more practical guidance for use in the qualification process?

Answer Options	Response Percent	Response Count
Design of Experiments	14.3%	12
ANOVA Analysis	2.4%	2
Statistical Equivalence of Methods	17.9%	15
Mapping the operating space of a method	28.6%	24
Justification of Specifications	23.8%	20
Determining Equivalence with changes to critical reagents	6.0%	5
Assessing impact of process change on method	7.1%	6
Other (please specify)		7
answered question		***84***
skipped question		***10***

that only the minority of the participants thought that only references to statistical work was sufficient.

The answer to **Question 12** also supports the premise that statistical and analytical tools are needed within the AMD report, including the use of examples throughout the report which will include analytical techniques such as analysis of variance (ANOVA) and design of experiments.

Transfer of Method

Again, we examined the comments to understand why 17.6% disagreed with statement six.

One respondent said that "It depends on the stage of validation. For example, transfer can be part of intermediate precision if the validation is being performed for the first time. Otherwise, a protocol is necessary and a SOP defines the process of transfer."

This may indicate the concept of transfer occurring through the joint activity of the precision section. However, if true, this model would not determine accuracy equivalence, so this concept would not be a best practice as is, but may need further exploration to fully understand in action. There are further comments on the use of protocols and whether or not they might contain acceptance criteria if the method were qualified. This will prove to be an interesting area within the task force report as it relates to the method qualification status and what it means.

Other respondents said, "There is a need for preapproved protocol that defines testing, samples to be tested and acceptance criteria. Too many companies have the criteria set as must meet specifications. This is not acceptable, as one lab could be on one end of the spec. range while the other lab is on the other end," and that "transfer of qualified methods is less stringent than validated method transfer–both are guided by procedures." These comments addressed topics that are being tackled within the Task Force.

Documentation

In **Questions 13** and **14**, we were trying to see the current industry practices regarding documentation and reports for the development and qualification phase. The majority of respondents agreed that Method Development and Method Qualification report content areas are important to have in the AMD report. From that, we concluded that there is a need to define expectations of report content.

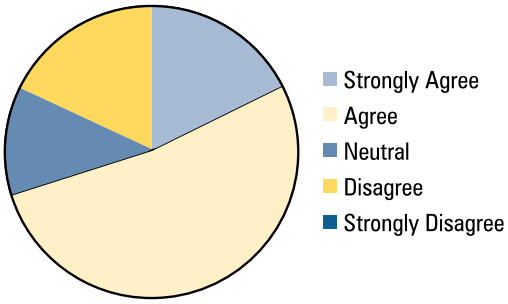
Areas for Discussion

Some questions were designed to encourage discussion and comments. Questions 7, 8 and 11 were designed with this in mind. Sometimes the wording of the question was purposely obtuse to further encourage responses.

Question 7's statement about changing a qualified method without requiring a requalification to changes made to the operating space of the method generated many comments from respondents including:

- "How is operating space to be defined? This is not commonly done for ana-

Transfer of qualified method follows the same process as the transfer of validated method. Do you agree with this statement?



Question 13: Should the Task Force report contain detail of the Method Development Report content areas?

Answer Options	Response Percent	Response Count
Strongly Agree	23.0%	20
Agree	59.8%	52
Neutral	13.8%	12
Disagree	3.4%	3
Strongly Agree	0.0%	0
Other (please specify)		4
answered question		***87***
skipped question		***7***

Question 14: Should the Task Force report contain detail of the documentation needs for the Method Qualification Report?

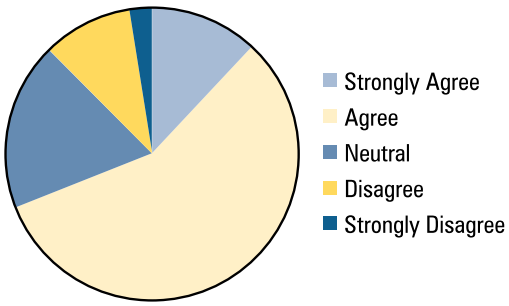
Answer Options	Response Percent	Response Count
Strongly Agree	32.2%	28
Agree	52.9%	46
Neutral	10.3%	9
Disagree	4.6%	4
Strongly Agree	0.0%	0
Other (please specify)		3
answered question		***87***
skipped question		***7***

lytical methods. During qualification stage, changes can be assessed by technical expert (analytical chemist) as to whether and what amount of requalification is required."

- "This question has a peculiar wording, but I think I got the point. Any change of this sort requires adherence to a company's change control policy. The request for change document should explain and provided justification for the change. If the "operating space" is defined in the method development reports, then there may not be the need to repeat requalification. However, this decision needs to be made by the subject matter expert who knows the background and application. As I stated above, there could be other reasons to conduct requalification, such as to understand how the reference standard will behave with the new procedure…"

Question 7 Changing a Qualified Method Without Requalifying it

Changes to a qualified method can occur without requiring requalification if the change is within the operating space of the method. Do you agree with this statement?



Question 8 asked whether the following was true: Method Design Space is part of the Development phase for a method. While 76% responded yes, the 23 comments it generated indicates there is a great need to define and discuss what is meant by this statement. Further exploration of this topic is needed within the Task Force as there was great disagreement over what was meant by this question by the survey participants.

Question 11 asked for which case studies for development and qualification would provide the best practical guidance and reference for best practices? Respondents were allowed to answer more than once: 82% responded HPLC Purity analysis; Elisa (quantitative impurity) came in at 40%; and Electrophoresis came in third at 15%.

QbD and Operating Space

Questions 9, 10 and **15** examined design space, operating space and QbD within the method development-qualification life cycle. The individual comments to the questions indicated where detailed guidance may need to be given by the task force.

For these questions, a total of 42 separate comments were obtained. Like some of the questions above, some were designed to be slightly obtuse to generate additional comments for discussion.

80% agreed with **question 9** when asked, "Within the Design Space, a method platform can be requalified for a new product using the same method?"

Question 10 asked, "Within the Operating space, a qualified method can be revised for changes to critical reagents, equipment and steps and as long as it fits in the Design space, does not require requalification" which only 57% agreed with.

Again, the questions were designed to probe and encourage comments, such as, "This could only be no if the operating space, even though qualified, is not fully within the design space as that would be a contradiction in itself," and "A method should be defined with acceptable ranges and practical precision for inputs (such as temperature, pH, etc). You might have procedures to qualify new reagents or column lots, those should be defined in the method. You might have allowances to adjust conditions as needed, but those should be defined in the method."

88% agreed with **question 15** when it stated, "QbD elements within Design, Development and Qualification stages of a method with detailed examples should be part of the Task Force report" to.

These questions enhanced the ability of the survey to effectively gather a broad snapshot of current industry practices and expectations in the subject area of QbD applications to the method life cycle.

What Topic Interests you?

The final question, **Question 16** asked, "What particular topic would you like to see addressed within the Analytical Method Development and Qualification Report?" We received 42 responses which far exceeded our expectations. Each of the responses was an individual comment and none were identical. The range of topics covered a vast array of topics.

Below are a few of the responses received for question 16:

- The original list (question 11) is good. My request would be to keep the report simple and practical. The report should be able to provide guidance to an audience that spans a wide range from small to large organizations as well as contract labs
- Qualification level at different stages

in clinical development
- Example of what is required as a minimum for method development
- The method should be suitable for its intended use and therefore what should the acceptance criteria for the applicable parameters to set based on the product specifications
- Use of assay controls where no standard exists
- Justification of specifications
- Details of comparability parameters between two different methods
- I have seen many companies struggle with knowing what is required at Phase 1, versus Phase 2 and 3. Examples of how to choose the various validation elements at the appropriate phases, and how to implement for qualification versus validation would be beneficial.

The high response to our questions indicates a strong interest in the Method Development and Qualification area. The detailed comments received for each question help guide us in terms of content needed (statistical tools), details and definitions needed (qualification versus validation versus phase appropriate validation), and where more discussion may be needed (QbD elements) in order to generate a task force report that is a practical guidance to best practices.

We would like to thank the PDA membership for helping us obtain this valuable insight into drafting a practical guidance for your use.

About the Author

Melissa Smith is the Founder and Principal Consultant of MJQuality Solutions, LLC, a consulting firm that is involved in the Quality and Analytical fields with experience in the industry for over 25 years.

Technology Trend, continued from page 19

a stainless steel facility, particularly in the disposal of CIP chemicals; whether they are caustics or acids they need to be neutralized and dealt with through the liquid waste treatment. The use of disposables greatly reduces the water for injection and steam that needs to be generated both for cleaning and sterilization purposes. Single use systems can reduce caustic chemicals by 20%; acids by 85%; SIP by 100% and WFI by at least 50%. Sterilization by gamma irradiation (applied to an entire lot of single-use systems for multiple product batches) also significantly reduces energy requirements and carbon emissions relative to moist heat (steam) sterilization of stainless systems, conducted on a per product batch basis..

"If you look at waste in terms of carbon footprint, you can reduce your carbon footprint by over half by going to disposables. The amount of carbon utilization necessary to produce all that water you need is then balanced by the much lesser need in carbon footprint derived from the production, delivery and waste of disposable plastics."

Advantages

Advantages of single-use systems are many. A decreased set-up time allows for increased flexibility because the total set up consists of a bag being placed in the reactor. In addition to low installation costs (which consists of disposable bags), cleaning costs, maintenance and assembly costs are reduced since the bags arrive pre-sterilized and validated per ISO 11137 and ANSI TIR 33 to the facility.

Firms that do invest in a single-use system can expect to see a reduction in the cost of manufacturing biopharmaceutical goods.

This in turn reduces the need and delay for sterilizing and cleaning as well as the time to validate those actions.

With the elimination of risk of product cross-contamination since a bag is discarded when the process has finished, there is no need to develop suitable cleaning processes, perform cleaning verification, method development and validation or equipment sterilization or sterilization validation, which again leads to a time and money savings.

Cost

When people look at the cost of operating a stainless steel plant, the idea is 'oh, I could just clean it and be done. I don't have this cost of the disposable.' They fail to consider that it takes a day to clean, resterilize and reset up equipment; whereas, with a single-use system, once the bag is taken out all you need to do is put a new one in. But if they take a closer look at the opportunity cost of the turnover time, it is more cost effective to go in single-use if you are operating at a clinical scale or in a small scale production up to a few thousand liters a batch.

However, Martin said that very large scale productions like monoclonal antibodies facilities, which operate with 10, 000 or 20,000 liter bioreactors, it is probably going to be more cost effective to operate in a stainless steel system because there are not good disposable options yet. There are some efforts to increase the size of disposable bioreactors. The largest ones that are currently available in the market are about 1,000 liters. There are some prototypes that are 2000 and 5000 liters, but there is a limit to that in terms of handling that large a bag.

Future of Stainless Steel vs. Plastic

While it is a difficult decision to make if you already have a stainless steel facility, moving forward, Martin said that it looks like manufactures will convert to

single-use systems when expanding their facilities or introducing new products. In 2009, according to the *BioProcess International* survey, there was a 9.6 % increase in firms that were implementing single-use systems with new processes from the previous year. Firms that do invest in a single-use system can expect to see a reduction in the cost of manufacturing biopharmaceutical goods.

PDA's Who's Who

Jerry Martin, Senior Vice President, Global Scientific Affairs, Biopharmaceuticals, Pall Life Sciences, is responsible for technical communications and industry/regulatory liaisons related to biotechnology and pharmaceutical process separations. He has over 30 years experience in the bio/pharmaceutical industry in QA/QC, Technical Support, R&D and Marketing of filtration, in vitro diagnostic, medical device and molecular biology products. Jerry is also the Chairman of the Board of the Bio-Process Systems Alliance trade association as well as an active member of ISPE and PDA.

Journal POV, continued from page 19

to predict clinical safety and efficacy

- Complexity of the processes that are used to manufacture these protein products along with the raw materials that they use

It will take some time for the regulators and industry to create a framework that addresses these gaps.

What is needed to ensure QbD adoption by the biotech industry? Alignment across global regulatory agencies on the requirements and the benefits is very important. Some of this may be achieved via the forthcoming ICH Q11 guidance document, which focuses on drug substance manufacturing and is the counterpart of ICH Q8 *Pharmaceutical Development,* which focuses on drug product manufacturing. Continued partnership between the regulators and the industry through various professional organizations (such as PDA) or expansion of formal programs such as the QbD Pilot Program is required. Workshops, where the regulators can present the outcomes of such programs to the biotech community in general, are critical for the QbD effort to gain the credibility needed for a wider engagement of the biotech industry. Finally, academia, in partnerships with the regulators and the industry, could also play a critical role in creating tools and approaches that serve as enablers for QbD implementation.

The *PDA Journal of Pharmaceutical Science and Technology* welcomes submissions of papers in these areas and would serve the broader community as a repository of QbD applications.

sartorius stedim biotech

SINGLE-USE TECHNOLOGY

New sterile filters Sartopore® 2 XLG and XLI.
A quantum leap in flow rate and throughput.

With their unique hydrophilic, heterogeneous double-layer polyethersulfone membranes, new Sartopore® XLG and XLI provide broad chemical compatibility, high-thermal resistance and significantly higher throughput and flow-rate than any other sterilizing grade filters.

Typical applications include sterilizing grade filtration of:

- Buffer
- Media
- Biologics (intermediate & terminal)
- SVPs and LVPs
- Ophthalmics
- Antibiotics
- APIs

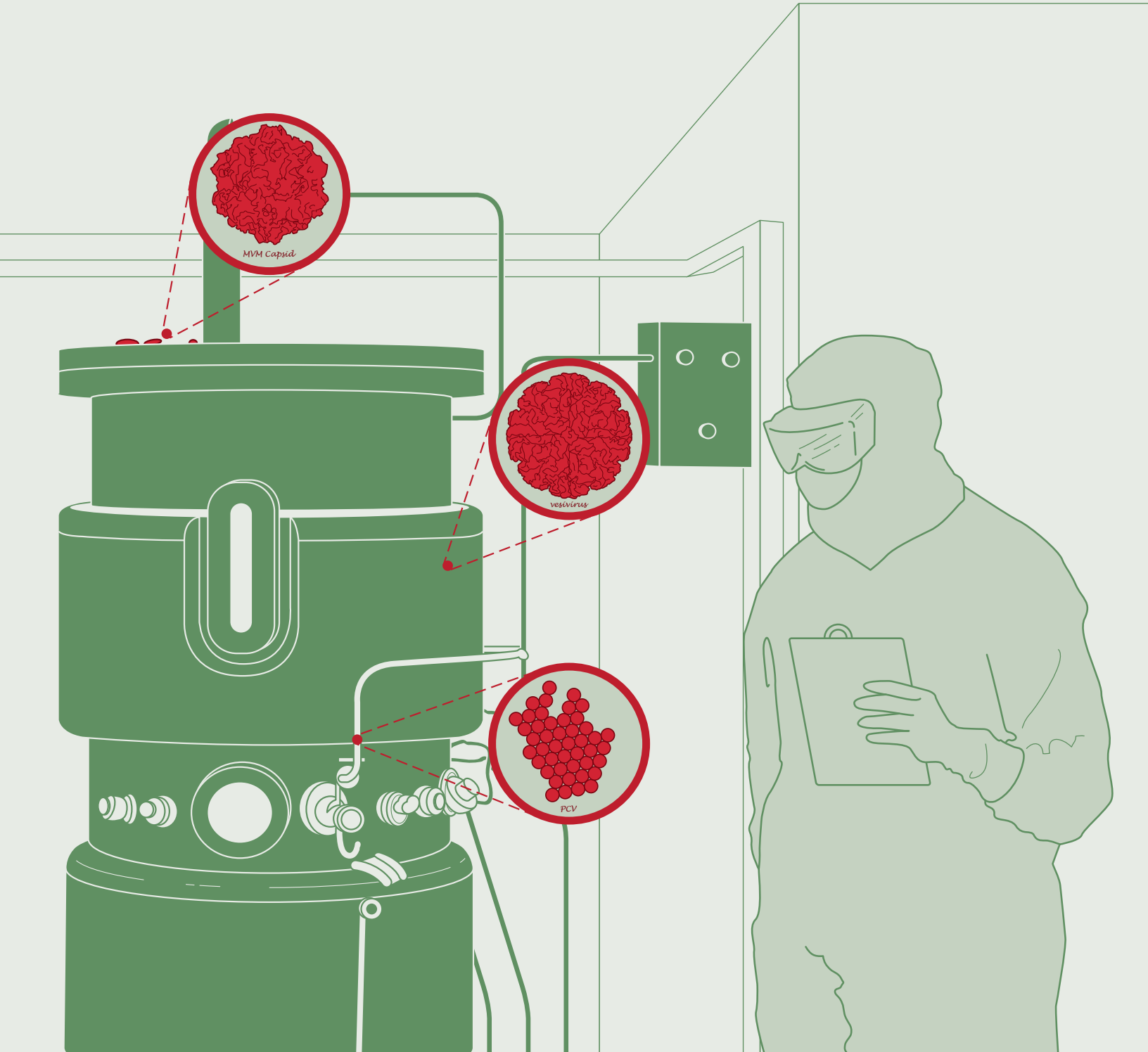
www.sartorius-stedim.com/sartopore2
turning science into solutions

Sartorius Stedim Biotech
USA +1.800.368.7178
Europe +49.551.308.0

U.S. FDA, Industry Meet to Share Notes on Virus Control

Walter Morris, PDA

Virus contamination is not a common occurrence in the tightly controlled world of vaccine and therapeutic biotech manufacturing. Yet the issue was suddenly thrust into the spotlight in 2009 and 2010, as two high-profile cases of product/process contamination made headlines.



The first case was an isolated cell bank contamination affecting two sites and attributed to a cell culture nutrient. The other case involved vaccines by two different firms, but the route of contamination was the same—a common processing material. Both had large consequences for the firms involved, patients and regulators.

As part of its effort to facilitate solutions to these problems in the future, the U.S. FDA partnered with PDA to hold the workshop, Adventitious Viruses in Biologics: Detection and Mitigation Strategies. The workshop drew participation from large and small companies, as well as regulators from Europe.

[Editor's Note: The program planning committee is currently working with conference speakers and PDA to develop and publish full proceedings. As such, the following report is limited mostly to a review of key points from the regulatory representatives.**]**

While the meeting was developed in the wakes of the high-profile contaminations, the presentations demonstrated that much is being done by both industry and regulatory authorities to help reduce the risks of this complicated manufacturing threat.

Anthony Lubiniecki, Sr. Fellow, CMC Strategy, Janssen (a J&J affiliate), opened the meeting with an instructive discussion about the evolution of viral safety approaches. Lubiniecki, who was a member of the workshop planning committee, wended through the history of early vaccine procedures and gave an overview of modern control approaches for rDNA products. He ended his talk with the following question (from his slide), which helped set the stage for the remainder of the conference:

Given that substantial time is required to develop some of these technologies or establish their relevance, and demonstrate a lack of effect on product stability where appropriate, what is an appropriate time frame in which to expect adoption of proven new technologies to occur?

The following series of presentations highlighted the current regulatory expectations for viral contamination control, with talks from two FDA officials and a representative from the Paul-Ehrlich-Institut.

FDA's **Philip Krause,** MD, Acting Associate Director for Medical Policy and Vaccine Safety, Center for Biologics Evaluation and Research (CBER), started the session by focusing on vaccines.

Krause described the evolution of methods from the early years of vaccine manufacture, but his talk quickly turned to CBER's approach to evaluating porcine circovirus 1 (PCV1) in vaccines—the unwanted guest in the rotavirus vaccines that hit the press in 2010. After findings of PCV1 in rotavirus vaccine surprised third party researchers looking at the GlaxoSmithKline's version brought the issue to light, FDA first set out to determine if the contamination likely to represent infectious virus. It was later found that Merck's version of the product was similarly contaminated.

Rosenberg spent some time dwelling on mitigating risks posed by animal-sourced raw materials

FDA performed a battery of molecular studies and cell culture studies to answer a series of questions, including:

- Do vaccine-inoculated cells show evidence of virus infection?
- Can PCV nucleic acid be detected in vaccines?
- How does sequence of PCV1 from vaccines compare with sequence of known PCVI?

CBER utilized quantitative PCR for these studies and the conclusions have been well publicized.

Following this discussion, Krause noted that the next challenge is determining how to incorporate the new methods in product evaluation.

In conclusion, Krause emphasized that adventitious agent detection for vaccines relies on the use of "multiple, overlapping strategies"—a notion which would be echoed by a number of speakers. He also noted that detection methods for adventitious agents are evolving, driven by improving technology. These technologies, in turn, offer a "powerful means" for supporting safe product development.

Strategies for preventing contamination of biotech products were presented next by FDA's **Amy Rosenberg,** MD, Division of Therapeutic Proteins Director**,** Center for Drug Evaluation and Research (CDER), following Krause's presentation.

Rosenberg first outlined four "complex" risks involved with viral contamination in biotech products, the risks to:

- Patients/personnel from infection
- Product availability
- Other products in a facility
- Product quality

The "predominate" cause of viral contamination in fermentation processes, Rosenberg said, is animal-sourced raw materials. Cell banks, human error and environmental factors represent other common sources. She listed another of regulatory resources to help companies develop prevention strategies, including the International Conference on Harmonisation (ICH) quality guideline Q5A (1998), several FDA documents and regulations, and a 2008 European Medicines Agency guideline on virus safety in biotech products.

In light of the problems experienced by Genzyme, the firm involved in the other headline-making case mentioned above, Rosenberg spent some time dwelling on mitigating risks posed by animal-sourced raw materials. She noted that the vesivirus 2117 that plagued bioreactors in Genzyme's Allston and Geel facilities in 2009 was likely introduced through a cell culture nutrient. While human infection was not considered a threat, the company suffered productivity declines. Standard testing was unable to identify the culprit of the cell bank productivity drop, so Genzyme developed a PCR assay which got the job done.

Rosenberg highlighted the following lessons and suggestions:

- Manufacturers that use bovine serum should employ sensitive PCR assays to detect known viral contaminants
- Manufacturers that use bovine serum should employ broad based and sensitive PCR methods for detection of emerging/potentially zoonotic viruses (universal biosensor)
- Manufacturers that use bovine serum should employ inactivation steps commensurate with preservation of product quality
- Vendors that produce bovine serum and/or manufacturers should assess both fetal and maternal serum for evidence of recent viral infection: antibodies to viruses such as vesivirus

With respect to emerging viruses and cross species infectivity, Rosenberg held out hope for "universal biosensor" evaluation of animal based raw materials and fermentation culture at early time points. She highlighted two papers (see box below) that discussed such an approach.

The Paul-Ehrlich-Institut's **Johannes Blümel,** Head of Virus Safety Section, Vaccines and Biomedicines, outlined current European regulations on adventitious virus safety.

Like Rosenberg, Blümel outlined several principles for "improved virus safety" with respect to animal-derived materials. These were:

- Avoid bovine serum whenever possible
- If bovine serum is used, end of production testing is recommended
- Use only virus-inactivated serum
- Use only virus inactivated porcine trypsin (40 kGy)
- Replace porcine trypsin by other (safer?) trypsin (recommended)

Other FDA representatives appeared to discuss pre- and post-approval CGMP expectations both from CBER's and CDER's perspectives.

CDER's **Barry Cherney,** PhD, Deputy Director, Division of Therapeutic Proteins, provided a thorough review of "gaps" in virus contamination prevention efforts.

One gap is in the control of raw materials. The problem here is multi-tiered. For one, Cherney said, high-risk materials, ➤

Cell Substrate Task Force Scope

- Issues that impact cell substrate safety/quality
- Resulting from scientific/technical advances over a decade
- All banked non-microbial cell substrates
- Parental cell line to testing of the unprocessed bulk
- Use case studies as a basis
  - Approaches to address these issues scientifically
  - Attention to current global regulatory guidelines
  - Consistent with global regulatory expectations

Taken from Kathryn King's slide deck

Biotest

From Nature for Life

NEW

RCS High Flow Touch

Microbial safety at your fingertips

- Reliable - Proven RCS technology
- Convenient - Flexibility and mobility with an easy touch
- Validated - Complete system with standardized media

Biotest Microbiology Corp.
400 Commons Way
Rockaway, NJ 07866
USA

Tel.: +1 973.298.8596
Fax: +1 973.625.9454
CustomerService: 877.210.5103
CustomerService@biotestusa.com
www.biotestusa.com

Five compendial strains.
One convenient package.

Licensed, traceable growth promotion testing.

Introducing:

ez accu shot™
GROWTH PROMOTION TESTING
Select

One container, five compendial strains
- less inventory needed
- reduced waste

Traceable
- licensed

Five peel-off labels (one for each strain)

Five vials of hydrating fluid
- 1.2 mL in each vial

Instant dissolve
- No preincubation
- 8 hour stability

Five different compendial strains
- 1 lyophilized pellet per vial

Includes these five traceable strains:

- Catalog # 0392A *Aspergillus brasiliensis* ATCC® 16404™*
- Catalog # 0486A *Bacillus subtilis* subsp. *spizizenii* ATCC® 6633™*
- Catalog # 0443A *Candida albicans* ATCC® 10231™*
- Catalog # 0484A *Pseudomonas aeruginosa* ATCC® 9027™*
- Catalog # 0485A *Staphylococcus aureus* subsp. *aureus* ATCC® 6538™*

NO DRY ICE & TRACEABLE

Microbiologics®
A safer, healthier world.
www.microbiologics.com

ATCC Licensed Derivative®

** The ATCC Licensed Derivative Emblem, the ATCC Licensed Derivative word mark and the ATCC catalog marks are trademarks of ATCC. MicroBioLogics, Inc. is licensed to use these trademarks and to sell products derived from ATCC® cultures.*

Not intended for clinical use.

like bovine serum and trypsin, but drug manufacturers often only rely on supplier testing to reduce the risk of viral contamination.

However, he said, "AV testing alone will not prevent the entry of bovine viruses into the production process due to assay limitations. It may only take one infectious virus to crash a fermentor."

"AV testing alone will not prevent the entry of bovine viruses into the production process…"

Replacement of these materials is one option, though one that poses other kinds of risks. These include decreased yields or potential mycoplasma contamination. Treating animal-derived raw materials is another option, but the procedures to do so introduce other kinds of risks.

In the end, Cherney explained how the Agency is acting to improve virus safety. On the one hand, it is pursuing directed research projects in three areas:

- Determining robustness of various viral safety technologies
- Creating a viral clearance database of submitted regulatory documents
- Comparing new purification technologies

Partnering with organizations like PDA is another strategy both in formulating evens like he workshop and developing technical reports, he explained.

An example of FDA involvement in technical reports was provided by CDER's **Kathryn King**, Phd, Office of Biotechnology Products, who co-chairs the PDA Cell Substrate Task Force with **Michael Wiebe,** PhD, Quantum Consulting. The Task Force is divided into three working groups, one of which is looking at virus testing of cell banks and unprocessed bulk. The group is aiming to publish a technical report in mid-2012.

G.K Raju, PhD, MIT, closed the workshop by presenting three broad steps for moving forward:

1. Describe and characterize the general problem
2. Describe and characterize the solution
3. Develop collaboration and communication processes to enable solutions.

By all accounts, the workshop met its goals of focusing attention on emerging methodology, brainstorming solutions to fill gaps and enhance controls, outline regulatory expectations, and present case studies of real-life contamination discovery and mitigation actions.

snapshot

Harmonization *Report*

Status of Various Guides Updated at Fukuoka ICH Steering Committee Meeting

Dr. –Ing. Stephan Roenninger, F. Hoffmann-La Roche, with Emily Hough and Jim Lyda, PDA Staff

The International Conference on Harmonization (ICH) Steering Committee Meeting took place in Fukuoka, Japan from November 6-11 in 2010. This meeting marked the 20th anniversary of this highly recognized and accomplished international harmonization initiative for human drugs **(1)**.

The following Quality topics were discussed in detail: ICH Q4B, ICH Q11, ICH Q-IWG and the joint topics with safety experts on ICH Q3D and ICH M7.

ICH Q4B: Pharmacopoeial Harmonization

For the ICH Q4B Guideline *(Evaluation and Recommendation of Pharmacopoeial Text for Use in the ICH Regions)* a new revision on the Dissolution Test (Annex 7(R2)) was adopted for implementation (Step 4). Further discussions focused on the future of the ICH Q4B project will take place to determine if alternate approaches for pharmaceopeial acceptance should be considered.

ICH Q11: Development and Manufacture of Drug Substances

Good progress was made in the discussions of the Expert Working Group (EWG) on ICH Q11, *Development and Manufacture of Drug Substances (chemical entities and biotechnological/biological entities)*. The EWG worked on details in the text and did not identify any major barriers to progress based on the content. It is hoped that an agreed step 2 document for public comments will be issued in spring 2011. PDA will then form a task force and compile comments.

Q-IWG

At the meeting, the Quality Implementation Working Group (Q-IWG) continued its goal to support of harmonized implementation of ICH Quality guidance, Q8, Q9 and Q10. The focus was on clarification of terminology and the interrelationship between the three guidances and to discuss the contribution to training outside the ICH region.

The Q-IWG celebrated the success of the three regional training workshops on the ICH Q8, Q9 and Q10 guidelines. For this, the Q-IWG developed materials (cases study, development, assessment, manufacturing implementation, inspection) and key messages on design space, control strategy, pharmaceutical quality systems and quality risk management as presentations to be published for training **(2)**. They are designed to explain the interrelationship of Q8, Q9 and Q10 **(3)**. The EU and US events, co-sponsored by PDA, were well-attended and considered successful by both regulatory and industry participants.

The Q-IWG agreed to a number of public Q&A's about these ICH quality guidelines and liaised with the Global Cooperation Group and the ICH observers (e.g., Health Canada, EFTA represented by Swiss Medic) for further workshops. These documents and other training materials from the workshops are scheduled to be released on the ICH Web site **(2)**.

The Q-IWG summarized the training workshops* by listing questions, comments and statements. Evaluations showed that technical and regulatory gaps still need to be addressed such as level of detail in submissions, details on the control strategy and batch release, critical/non-critical, process validation/continuous process verification, role of modeling and design space. The goal is to publish them in one year's time.

ICH Q3D: Heavy Metal Impurities

Following the Tallinn steering committee discussions, there was further work on developing the guideline on the basis of the concept paper for metal impurities, including the first discussions on the scope of the guidance and preliminary safety limits that will be defined for each metal impurity.

Several approaches may be taken to assess the presence of metal impurities. The need for analytical testing would be based on a determination of the potential for metals to be present in the drug product; the control strategy should be appropriate for the level of risk. Any application of this guideline to existing marketed drug products are under consideration.

A preliminary list of metalsis being considered and may include, e.g., Arsenic, Mercury, Lead, and, Cadmium and their respective preliminary permissible daily exposure.

2010 ICH Quality IWG Workshops: *June2-4, Tallinn, Estonia; October 6-8, Washington, D.C.; October 27-29, Tokyo, Japan.*

Objectives of these workshops were to support consistent implementation of ICH's most recent quality guidelines: ICH Q8, Pharmaceutical Development*; ICH Q9,* Quality Risk Management*; and ICH Q10* Pharmaceutical Quality Systems*. The EU and US workshops were co-sponsored by PDA and the ISPE. In Japan, they were co-sponsored by the Japan Pharmaceutical Manufacturers Association and the Pharmaceutical and Medical Device Regulatory Science Society of Japan.*

ICH M7: Genotoxic impurities

The discussion on topic ICH M7, *Genotoxic Impurities*, included six party reviews of positions and experience since previous regional guidance on the topic was published. The structured-activity relationship assessment provided clarity and consistency regarding which areas needed to be addressed. There was interest in the use of a specific "threshold of toxicological concern" for structurally similar genotoxic impurity classes. The intent of the M7 guidance is to focus on carcinogenic risks of mutagenic impurities.

The title of M7 was considered in the

continued at bottom of page 42

Environmental Monitoring **Simplified.**

Real-Time Microbial Monitoring

Microbial Sampling

Integration and Validation

Particle Counting

Viable and Non-Viable. Together. **VALIDATED.**

PARTICLE MEASURING SYSTEMS

Without measurement there is no control.
www.pmeasuring.com • 1(303) 443-7100

2011 PDA Europe Conference, Exhibition + Training Courses

Pharmaceutical Microbiology – Mycoplasma

Enhancing Quality in Process and Product

15-18 March 2011 | Berlin, Germany

This conference will give a comprehensive overview on current and emerging trends in pharmaceutical microbiology topics, including virus, mycoplasma, modern microbiological methods, environmental monitoring, contamination control and sterility assurance as well as regulations. Key Topics are:

- detection and identification of virus, mycoplasma
- modern microbiological methods
- environmental monitoring and contamination control
- sterility assurance and regulations.

Meet regulators, industry experts and suppliers to find out what challenges you will face.

CONFERENCE, EXHIBITION 15-16 March
TRAINING COURSES 17-18 March

https://europe.pda.org/Microbiology2011

Remember the Annual!

San Antonio, Texas • April 11–15 • www.pda.org/annual2011

Jeffrey L. Hartman, Merck

The Program Planning Committee is very pleased and excited to showcase the *2011 PDA Annual Meeting* that will be held at the JW Marriott in the beautiful and historic San Antonio Hill County, San Antonio, Texas, home of the Alamo. The committee has been very busy selecting an excellent panel of presenters, plenary speakers, programs and activities that are sure to be educational and fun. This is PDA's "flagship" event and continues to be considered the year's most valuable networking opportunity. With some of the new venue and workshops being offered, we anticipate an even greater audience and are confident that this year's meeting won't disappoint you.

The Program Planning Committee has selected *Harnessing the Power of Knowledge* as the theme for our 2011 event. Today, information and technology is growing and changing exponentially, including the challenges in processing and handling all of this data. Furthermore, how does one gain the knowledge to assess and evaluate whether these technologies are suitable for your company or organization? Companies face challenging questions and decisions on single-use systems, applying rapid microbiology methods and how to improve their supply chain management. Knowledge is power and dissemination of that knowledge will better drive world class science and technology into your organization. Join us and the Subject Matter Experts in San Antonio and you may better learn how to harness this knowledge.

In keeping with the meeting's theme, the Program Planning Committee is introducing a new one day fundamentals track. The fundamentals course is designed to cover all of the critical areas in the pharmaceutical/ biopharmaceutical industry including:

- Validation
- Operations
- Microbiology
- Quality and Regulatory Affairs
- Aseptic Processing

Many of these sessions will be lead by the same instructors who teach at the PDA Training Center. This course is ideal for those new to the industry, or for those looking to harness the resources available to them through the PDA.

The meeting will also include the traditional format with three parallel conference tracks. Over 45 presentations are being offered covering many of the new advances in environmental monitoring, microbiology, manufacturing/process science, supply chain management, outsourcing, protein manufacturing, developmental and quality science. After the sessions, there are 14 Interest Group meetings scheduled for the first two days. In between and among sessions, there will be the opportunity to review and discuss over 30 poster displays. In the Exhibit Hall, representatives and venders from leading companies worldwide will be available to share new innovations, answer any questions and help resolve some of your company's issues. As always, we want this conference to be as interactive as possible. We encourage you to come, be engaged and share your knowledge. The exchange of thoughts and ideas is great opportunity to gain knowledge and conquer the challenges you face.

The plenary sessions always contribute to a great meeting and this year is no exception. For the opening plenary session, the committee is pleased to present **Piotr Krauze**, Scientific Administrator, Manufacturing and Quality Compliance, European Medicines Agency, who will provide the EMA perspective on knowledge management. Also presenting will be Professor **Janet Walkow**, Director, Drug Dynamics Institute, University of Texas. Professor Walkow will discuss opportunities for academic-industry collaboration and will be introduced by **Lynn Crismon**, Dean, College of Pharmacy, University Of Texas. For the closing plenary, we will hear the U.S. FDA discussing knowledge management with respect to Continuous Process Verification (Stage 3) and the life cycle of process validation as well as the Center for Disease Control (CDC). For the CDC, accessing and harnessing knowledge worldwide is a critical operation with today's risks of new diseases and bioterrorism.

To top off a great conference, there will be plenty of activities including a "dine around the river walk." What better setting than San Antonio, in April to enjoy a relaxing river walk, a visit to the historic Alamo and an opportunity to network with old friends and meet new ones.

The 2011 Program Planning Committee is committed to making this meeting a valued, informative, and knowledge building experience. So please, *Remember the Annual* and join us, April 11-15 in San Antonio, Texas.

PDA's meeting is in the home of the historic Alamo

PDA/FDA Conference to Focus on Quality and Compliance

Washington, D.C. • September 19-23 • www.pda.org/pdafda2011

Sue Schniepp, OSO Biopharmaceuticals

The *2011 PDA/FDA Joint Regulatory Conference* Steering Committee is hard at work planning the 2011 Conference scheduled to take place September 19-21 at the Renaissance Hotel in Washington, D.C. The tentative theme of the conference is being finalized but will build upon the 2010 conference by continuing the focus on improving quality and compliance. The 2011 conference will explore strategies and approaches companies should consider for ensuring conformance to regulations while empowering their quality and regulatory personnel to act responsibly when assessing products and processes in order to meet safety and effectiveness requirements. By being proactive, firms will be able to maintain an efficient, compliant operation while working effectively with regulatory agencies. In the end, companies will save considerable time and resources by not having to remediate nonconforming and undesirable practices.

The PDA/FDA Joint Regulatory Conference offers the unique opportunity for you to join U.S. FDA representatives and industry experts in face-to-face dialogues. Each year, FDA speakers provide updates on the current state of efforts impacting the development of global regulatory strategies while industry professionals from some of today's leading pharmaceutical companies present case studies on how they employ global strategies in their daily processes. Hear directly from FDA experts and representatives of global regulatory authorities, and take home best practices for compliance. You won't find this level of direct information exchange with FDA at any other conference! PDA is also offering an exhibition during the conference and the PDA Training and Research Institute will host courses immediately following the conference, September 22-23, to complement what you learn at the meeting.

Be sure and mark your calendar now so you don't miss this unique opportunity and keep reading upcoming editions of the *PDA Letter* and check www.pda.org/pdafda2011 to hear more about the conference as the committee solidifies the program.

TRI Courses to Consider

The PDA Training and Research Institute will be offering these courses after the PDA/FDA Joint Regulatory Conference:

"Effective Investigations and Corrective Actions (CAPA)"
"Quality by Design for Biopharmaceuticals: Concepts and Implementation"
"Active Pharmaceutical Ingredients - Manufacture and Validation"
"Role of the Quality Professional in the 21st Century"
"Preparing for Regulatory Inspections for the FDA and EMA"
"Documenting and Conducting OOS Investigations"
"GMPs for Manufacturers of Sterile and/or Biotechnology Products"

Atypical Actives Workshop Seeks Regulatory Pathway

Bethesda, Md. • March 9-10 • www.pda.org/atypicalactives2011

Bob Dana, PDA and Maria Guazzaroni Jacobs, Pfizer

Sodium chloride, isopropyl alcohol and glycerin–what do all these have in common? Not sure? Well, all three are commonly used as excipients and/or adjuvants in drug products. But, as they say in the TV commercials: "wait there's more." All may be active ingredients in drug products. Normal saline, hand sanitizers and glycerin suppositories would all list these as active ingredients. They are not typically considered to be such, but in some circumstances, they may become active pharmaceutical ingredients (APIs). So if they are not typically considered to be APIs, what are they when used in products such as those mentioned above? They are, in fact, atypical active ingredients. Why is that important?

Well, as I'm sure we are all aware, the manufacture of APIs is required to be done in compliance with current good manufacturing practices. This means that, taken literally, these APIs must be manufactured in compliance with the criteria in ICH Q7, Good *Manufacturing Guide for Active Pharmaceutical Ingredients*. How realistic is that? Do the manufacturers of these and other atypical active ingredients, who prepare literally thousands of tons or more of these chemicals, do so in compliance with ICH Q7? We are not in that business, but if asked to speculate we would guess not.

What would happen if they needed to comply with all the criteria of ICH Q7 to continue to supply the pharmaceutical industry? Would their business model support the costs associated with the additional controls necessary to comply with all the ICH Q7 criteria? Again, we can only speculate, but we would guess not. What then would happen to the drug products using these atypical active ingredients? Continued speculation leads to the possibility that they might disappear from the market.

The Parenteral Drug Association presents...

PDA/FDA Atypical Actives Workshop

Coming Together to Develop Solutions

March 9-10, 2011

Hyatt Regency Bethesda
Bethesda, Maryland

Conference brochure now available. Request yours today!

Atypical Actives are chemicals that do not have an obvious medical function and yet have been designated as the API in marketing authorization. These Atypical Actives may not always be manufactured according to ICH Q7 because they are intended for use in other industrial sectors. **Continued use of APIs not manufactured according to ICH Q7 brings the drug product holder in conflict with regulatory requirements.**

Join together with industry and regulatory experts, including FDA and EMA representatives, to openly discuss and debate these important topics.

Plenary sessions with over 15 presentations will discuss:

- Perspectives from the users, makers and regulators
- Liability issues from both the makers side and the user side
- US and EMA regulatory perspectives
- Case studies and breakout sessions
- What happens when your Excipient is used as an Atypical Active?
- *And so much more!*

The breakout sessions at this workshop will cover **Technical Considerations** and **Regulatory Considerations**.

For details and to register, visit
www.pda.org/atypicalactives2011

What is PDA?
The Parenteral Drug Association (PDA) is a global non-profit organization of over 9,500 members. Our focus and emphasis is in the areas of **sterile product technology, biotechnology and quality and regulatory compliance concepts and systems** - become a part of our community, join PDA today!
www.pda.org/join

Recognizing this dilemma, PDA and the U.S. FDA have teamed up to develop the a workshop on atypical actives. The *2011 PDA/FDA Atypical Actives Workshop* will be held in Bethesda, Md., on March 9–10. It will explore the complex issues and questions surrounding the manufacture and use of these compounds. The workshop will feature plenary sessions on day 1, allowing users of atypical actives and regulators to provide their perspectives. Legal aspects will also be covered in a day 1 plenary session as will a discussion of some of the sourcing and marketing issues associated with these compounds.

Following a discussion of case studies on day 2 presented by manufacturers, users and regulators, the workshop will split into breakout sessions where the real work will take place. Attendees will have the opportunity to discuss the technical considerations and regulatory considerations associated with the manufacture and use of atypical actives. The workshop will be structured so these breakouts are repeated a second time, allowing attendees to participate in both breakouts.

The workshop will conclude with a summary of the breakout sessions, including major issues and recommendations for a way forward to resolve these issues. What better way to participate in helping to shape the future of the manufacture, use and regulatory scheme for atypical actives than to participate in this workshop?

The workshop will be held at the Hyatt Regency Bethesda, conveniently located at the Bethesda station on the Washington, D.C. Metro, just 45 minutes from Reagan National Airport, Dulles International Airport, and Baltimore/Washington International Airport and only 30 minutes from Amtrak's Union Station. With any luck, Washington, D.C.'s cherry trees will be in blossom and, take it from those who know, they are absolutely spectacular.

The convenience of the venue, the desirable attributes of the Washington, D.C. area, and most of all, the critical importance of this topic make attendance an absolute must if you are involved in the manufacture, use or regulation of atypical active ingredients, including those involved with purchasing, supply chain and contract manufacturing operations, as well as more traditional functions such as manufacturing, quality assurance and regulatory affairs. Visit the workshop website, www.pda.org/atypicalactives2011, for more details including a detailed agenda and information on how to register. On behalf of the Program Planning Committee, we look forward to seeing you there.

Conference Focuses on Solutions to Supply Chain Issues

Bethesda, Md. • March 1-4 • www.pda.org/coldchain2011

Conference Chair Rafik H. Bishara, PhD, PDA's Pharmaceutical Cold Chain Interest Group Leader

In its sixth consecutive year, the *2011 PDA Pharmaceutical Cold Chain Management Conference* will focus on the various challenges, solutions and case studies regarding integrated supply chain management and Good Distribution Practices (GDP). Representatives from the United States Pharmacopeia, industry and cold chain solution providers will discuss, review and debate many of these cold chain issues as it pertains to importation, naturalization and distribution. Experts from Brazil with industry experience will share their regulatory objectives, key compliance activities and solutions to the common problems that shippers experience in their efforts to import, export and distribute pharmaceutical products in this region of the world.

We have designed a session on how to set up a stability budget. This session will describe and justify studies using scientific data and rationale necessary to determine an appropriate stability budget for a drug substance or drug product. A stability budget considers the results of long term, accelerated, freeze/thaw, and temperature cycling studies to determine the amount of time out of storage that a drug may experience without any significant risk to its quality. Firms have used the idea of a stability budget to assign permissible time out of storage for packaging and labeling operations for refrigerated drug products for some time. This concept has been expanded by the PDA task force into a draft document to include storage and distribution as well. It is intended to complement existing guidance on stability studies and maintaining the quality of pharmaceuticals during distribution.

With the overwhelming number (and volume) of GDP regulations and guidelines from both industry and MOH's, a special session will address what are "they" asking us to do? This session will identify the 30+ GDP world-wide regulations, guidelines and position papers on the GDPs and will outline and summarize a clear understanding of what is expected. Topics including temperature management, supply chain integrity and information control/sharing will be discussed.

Smart shippers and the reusability of containers will demonstrate will be discussed. A first time review of the recommended guidance by the PCCIG's Active Packaging Systems Task Team will also be presented.

On behalf of the Program Planning Committee, I extend a personal invitation to you and your colleagues to join us on March 1 – 2 in Bethesda, Md., for what is promising to be an informative, stimulating and engaging conference. I also you to extend your stay in Bethesda for the PDA Training and Research Institute course, "Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems" March 3-4 at the PDA Training and Research Institute in Bethesda, Md.

For more details on the conference, course, agenda and to register online, please visit www.pda.org/coldchain2011.

The Parenteral Drug Association presents the...

2011 PDA Pharmaceutical Cold Chain Management Conference

Cold Chain – Reaching for Global Scientific Consensus for Patient Safety

Conference Brochure Just Released!

March 1-4, 2011

Bethesda North Marriott Hotel
Bethesda, Maryland

Attend this conference to participate in over 19 presentations in sessions that include:

- Regulatory Updates
- Case Study – Compliance with Cold Chain Importation/ Nationalization/Distribution of Product Requirements in Latin American Countries
- Global Comparison of Cold Chain/GDP Regulations
- A Stability Budget as a Means of Protecting Drug Quality in the Distribution Environment
- Smart and Reusable Containers for Good Cold Chain Management
- Update from Academia
- Update on Shipping System Qualification and Process
- Compliance with GDP, GIP and Labeling Requirements

Expert speakers from: USP; FDA (invited); Abbott US and Brazil; Eli Lilly US and Argentina; FedEx Custom Critical; Johnson & Johnson; Kirsen Global Security; University of South Florida Polytechnic; Packaging Science Resources; Sensitech, Inc. and more!

Advance your cold chain knowledge by attending the PDA Training and Research Institute (PDA TRI) course, *Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems*, March 3-4.

CONFERENCE March 1-2 **EXHIBITION** March 1-2 **COURSE** March 3-4

www.pda.org/coldchain2011

A New Standard for GMP and Quality Discussions in Europe

London Heathrow, UK • May 3-6 • europe.pda.org/pdaema2011

Jim Lyda, PDA

PDA and the European Medicine Agency are pleased to co-sponsor the *2011 PDA/EMA Joint Conference* in London. This year's conference, the fourth since 2006, has an increased scope beyond GMP to include an array of quality issues around pharmaceutical development, production and quality management. Input from European Medicines Agency's Quality Working Party, Biologics Working Party and the GMP/GDP Inspectors Working Group can be seen in the scope of the agenda including increased CMC-related topics. The program has been extended to two and a half days, and the number of concurrent tracks increased to ten to make room for the expanded content.

This conference will supply critical and useful information to all companies and individuals, including small to medium enterprises involved in the development, production and quality management of medicinal and biopharmaceutical products. The plenary sessions on each morning of the conference will address universal themes of interest to the all segments of our business.

The ten parallel tracks on the afternoons of May 3 and 4 will provide coverage of more detailed technical or regulatory topics. The parallel tracks include:

- Process optimization
- Quality
- Regulatory Affairs
- Advanced Therapies
- Supply Chain
- Trends in Manufacturing
- Biologics
- Orphan Drugs

The planning committee has specifically focused on issues of interest to start-ups, small and medium enterprises. Over 25 speakers from the European Medicines Agency and the national Health Authorities will be present at the conference. The venue at London's Heathrow Airport makes access to the conference convenient for travelers from across Europe and the United States.

The conference will be useful for persons desiring technical and regulatory information on process optimisation, quality management, CMC and regulatory affairs, GMP, advanced therapies, supply chain, trends in manufacturing, biologics and orphan drugs. It will also be very helpful for persons involved in: inspection/audit, process development, validation, pharmaceutical R&D, CMC and regulatory affairs, manufacturing, QA/QC, compliance and related disciplines.

PDA extends sincere appreciation to the planning committee for development of this special program

Co-Chairs

Riccardo Luigetti, European Medicines Agency

Lothar Hartmann, F. Hoffmann-La Roche

Regulatory Authorities

David Cockburn, European Medicines Agency

Nick Gate, European Medicines Agency

Steffen Gross, Paul-Ehrlich-Institut, Germany

Anne Junttonen, Finnish Medicines Agency

Vasiliki Revithi, National Organization for Medicines, Greece

Peter Richardson, European Medicines Agency

Jean-Louis Robert, Laboratoire National de Sante, Luxembourg

Jean-Hugues Trouvin, AFSSAPS, France

Industry

Véronique Davoust, Pfizer

Gabriele Gori, Novartis

Frank Hallinan, Pfizer

Barbara Jentges, PhACT

José Luis Ortega Conejero, PharmaMar

Søren Pedersen, Novo Nordisk

Siegfried Schmitt, Parexel Consulting

PDA Staff

Georg Roessling

James Lyda

Robert Dana

Harmonization Report, continued from page 34

frame of the document's scope and in alignment with Q3D and Q11. A first draft for internal discussions (Step 1) is expected by the next ICH meeting.

The next ICH Steering Committee and its expert working groups is scheduled for Cincinnati, Ohio on June 11-16.

References

1. "ICH Steering Committee, Fukuoka, Japan, 10-11 November 2010," *ICH*, www.ich.org/ichnews/press-releases/view/article/fukuoka-japan-november-10-11-2010.html
2. "Quality Guidelines," *ICH*, www.ich.org/products/guidelines/quality/article/quality-guidelines.html
3. "ICH Q8/Q9 Q10,"*ICH*, www.ich.org/trainings/ich-trainings/ich-q8q9q10.html

PDA/EMA 2011 Conference

Regulation, Cooperation, Innovation: An Effective Partnership among Authorities and Industry in Europe

Register by 7 March 2011 and SAVE!

3-6 May 2011

London Heathrow, UK

The 2011 PDA-EMA Conference includes an expanded agenda with a full range of GMP, Quality and CMC issues relating to pharmaceutical development, production and quality management. Input from EMA's Quality Working Party, Biologics Working Party and GMP/GDP Inspectors Working Group have resulted in a conference which includes the following highlights:

- Over 25 speakers from EMA and National Health Authorities
- From over 15 speaker from industry & affiliated organizations
- Three morning plenary sessions
- Ten afternoon parallel tracks with open discussions
- Eight topic areas:
  - Process optimisation
  - Quality
  - Regulatory affairs
  - Advanced therapies
  - Supply chain
  - Trends in manufacturing
  - Biologics
  - Orphan drugs and SMEs
- Convenient venue at London Heathrow Airport

CONFERENCE, EXHIBITION TRAINING COURSES

https://europe.pda.org/PDAEMA2011

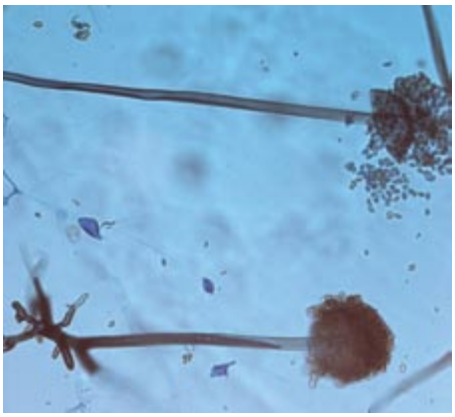
Teaching the Environmental Mycology Identification Workshop

Bethesda, Md. • April 26-28 • www.pdatraining.org/mycology

John Brecker, Fleet Laboratories

Two things I really look forward to every year are summer vacation and teaching the *Environmental Mycology Identification Workshop* for PDA's Training and Research Institute (PDA TRI). The workshop for me is both challenging and rewarding. Over the last ten years, this workshop has grown with more and more information added each year. Without a doubt, this workshop has allowed me to improve my ability as a trainer. Each participant brings enthusiasm and energy, making it such a great course because every participant has the opportunity to share their unique experiences in identifying molds. I have even found myself learning from the experiences shared by participants over the years. The course not only encompasses one-on-one instruction but also group discussions on current topics of interests such Quality Control and GMP compliance issues related to fungi.

The workshop is designed to give the participants the necessary tools to be able identify mold and yeast isolates with confidence, thus increasing their firm's compliance structure. The majority of the time will be spent in the laboratory where the workshop offers not only a large number of examples of fungal species but also examples of these species growing on different types of selective media. The laboratory setting at TRI is perfect for learning and practicing new techniques for identification. The participants will follow the identification procedure from detection to the preparation of sub-cultures using several recommended procedures and media. Participants will be challenged during the workshop to identify several unknown species of fungi using both macroscopic and microscopic observations.



The laboratory setting at TRI is perfect for learning how to identify species at a microscopic level

The identification of fungi found in raw materials or pharmaceutical products can present a big challenge to the QC Microbiology Laboratory. Regulatory guidelines for investigations and CAPAs when results exceed action limits will require the identification of microbial contaminants, including fungi. Key product or raw material release decisions and environmental monitoring trends are frequently contingent on the identification of fungi to, not only genus, but to the species level. Contract laboratories can be used for identification of fungal isolates; however, it is possible to save both time and money if the identification process can be conducted in-house.

There is one question I hear a lot: Which reference books would I recommend for a QC Microbiology Lab? There are many good reference books out there and we cover a lot of them in the workshop. But, I would have to say one of my favorites is, *Illustrated Dictionary of Mycology* by **Miquel Ulloa** and **Richard Hanlin**. This book has excellent drawings and photographs of microscopic images to assist in visual identifications. The definitions of technical terms are very helpful for drafting a standard operating procedure for identification.

SOPs are an essential part of the identification process. The steps necessary to establish an SOP for identification of fungi will be discussed in the course. Maintaining in-house cultures for fungal isolates, rapid methods for mold identification and an exercise for designing dichotomous keys for in-house isolates will also be included in the workshop. Each participant will be given a copy of the detailed workshop manual that includes microscopic images. A reference book will also be given to each participant.

John Brecker helps a student during his course at TRI

It is an inspiration to me when I see the look of self-confidence on the face of the participants when they realize they can apply their knowledge and experience to identify unknown, environmental mold isolates. The demand is high and seating is limited so it is important to register as early as possible. Do not miss this exciting and valuable course.

For detailed course information and to register, visit www.pdatraining.org/mycology. If you would like additional information about this or other laboratory courses, please contact **James Wamsley** at wamsley@pda.org.

About the Author

John Brecker, Senior Microbiologist, Fleet Laboratories is certified as a Registered Microbiologist, Consumer Products and Quality Assurance through the American Academy of Microbiology-National Registry of Microbiologists. He has spent thirty years as a Quality Control Microbiologist for pharmaceutical, biopharmaceutical and personal care product manufacturers. His expertise includes microbial identifications, microbiological testing and validations, environmental monitoring as well as research and development.

Parenteral Drug Association Training and Research Institute (PDA TRI)

Upcoming Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

Save **10%** by registering early! *

Become a PDA member and save even more on your course registration!

March 2011

Hosted in conjunction with the *2011 PDA Pharmaceutical Cold Chain Management Conference:*

Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems

March 3-4, 2011 | Bethesda, Maryland | www.pdatraining.org/globalregulations

Aseptic Processing Training Program: Session 2

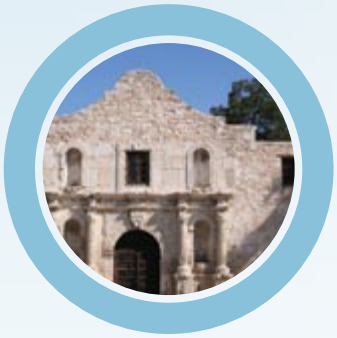
Week1: March 7-11, 2011
Week 2: April 4-8, 2011
Bethesda, Maryland | www.pdatraining.org/aseptic

Prefilled Syringe Week

March 21-25, 2011 | Bethesda, Maryland | www.pdatraining.org/prefilledweek

- Solving Strategic Quality, Regulatory and Technical Issues During the Development of Prefilled Syringes, AutoInjectors and Injection Pens (March 21-22)
- Development of Prefilled Syringes (March 23-24)
- Syringes and Elastomers: Understanding the Effects on Quality and Demonstrating the Production Process, Influences and Needs (March 25)

April 2011



The 2011 PDA Annual Meeting Course Series

April 13-14, 2011 | San Antonio, Texas | www.pdaannualmeeting.org/courses

- GMP 101
- Steam Sterilizers – Getting It Right from the Beginning – *New Course*
- Rapid Microbiological Methods: Overview of Technologies, Validation Strategies, Regulatory Opportunities and Return on Investment
- DoE Basics for Validation by Design – *New Course*
- Cleanroom Management
- CMC Regulatory Compliance of Biopharmaceuticals
- Six Sigma in Process Validation – *New Course*

Environmental Mycology Identification Workshop

April 26-28, 2011 | Bethesda, Maryland | www.pdatraining.org/mycology

Laboratory Courses

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

* PDA's Aseptic Processing Training Program is not eligible for any discounts.

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

Editor's Message

A Virus of a Different Sort Hits the Letter!

This issue features my report from the PDA/FDA Adventitious Virus Workshop held last December. There's not much more I can say here about that meeting that's not already said in the article. It was an informative and helpful event from beginning to end. Look for more information on proceedings that PDA plans to publish later this year. The committee already is working on a follow up event, and the Letter will keep you informed of that as well.

There is another kind of virus that all manufacturers need to worry about, whether working with cell banks, vaccines, or traditional drugs. In fact, businesses of all stripes need to watch out for them, as should anyone who works with a computer at home or has a smartphone or a tablet device. Yes, computer viruses. What a strange twist of fate that my workstation at PDA would be infested and nearly completely destroyed by a Trojan Horse virus the same week I received my February issue of *Wired* magazine, which included an article on off-the-shelf hacking software, and during the same month I wrote a report from an adventitious virus meeting. So, not only was I reminded of my desktop's ailments every time I entered my office and saw the gaping empty space where the machine used to sit, but I thought about it at home when I read my magazine and as I edited the *Letter*.

Fortunately, all of my important work is stored on PDA's network. Nevertheless, much damage was done, unfortunately, though nothing as bad as what would happen when a plant is infected with a real, living virus. But, it leaves one wondering: What was on the computer that I need? What was on there that was confidential or personal that now could expose me to identity theft or worse crimes? Can we recover anything?

Then you start thinking about how you got the virus and how dumb you feel for opening up your computer to it. In this case, I was scanning Google images to get ideas for the March cover of the *PDA Letter*. Several pages into the results, I clicked on a really cool photo and, sure enough, all hell broke loose. Two fake antivirus programs launched. At first I couldn't tell if they were PDA's programs or the Trojan Horse viruses that are common. I quickly realized what was happening and unplugged my computer from PDA's network. The IT folks came over and deactivated all of it, and then the hard drive crashed.

Thankfully, as I was actually writing this, I received word that they will be able to recover data from the hard drive (without sending it out to the "Geek Squad" which I'm wary to use under any circumstances—sorry Best Buy). As to what can be recovered, that remains to be seen.

So that's my personal adventitious virus story (all true, unfortunately). I hope it serves as a warning to be very careful when browsing the internet. I shudder to think of all the time my own middle-school aged son has gone on Google on my home PC to get images for projects. That will be ending, for sure!

PDA Letter

The PDA Letter is published 10 times per year, exclusively for PDA members.

Subscriptions are not available.

PDA Global Headquarters — Bethesda Towers

4350 East West Hwy., Suite 200
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900 Fax: +1 (301) 986-0296
info@pda.org
www.pda.org

PDA Europe — Adalbertstr. 9

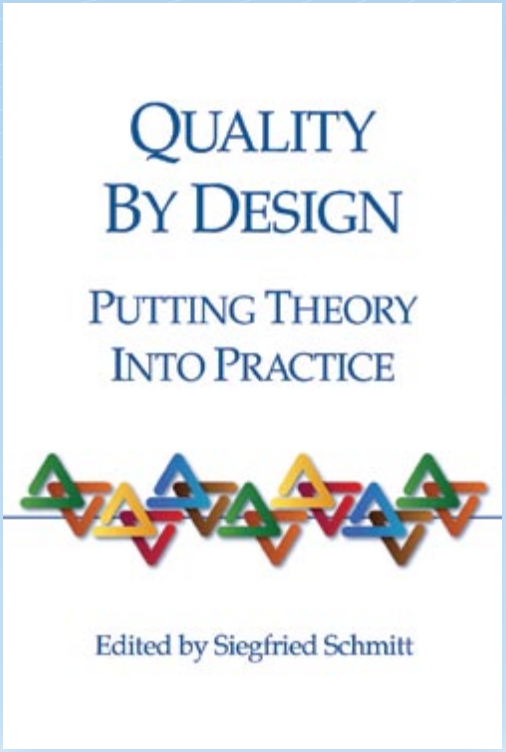
16548 Glienicke/Berlin Germany
Tel: +49 33056 23 770 Fax: +49 33056 23 7777
petzholdt@pda.org

PDA Training & Research Institute

4350 East West Hwy., Suite 150
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900 Fax: +1 (240) 482-1659
info-tri@pda.org

Last Call for Pre-orders!
Save 10% by ordering your copy before February 28th!

New Release at the PDA Bookstore



Quality By Design: Putting Theory Into Practice

Edited by Siegfried Schmitt

The process of adoption, implementation and interpretation of Quality by Design is currently the key driver to help industry bring products to market faster and at the same time provide maximum assurance of product quality. Though pharmaceutical companies need to abide the law and therefore comply with the applicable laws, rules and regulations, their goal must be to be profitable. A business case must therefore not only outline how compliance can be achieved, maintained and improved, but also how this will result in a positive financial impact.

In this publication, global subject matter experts offer invaluable information that will guide companies who wish to:

- Proactively address regulatory trends
- Reduce or eliminate the number of reworked batches
- Achieve better manufacturability and process robustness
- Drastically reduce recalls
- Achieve leadership in the industry

This publication was written with all stakeholders in mind; the regulatory agencies and the healthcare industry, including their suppliers.

www.pda.org/QualitybyDesign

The PDA Bookstore's January Top 5 Best Sellers

1 **Recent Warning Letters Review for Preparation of an Aseptic Processing Inspection**
By Jeanne Moldenhauer
Item No. 17292
PDA Member
$280
Nonmember
$349

2 **Cleaning and Cleaning Validation, Volume 1**
Edited by
Paul L. Pluta
Item No. 17288
PDA Member
$335
Nonmember
$419

3 **Environmental Monitoring: A Comprehensive Handbook, Volume IV**
Edited by
Jeanne Moldenhauer
Item No. 17291
PDA Member
$335
Nonmember
$419

4 **Practical Aseptic Processing: Fill and Finish, Volume I and II**
Edited by
Jack Lysfjord
Item No. 17283
PDA Member
$425
Nonmember
$530

5 **Validation by Design®: The Statistical Handbook for Pharmaceutical Process Validation**
By Lynn D. Torbeck
Item No. 17266
PDA Member
$265
Nonmember
$329

www.pda.org/bookstore | Tel: **+1 (301) 656-5900** | Fax: **+1 (301) 986-1361**

The Parenteral Drug Association Presents...

2011 PDA ANNUAL MEETING

Harnessing the Power of Knowledge to Drive World Class Science and Technology

Over 45 Presentations by Industry and Regulatory Experts

1946 65TH ANNIVERSARY 2011

April 11-15, 2011

JW MARRIOTT SAN ANTONIO HILL COUNTRY
SAN ANTONIO, TEXAS

www.pda.org/annual2011

Join PDA for the 65th PDA Annual Meeting, themed *Harnessing the Power of Knowledge to Drive World Class Science and Technology*, which will support over 45 presentations in sessions which will include:

- Submissions – Perspectives from Both Sides
- Advances in Single-Use-Systems
- Advanced Approaches in Environmental Monitoring
- Applications for Integrating Risk Management
- Moist Heat Sterilization
- Freedom From Paper and Efficient IT Systems for cGMP's QC/QA Environments
- Post Implementation – Maintaining a Change Control Program
- Contamination Control
- Manufacturing Protein Therapeutics
- Plus many, many more excellent topics to be discussed!

New Fundamentals Track! April 12, 2011	Process Validation Post Conference Workshop, April 13-14, 2011	PDA TRI Courses, April 13-15, 2011
Are you new to the industry or have recently changed jobs? This is the perfect time to join us for our **New Fundamentals track** aimed at those who are new to the pharmaceutical/ biopharmaceutical industry, or have recently changed jobs with an associated change in focus.	Hear Directly from FDA Guidance Authors. This workshop will explore US and International regulations, technology transfer, documentation strategies, post approval reporting and so much more!	Seven PDA Training and Research Institute (PDA TRI) courses like: **GMP 101, Steam Sterilizers: Getting It Right from the Beginning – *New Course*, DoE Basics for Validation by Design – *New Course***, plus many more.

www.pda.org/annual2011

MEETING April 11-13 | **EXHIBITION & CAREER FAIR** April 11-12
PDA PROCESS VALIDATION GUIDANCE POST CONFERENCE WORKSHOP April 13-14 | **COURSES** April 14-15