People • Science • Regulation

PDA Letter

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Considerations for Successful Design, Operation and Maintenance of an Ultrapure Water System

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Results from PDA's Benchmarking Survey on Glass Quality will be shared at this conference.

The Parenteral Drug Association presents the...

PDA/FDA Glass Quality Conference

June 4-5, 2012

Renaissance Downtown Hotel | Washington, D.C.

The *PDA/FDA Glass Quality Conference* will carry on the mission of continuous learning to understand the risks associated with glass containers and use with pharmaceutical and biopharmaceutical products. Trends toward novel products such as imaging for diagnostics, biomarkers, tissue engineering, nano carriers and stem cell therapies can potentially bring a host of issues not yet discovered.

This conference will convey an in-depth understanding of glass materials, manufacturing, handling and strategies for qualification and control.

Highlights include:

- **HOT TOPIC:** Keynote Speaker **David Jaworski**, Acting Branch Chief, Domestic Compliance Branch, Division of Domestic Drug Quality, *FDA* will present on FDA Regulatory Expectations and Lessons Learned on Glass Recalls.
- **Plenary sessions on:**
  - Development Considerations/Glass
  - Pharmaceutical Packaging in Glass
  - Glass Handling Equipment Manufacturers Perspective
  - Quality Control Issues
  - Distribution/Packaging/Transportation
  - Monitoring Customer Feedback & Other Factors to Consider in Glass Defect Prevention
  - What Are We Going To Do To Make It Better?
- The PDA has conducted a benchmarking survey to understand glass quality and your perceptions of glass quality and glass suppliers. The results of this survey will be compared with the 2011 survey and shared with the attendees at the conference.
- And much more

Immediately following the conference, PDA's Training and Research Institute (PDA TRI) will be hosting two stand-alone training courses on-site on June 6-7.

Visit **www.pda.org/glass2012** for more information and to register

Exhibition: June 4-5 | Courses: June 6-7

Rebecca Rodriguez, National Drug Expert Investigator, *ORA, FDA* will give a presentation on *Validation of the Aseptic Process and Inspection Trends From a Regulatory Perspective*

The Parenteral Drug Association presents the...

2012 PDA Innovation & Best Practices on Sterile Technology Conference

Sterility Assurance for Aseptic Processes and Terminal Sterilization

June 18-19, 2012 | Conrad Chicago | Chicago, Illinois

The *2012 PDA Innovation & Best Practices on Sterile Technology Conference* will concentrate on the state of sterile product manufacturing for the healthcare industry including updates on regulatory expectations, innovative technologies, process design and decision making methods and sources of valuable knowledge.

Highlights of this meeting include:

- **Opening Plenary Session: Applying Quality Risk Management in Sterile Manufacturing – Case Studies.** This opening session will explore the integration of ICH Q8, Q9 and Q10 to develop, implement and sustain a sterile drug product manufacturing control strategy and utilization of quantitative risk modeling to rapidly assess risk of bioburden ingress during aseptic filling.
- Additional sessions include:
  - Contamination Control and Remediation
  - Application of PDA TR No. 1 Sterilization Science Concepts
  - Evolving Novel Sterilization Technology
  - Case Studies on Risk Based Approaches for Sterile Product Facility Design
  - Trends in Sterile Product Manufacturing Regulatory Expectations
  - PDA Technical Report: Answers to Your Sterile Product Questions
  - Ask the Experts Panel Discussion – The Future of Sterile Product Manufacture – Trends, Issues and Solutions
- Interest Group meetings for Clinical Trial Material and Sterile Processing/Blow-Fill-Seal
- A series of new and revised PDA Technical Reports on sterilization and aseptic processing will be showcased as well as a brief update to USP's Sterilization Chapters and the rewrite of USP ‹1207›.
- And much more

Immediately following the conference the PDA Training and Research Institute (PDA TRI) will be hosting four on-site stand-alone courses June 20-21.

Visit **www.pda.org/steriletechnology2012** for more information and to register.

Exhibition: June 18-19 | Courses: June 20-21

Photo Courtesy of Sartorius Stedim Biotech

PDA Letter

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22 Considerations for Successful Design, Operation and Maintenance of an Ultrapure Water System

Water is undoubtedly the most fundamental requirement in the pharmaceutical manufacturing environment, but it is often an overlooked commodity in terms of maintenance and assurance of low bioburden levels. While multiple preventive measures are implemented into most water purification systems, contamination of the water by microorganisms remains a cause for concern.

29 Biofilm Myths

The following was adapted from the presentation, "Design and Control Strategies to Minimize Biofilm Risk," given on April 17, 2012 at the *2012 PDA Annual Meeting*.

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The scope of *PDA Technical Report, No. 55, Detection and Mitigation of 2,4,6-Tribromoanisole and 2,4,6-Trichloroanisole Taints and Odors in the Pharmaceutical and Consumer Healthcare Industries* provides guidance on how to detect and mitigate 2,4,6-tribromoanisole and 2,4,6-trichloroanisole taints and odors from tribromophenol-treated wood pallets.

36 Tracking (and Tracing) Counterfeits in the Supply Chain

The U.S. FDA is pushing harder for the implementation of track and trace methods for drug products to protect patients from dangerous, low-quality fakes. Recent findings of counterfeit Avastin, a Roche anticancer drug, only heighten FDA's concern over the growing threat to patient safety in the United States.

Staunch Contributors Honored at Annual Meeting Banquet

Each year, PDA recognizes the dedicated contributors who have help shape the Association in recent years at the Annual Meeting Awards Banquet, traditionally held the night before the conference begins. The banquet is a joyous occasion where awardees and their guests are celebrated and have a chance to meet other PDA volunteers.

PDA congratulates each winner and thanks them for their service to the Association. Look for detailed coverage on each award winner throughout the year leading up to the 2013 Annual Meeting in Orlando, Fla.

Honorary Membership

This is PDA's most prestigious award, conferring lifetime membership benefits to the recipient. The award is usually given in recognition of very long service, of a very significant nature, to PDA. This year's recipient is:

James Agalloco, Agalloco & Associates

Gordon Personeus Award

This award is intended to honor a PDA member, other than a member of the PDA Board of Directors, for long-term acts or contributions that are of noteworthy or special importance to PDA. This year's recipients are:

Richard Friedman, U.S. FDA

Dr.-Ing. Stephan Rönninger, PhD, F. Hoffmann-La Roche

Frederick J. Carleton Award

This award is designated for a past or present member of the PDA Board of Directors whose services on the Board are determined by his/her peers as worthy of such recognition. This year's recipient is:

Kathleen Greene, Novartis Vaccines and Diagnostics

PDA/DHI Editor/Author Award

This award is presented annually for the best editor/author of PDA/DHI co-published books as selected by PDA members. This year's recipient is:

Siegfried Schmitt, PhD, Parexel

Distinguished Service Award

This award is given in recognition of special acts, contributions or services that have contributed to the success and strength of PDA. This year's recipients are:

Scott Bozzone, PhD, Pfizer

Vince Mathews, Eli Lilly

Edwin Rivera Martinez, Sanofi-Aventis

Michael Wiebe, PhD, Quantum Consulting

Lothar Hartmann, PhD, Crucell

Service Appreciation Award

The Service Appreciation Award is presented annually for special acts, contributions or services that have contributed to the success and strength of PDA. This year's recipients are:

Stefano Maccio, PhD, CTP Tecnologie di Processo

Peter Noverini, BioVigilant Systems

Myron Dittmer, MFD & Associates

Patricia Brown, Agilent Technologies

Ano Xidias, PharmOut

Maik Jornitz, Sartorius Stedim

Amy Scott-Billman, GlaxoSmithKline

Jens Eilertsen, PhD, Novo Nordisk

Norbert Hentschel, Boehringer Ingelheim Pharma

Frederick D. Simon Award

The Frederick D. Simon Award is presented annually for the best paper published in the P*DA Journal of Pharmaceutical Science and Technology*. This year's recipients are:

Guenther Gapp, PhD, Sandoz

Peter Holzknecht, Sandoz

James P. Agalloco Award

The James P. Agalloco Award is presented annually to the PDA faculty member who exemplifies outstanding performance in education. This year's recipients are:

Ed Trappler, Lyophilization Technology

Wenzel Novak, PhD, Groninger & Co

Michael S. Korczynski Award

This award funds travel expenses for an international guest to deliver the "Korczynski Paper" at a PDA Meeting. This year's recipients are:

Georg Roessling, PhD, PDA

Rafik Bishara, PhD, RHB Technical Advising

President's Award

This award recognizes a PDA staff member, other than Senior Staff, whose exemplary performance has contributed to PDA's success during the previous year. This year's recipients are:

Ailyn Kandora, PDA

Andrea Viera, PDA

On the forefront - Mab developments in Europe

Emerging Trends for Therapeutic Monoclonal Antibodies and Related Products

Considerations for Quality Attributes throughout the Development Continuum and Registration

Session 1: Development for biological IMPs

- What is the appropriate level of quality detail needed for biological IMP dossiers?
- Are acceptance criteria and details for in-process control required for early stages?
- How can an IMP dossier be built based on QbD principles?
- Degree of characterization of IMPs in early drug development?
- To what extent can shelf life dating be based on supportive data?

Session 2: Molecular Approaches to Optimization

- Can certain routine testing be eliminated based on molecule optimization strategies?
- Is it possible to optimize a monoclonal antibody drug substance to the point of having no critical quality attributes related to its molecular properties?
- How should molecule design features be communicated in the market application?
- What are the expectations for in vitro bioassays when more than one cell-killing target is involved?

Session 3: Late-stage Process Development

- How is process parameter criticality assessed and confirmed?
- How much can we rely on prior knowledge to support process characterization?
- What are the most frequent questions health authorities ask regarding the control strategy. What are the major missing elements in the dossier?
- What information on the control strategy needs to be provided during an inspection? How far back into process development does the inspector look?

Session 4: Development, Regulatory and Future

- What are Molecular particulars and how are they characterized?
- How do we characterize the starting material used to manufacture the Antibody Drug Conjugate (ADC)?
- What are the test methods used to investigate and quality control ADC and multifunctional antibodies?
- How do we characterize the linker-quality, its mechanism in-vivo and the relevant data requirements?
- What are the unique dossier structure and data requirements for ADC and multifunctional antibodies?

Not to be missed: Nathan Ihle, PhD, Seattle Genetics!

Workshop Co-Chairs:
Steffen Gross, *Paul-Ehrlich-Institut, Germany*
Michael DeFelippis, *Eli Lilly*

12-13 June 2012

Hotel NH Danube City
Vienna | Austria

WORKSHOP 12-13 June | **EXHIBITION** 12-13 June

Volunteer

Peter Noverini, Field Applications Scientist, BioVigilant Systems

PDA Join Date: November 2, 1999

Interesting fact about yourself: A few years ago, I took up homebrewing as a hobby, which requires proper sanitization practices, good aseptic technique and an understanding of how to properly grow and culture yeasts. This has allowed me to finally make my peace with microorganisms outside of my professional role of ensuring that they are properly controlled in clean rooms. The yeasts I use in homebrewing, however, have to promise to behave and never cause me late nights of dealing with adverse trend excursions ever again! I've also recently entered the exciting world of auto racing; the secret is that it's all about rapid risk management!

Why did you join PDA? In 1999, I had just transitioned into the pharmaceutical industry from the food industry, and I needed to come up to speed quickly on standards and guidelines in the pharma field and keep abreast of recent studies and happenings. The ubiquitous green journals provided a source of useful technical information and gave me a lens into the science and technology of parenteral manufacturing. Just as important, however, PDA gave me a network of individuals I could speak to at conferences and PDA chapter events for general discussion, advice and input.

Of your PDA volunteer experiences, which have you enjoyed the most? The chapter experience is the one that has brought me the most joy. Through interacting at the chapter level, I have made friendships and professional contacts that have lasted and grown over the years. In addition to dinner meetings, we have also had several day-long events, such as our upcoming contamination control event on June 8. We also have an annual golf outing (this year on August 10) that has continued to be a fun way for technical-oriented scientists to break out of their routine for a bit and meet up with other scientists and suppliers in the industry.

How has volunteering in PDA benefited you professionally? Volunteering has allowed me to have more face-to-face contact with industry experts, allowing their personal experiences to become more alive beyond the content of their written contributions. Two-way communication with these experts has allowed me to learn from these individuals in a more vibrant way and contributes to my knowledge and understanding of current science practices.

Which PDA conference/training course is your favorite? The annual microbiology conference has been the place for me to learn and speak to fellow individuals on my specific area of concentration: environmental microbiology and sterilization. I rely on this conference to give me cutting-edge information and new perspectives on where we are as an industry and to meet with representatives from companies who can facilitate these new paradigms. This conference has been so big and so expansive that we've had to create a new conference: the *2012 PDA Innovation & Best Practices on Sterile Technology Conference,* which will occur June 17-18 in Chicago, Ill. This conference will specifically focus on areas of innovation in sterile process technology. I'm on the planning committee for this meeting and look forward to this being an equally as informative conference.

What would you say to somebody considering volunteering with PDA? Absolutely volunteer. It is a must. If you signed up as a member for only the technical reports and journals, you are only getting a fraction of the full PDA membership experience. PDA can boast of a network of knowledgeable professionals who have contributed to the industry and whose professional experiences beyond the written word can breathe perspective and insight into your day-to-day operations. These experiences have helped round out my understanding the art and science of our industry and have better prepared me to address questions and solve issues within my own company.

If you would like to learn more or volunteer for a PDA chapter contact **Trevor Swan,** Manager, Membership and Chapters at swan@pda.org

Missouri Valley Holds Meeting on Industry, Enforcement Trends

Eldon Henson, Covidien

The PDA Missouri Valley Chapter held a dinner meeting at the Kansas City Airport Hilton Inn on current industry and enforcement trends in March.

Following networking and dinner, the chapter was addressed by two excellent speakers. **Miguel Hernandez** spoke first about compliance and enforcement issues as well as what was new at the U.S. FDA's Kansas City District Lab. Miguel provided an overview of FDA's current approach to compliance enforcement. He also provided some background on how the Compliance Branch of the District Office collaborates with the investigations team to ensure compliance. Miguel mentioned that the FDA is applying risk management in assessing GMP compliance of firms. A key element of their assessment involves the potential risk to the patient. When patient risk is high, FDA's action will be more direct and swift. When risk is low, FDA will generally exercise more flexibility unless repeat issues are noted.

To learn more about the Missouri Valley and other PDA chapters visit www.pda.org/Chapters.aspx

Miguel emphasized that his philosophy (and FDA's in general) is to work closely with industry—the earlier, the better—when issues or concerns are noted.

The next speaker, **Jim Polarine** provided an excellent overview of current industry trends including cleaning and disinfection, disinfection validation and current warning letter activity. He shared recent FDA warning letters and gave some of the background behind the citations. Jim also shared some ideas to prevent similar issues. His presentation gave a number of excellent reference materials to chapter members. Several members noted that his comments directly addressed current issues that they struggle with in their operations.

Next, each sponsor was introduced and was provided an opportunity to share brief information on their products and/or services. These sponsors included:

- cGMP Validation (represented by **Laura Gillikan**)
- Stantec (represented by **Kishore Warrier**)
- Regulatory Compliance Associates (represented by **Mike Silvola**)
- Commissioning Agents (represented by **David Shenberger**)
- Particle Measuring Systems (represented by **Mark Hollworth** and **Beth Lyons**)
- ACH Foam (represented by **Keith Baechle**)
- ProPharma Group (represented by **Ben Frey**)

We thank the sponsors for their continued support of our chapter.

Finally, the new chapter officers were introduced:

- **Eldon Henson**, President
- **Jeff Hargroves**, Vice President
- **Gary Klaassen**, Secretary
- **Keith Koehler**, Treasurer
- **Valerie Welter**, Board Member
- **Luann Wolfgram**, Board Member

Approximately 65 members, sponsors and guests attended. Our next chapter event is tentatively scheduled for mid-September in the St. Louis, Mo. area.

PDA Who's Who

Jeff Hargroves, President, ProPharma Group, and PDA Missouri Valley Chapter Vice President

Eldon Henson, Director, Operations, Technical Services, Covidien and PDA Missouri Valley Chapter President

Miguel Hernandez, Director, Compliance Branch, Kansas City District Lab, U.S. FDA

Gary Klaassen, Quality Assurance, Bayer Health Care and PDA Missouri Valley Chapter Secretary

Keith Koehler, Management, Certified Energy Labs and PDA Missouri Valley Chapter Treasurer

Jim Polarine, Technical Services Manager, Steris Corporation

Valerie Welter, Sr. Director, Quality Management, Teva Animal Health and PDA Missouri Valley Chapter Board Member

Luann Wolfgram, Chair, Biotechnology, Johnson County Community College, and PDA Missouri Valley Chapter Board Member

Faces & Places: 2012 Parenteral Packaging

March 13–15, 2012

(l-r)Claudio Buccardi,Bormioli Rocc;Lodovico Gavioli,Bormioli Rocco;Daniele Zuccato,Nuova Ompi;Claudia Petersen,Gerresheimer

(l-r) Georg Roessling, PDA; Thomas Schoenknecht, Schott

PDA Japan Chapter Holds 18th Annual Meeting in Tokyo

Japan Chapter Board Member Osamu Kawamata, PhD, SRL

The PDA Japan Chapter held a very successful 18th Annual meeting on November 8-9, 2011 at the Tower Hall Funabashi in Tokyo with 334 attendees. The meeting also included an exhibition and luncheon seminar sponsored by pharmaceutical and pharmaceutical-related companies.

The main theme of this meeting was *What Can We Do to Protect Our Lives—Work Together* and Meeting Chair **Izumi Saitoh**, PhD, gave an opening address.

A special session at the meeting, *The Earthquake and Reconstruction,* addressed the earthquake that occurred in Japan on Friday, March 11, 2011. The earthquake had a magnitude of 9 and struck off the coast of the Tohoku area. The resulting tsunami brought great destruction along the coastline and caused a number of nuclear accidents, primarily the ongoing Level 7 meltdowns at three reactors in the Fukushima Daiichi Nuclear Power Plant complex. Many factories were destroyed and roadways and airports suffered severe disruptions in this area. However, many pharmaceutical companies made great efforts to supply medicine to the people who were in the restricted area.

The presentations in this session focused on the efforts of the Ministry of Health, Labor and Welfare to stabilize medical supplies, the restorations of the factories that had suffered devastating damage and the continuous medical supplies Towa Pharmaceutical contributed to those who suffered during the earthquake.

During our annual meeting, we were also fortunate to hear from three overseas presenters. **Richard Johnson** spoke about PDA's Training & Research Institute, PDA's Paradigm Change in Manufacturing Operations (PCMO℠) initiative and PDA's planned activities with its Asia-Pacific Chapters. **Yi-Ching Liao** gave a presentation about implementing PIC/S GMP in Taiwan and our third presenter, **Edwin Rivera Martinez**, former Chief, International Compliance Branch, U.S. FDA, explained the Agency's January 2011 Process Validation Guidance.

We also had the opportunity to hear a presentation on current topics from the Pharmaceuticals and Medical Devices Agency.

During the Annual Meeting, each interest committee of the PDA Japan Chapter gave a presentation.

These interest committees covered a myri-

Validation/QS Event Success Signals Time for Texas Chapter?

Trevor Swan, PDA

On February 23, PDA held a half-day event on validation and quality systems in Austin, Texas.

PDA President **Richard Johnson** began the day with a discussion of the current state of pharmaceutical and biopharmaceuticals business, challenges and regulatory trends.

His presentation was followed by **Hal Baseman** who spoke about PDA's comprehensive response to the U.S. FDA's recently released guidance on process validation, which included significant commentary from PDA members via a special working group in conjunction with the PDA Process Validation Interest Group. The final version of FDA's revised guidance addressed much of the input discussed at the process validation's workshops that were held around the United States, Puerto Rico and Europe. Hal's talk also included a preview of the PDA technical report on process validation that will be published later this year.

The next presentation was given by **Sue Schniepp**. She highlighted some of the challenges that face contract manufacturing organizations, such as the importance of establishing a quality system that meets the requirements of a variety of clients. The significance of robust quality agreements and dynamic audit programs were central to the detailed account.

After lunch the meeting proceeded with a discussion of internal auditing of quality systems given by **Julie Thomas**. Her talk focused on the benefits of a well-constructed audit program. It is important, she said, to provide vital information that can support continuous improvement to upper management. This will give the firm the chance to prepare and practice for the "real thing."

The day's final topic was presented by **Mihaly Ligmond**. He provided a colorful account of the inspection of quality systems from an investigator's perspective. He spoke about what he looks for during an investigation and why. Mihaly also gave an overview of FDA's compliance program and encouraged the audience to take the time to actually read about it!

In addition to these "hot topics," the event was held in part as an effort to assess the interest in a PDA Texas Chapter. For years, PDA members in Texas have been part of the Midwest Chapter based in Chicago, Ill. The great turnout at this event was an indication to all that the time for a Texas chapter has come.

The meeting was supported by Platinum Sponsors Globiox, Particle Measuring Systems and Veltek Associates with additional support from Gold Sponsors Hach Company and Commissioning Agents.

If you would like to learn more about how you can support PDA chapter activities in Texas, contact **Trevor Swan** at swan@pda.org today!

PDA's Who's Who

Hal Baseman, COO, ValSource

Richard Johnson, President, PDA

Mihaly Ligmond, Drug National Expert, Division of Domestic Field Investigations, U.S. FDA

Sue Schniepp,Vice President, Quality, OSO BioPharmaceuticals Manufacturing

Trevor Swan, Manager, Membership and Chapters, PDA

Julie Thomas, Quality and Regulatory Consultant, Mirna Therapeutics and Senior Regulatory and Quality Assurance Consultant, Emergo Group

ad of topics, such as:

- ICH Q10
- Medical Device and Combination Products
- Nonsterile Drug Products
- Computerized Systems and Globalization
- ICH Q11
- Quality Assurance of Sterile Products

PDA's Who's Who

Richard Johnson, President, PDA

Yi-Ching Liao, Assistant Researcher, Taiwan FDA

Edwin Rivera Martinez, Vice President, U.S. Quality Liaison, Global Quality, Sanofi-Aventis

Izumi Saitoh, PhD, General Secretary, The Cell Science Research Foundation

Edwin Rivera Martinez explains FDA's January 2011 Process Validation Guidance at PDA's Japan Chapter's Annual Meeting

Please Welcome the Following Industry

Angel Adrovet, Genzyme

James Akers, Canadian Blood Services

Carol Anderson, Grifols

Nicole Arel, Shire HGT

Erika Barkley, Eli Lilly

Marcia Baroni, Eli Lilly

Michael Barron, Quality Chemical Laboratories

Dave Billingsley, Teva Animal Health

Mark Blanchard, EMD Millipore

Brenda Boone, Hospira

William Bost, DPT Lakewood

Craig Boyce, Intelligent Hospital Systems

Charity Boyles, Merck

Melinda Brock, Eli Lilly

Brian Brosdahl, ATS Labs

Karen Burns

Viviana Cambissa, GlaxoSmithKline

Matthew Camelio, Sanofi Pasteur

Gwen Carver, Merck

Karin Cedervall, CCS Healthcare

Lizzette Chung, Yung Shin Pharm

Carlos Cintron, Cubist Pharmaceuticals

Brian Clark, ImmunoGen

Neil Clayton, Pfizer

Cathelene Compton, CVC Consulting

Michel Comtois, Micom Laboratories

Robert Cote, ABC Laboratories

Frank Crisafulli, Vaisala

Carole Crowe, Agilent Technologies

Andrew John Crumpton, GlaxoSmith-Kline

Michael Cutter, Novartis

Veena Dayal, InnoPharma

Robert DeMasi, Allergan

Kuruppu Dharmasiri, MedImmune

Andrea Di Vora, Merck

Nicolas Dorange, BioMerieux

Nancy Duarte, Catalent Pharma Solutions

Stan Dube, Excelsior Medical

Celine Duhot, Merck Serono

Sheneka Dunn, Hospira

Susie Enache, W. L. Gore & Associates

Simon Evenden, GlaxoSmithKline

Melvin Faris, Commissioning Agents

Giorgio Ferrato, IMA Life

Todd Flanery, Getinge La Calhene

Guy Fonck, AFMPS

Julie Freburg, Genentech

Ichiro Funabashi, Becton Dickinson

Mirko Gabriele, Patheon

Michael Gatta, ICQ Consultants

Lodovico Gavioli, Bormioli Rocco & Figlio

Karen Gilligan, Allergan Pharmaceuticals

Liya Greenberg, Bio-Technology General

Evan Greger, Amgen

Mary Gresh, Endocyte

Joella Grossoehme, Teva Pharmaceuticals

Neil Grumbridge, Effective Pharma Support

Stefan Hafner, Baxter Innovations

Nils Hamann, Vibalogics

Melissa Hanna-Brown, Pfizer

Farah Hasan, Allergan

Joshua Hays, EMD Millipore

Dave Henderson, Oakwood Laboratories

Kristin Herndon, Seattle Genetics

Charlotte Hicks, Doe & Ingalls

Peter Holzknecht, Sandoz

Ken Howerton, Baxter

JoAnne Jacobs, Cook Pharmica

Luis Jimenez, Janssen Supply Chain

Jennifer Johns, Bristol-Myers Squibb

George Johnson, Pfizer

Anna Joyce, Ben Venue Laboratories

Sascha Karhoefer, West Pharmaceutical Services

Ryota Katsumi, Kyowa Hakko Kirin Co.

Hiroyo Kawafuchi, Toyama Chemical

Cynthia King, Hospira

Sok Tiang, Koh West Pharmaceutical Services

David Kolwyck, Amgen

Martina Kopp, Amgen

Takako Koshiro, Taiko Pharmaceutical

Angelika Kraft, Eli Lilly

Vasantha Kumar, Biocon

Palmer Lam, BioMarin Pharmaceuticals

Alexander Le, Gilead Sciences

Anne Leahy, EMD Millipore

Donna Lee, Grifols

Joann Lukasik, Ben Venue Laboratories

Warren MacKellar, Eli Lilly

Geena Malhotra, Cipla

Steve Martin, Gallus BioPharmaceuticals

Carl Martin, ASI

Thomas McGrath, AMRI

Greg McGurk, Irish Medicines Board

Leaders to the PDA Community

Holger Memmesheimer, Boehringer Ingelheim Pharma

Marla Meyer, West Pharmaceutical

Sandrine Miller, Abbott Laboratories

Eva Miller, Becton Dickinson

Sveta Minkin, SciClone Pharmaceuticals

Carmen Montalvo, Abbott Fermentation Products de PR

Elke MuehlbergAES Chemunex

Sibel Muratoglu, MN Pharmaceuticals

Roman Mysak, Genzyme

Dawn Nagel, EMD Millipore

Maria Nagy, Gedeon Richter

Yukio Nakata

Anil Narveker, Schott

Sile Ni Thuathail, Bioniche Pharma

Izehinosen Ogun, CIBA Vision Sterile Manufacturing

Sonalika Parashar, Glenmark

Jeffrey Peacock Bracco Diagnostics

Christopher Pierce, Jubilant Hollister-Stier

Michael Pietsch, Ben Venue Laboratories

Gordon Pugh, Alkermes

Alberto Quintana, Commissioning Agents

Nicholas Radio, Clarion Research Group

Thomas Raetz, Roche Diagnostics

Adrian Raiche, SiO2 Medical Products

Minna Rannikko, Ipsen

David Reifsnyder, Microbiological Environments

Derek Richards, Aptuit

Tilman Rock, Roche Diagnostics

Andrew Rockabrand, Eli Lilly

Guinet Roland, RGmp Compliance

Rene Rose, SGS

Dave Rottjakob, ATS Labs

Mike Rozbih, The Tungsten Shield Group

Noel Christopher Ryan, Mylan Institutional

Therese Ryan, ANSTO Health

Madhu Raju Saghee, Gland Pharma

Joanny Salvas, Pfizer

Kathleen Sampson, Genentech

Ana Sanchez, Rovi Contract Manufacturing

Michael Schafferius, Sartorius Stedim

Dawn Schrag, Valcom Services

Laurelle Sciola, EMD Millipore

Mary Scott, MPI Research

Audrey Scott, GlaxoSmithKline

Alessandra Seriacopi, Novartis

Irwan Setiawan, University College Ghent

Wendy Hirschelman Severs, Shire

Palak Shah, Gerresheimer

Umang Shah, Novartis

Sanjeev Sharma, Onyx Pharmaceutiucals

Hiroshi Shimaoka, EnBio

Pradeep Shiva kumar, Shilpa Medicare

Alan Silcock, Pfizer

Saurav Singh, Baxter

Ashley Slocum, EMD Millipore

Richard Smalley, Aptuit

Jody Snapp, Boehringer Ingelheim

Brigitte Soehling, IDT Biologika

Sushama Sontakke, Health Canada

Elizabeth Spies, Pfizer

V.A. Srinivasan, Indian Immunologicals

Daniel Stewart Antares Pharma

Sarah Stimpson, GlaxoSmithKline

Renato Surra, Soffieria Bertolini

Sarah Tanksley, Parexel

Dawn Tavalsky, Genyzme

Reza Tavana, Commissioning Agents

Christine Tayaba, Association of Cape Cod

Sergey Tesler, Amicus Therapeutics

Anne Toland, ATL Regulatory Consulting

Pamela Uetrecht, Covidien

Oliver Ullmann, Robert Bosch

Cuneyt Unutmaz, Crucell

Jorge Valentin, Amgen

William Vaughan, Hospira

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Hiring: Do It the Steve Jobs Way

Patrick Valtin

Jim was the perfect candidate with many years of solid experience as a professional sales rep and had an obvious talent of persuasion and communication skills. But the hiring manager had some strong reservations during the interview. Jim's strong focus on results "right now" and a certain aggressiveness that could probably overwhelm or upset clients were some of the weaknesses he was concerned about.

In regards to Jim's focus on the purposes of the company, its role in the community, the vital importance of innovation and unselfish dedication to excellence, he did the perfect job. He sold himself like never before and got hired.

Four months later, Jim was fired for lack of vision, lack of dedication and worst of all, for his lack of honesty in his intentions.

The manager knew he had to hire "the Steve Jobs way," but had no real clue as to how to do it. He hired what he saw and what he heard "at the moment." He was trapped into Jim's salesmanship talent. And he was fooled by Jim's hidden intentions: to get the job, "no matter what needs to be said…"

Steve Jobs' Hiring Philosophy

Steve Jobs was an amazing and unconventional leader in many respects. His reputation as the best entrepreneur of our time can be summarized in a few words: he and his top execs never compromised with the talents and qualifications required of their employees. He personally interviewed over 5,000 applicants during his career. He and his executives considered very different qualities in people than most business owners do.

When you thoroughly analyze Apple's philosophy of hiring, you find out that there has always been fundamental, uncompromising attributes needed to get a job at Apple.

You too can apply these attributes when you look at attracting top players and ensure you avoid trouble makers. To help you in the hiring process, here are the main "Apple selection attributes."

1. **Vision-minded:** Everyone joining the company must have a clear picture of its management vision–and fully agree to fight for it, to defend it and to live with it every day. Applicants who do not seem to get it are systematically rejected. When you hire people who don't seem to agree with, or care about your company vision, you are potentially employing future enemies.

2. **Innovation-minded:** Steve Jobs always emphasized the vital importance of hiring people who are innovative–willing to create something from nothing. Applicants are first chosen for their ability and willingness to constantly create, rather than for their technical competence.

3. **Future-minded:** Employees at Apple are driven by their leader's vision of the future and they contribute everyday to *creating* the future, more than just beating the competition. Each of them owns the future of the market because they know they can contribute to creating it. The eagerness to create, not follow the future is a vital attribute observed in top players, no matter the industry.

4. **Passion-minded:** Steve Jobs' first principle is: "Do what you love." People are hired because they love the product, the company and its vision. Applicants who do not demonstrate a genuine passion and "love" for the company's purposes and business philosophy will never make it.

5. **Contribution-minded:** A statement given by an Apple recruiter is clear enough: "We didn't want someone who desired to retire with a gold watch. We wanted entrepreneurs, demonstrated winners, high-energy contributors who defined their previous role in terms of what they contributed and not what they titles were."

6. **Engagement-minded:** Over two thirds of Americans are not engaged in their workplace. Apple management is strict on employees' level of commitment. Committed individuals who are inspired by a grand purpose make the whole difference in the most competitive conditions.

7. **Excellence-minded:** Steve Jobs was known for his passion of perfection. The company always tries things out until they are perfectly done. The same attitude is expected of every collaborator. Applicants who do not share that passion for excellence do not have a chance.

Other Critical Attributes to Evaluate

You will notice that these seven points enforced in the Apple's personnel selection are all personality-related attributes, also called soft skills. They do not always guarantee performance. But the chance

of selecting productive people is at least 200% higher when focusing on these vital soft skills. It is very well known that recruiters who focus on soft skills in their personnel selection process are, on average, 50% more effective in selecting top players.

So, in order to avoid falling in the *momentary personality trap*—as the hiring manager in the above example did, you should also focus on the following two *basic* soft skills:

1 **Honesty:** Did you know that one third of all business failures in the United States are due to employee theft? Also, 95% of all U.S. companies are victims of theft and yet only 10% ever discover it. So this is definitely a crucial criterion to evaluate. Everybody recognizes the importance of honesty so it would make sense to evaluate it PRIOR to evaluating any other soft skill, wouldn't it?

There are strong indicators which allow you to precisely evaluate honesty. Here are just a few: gaps in the resume, contradictory data between the resume and your standard job application, negative reaction or embarrassment from the applicant to your challenging questions and lack of accuracy in applicant's explanations of previous achievements.

2 **Willingness:** According to the U.S. Department of Labor, more than 87% of employee failures are due to unwillingness to do the job. You can't simply force someone to do something if they do not want to. Such persons will do what you want in order to keep their job or to avoid penalties. But they will not really put their heart into it.

Most applicants will tell you that they are willing, of course. The key to finding out if they are honest is to ask them to prove it. Challenge them to demonstrate that they have been willing to work hard, learn something new, question their old habits, work under tough conditions, etc… The way you do this is simply by asking them to give you specific examples when they had to display such willingness.

So, hire the Steve Job's way, by all means. But don't forget these two basic attributes in the same process. Inform applicants that your company values and management philosophy imply honesty and willingness/positive attitude as primary selection criteria, no matter the position – lack of either is enough to be considered unqualified!

About The Author

Patrick Valtin is the author of *No Fail Hiring* and a 24-year veteran coach and trainer in the fields of management and human resources. He is the President of M2-TEC USA. Patrick has trained 85,000 business owners and executives in the last 23 years about business strategies, leadership and people management, hiring, sales and marketing. For more information, please visit www.nofailhiring.com, www.m2-tec.com or call 877-831 2299.

snapshot

Task Force *Corner*

Technical Report on Bioburden and Biofilm in Pharma Processing Operations to be Published in 2012

Vince Anicetti, Keck Graduate Institute of Applied Life Sciences and PDA and Anastasia Lolas, Visionary Pharma Consulting

The Bioburden and Biofilm Management Task Force has set a goal to publish a new PDA technical report to address the important problem of bioburden and biofilm management in pharmaceutical processes in 2012.

The task force's urgency is driven by the lack of technical guidance in this area and recent biofilm problems that has been the subject of recent regulatory communications. Of particular note is the recent European Medicines Agency communication regarding the risk of endotoxins in certain peritoneal dialysis solutions. In this communication, the Committee for Medicinal Products for Human Use reported that endotoxins were being produced by biofilms; layers of bacteria that adhere to each other and are very resistant to cleaning processes ***(1).*** This problem left the manufacturer and the European Medicines Agency with the difficult choice of either potential supply shortages of life-saving products or continued use of potentially affected batches. Fortunately, this particular problem has been resolved through the diligent efforts of the manufacturer and Committee for Medicinal Products for Human Use. However, it illustrates the serious risk that biofilms present to today's pharmaceutical and biopharmaceutical processes.

A commonly used definition of a biofilm is a "microbial derived sessile (attached) community characterized by cells that are irreversibly attached to a substratum or interface or to each other, are embedded in a matrix of extracellular polymeric substances that they have produced and exhibit an altered phenotype with respect to growth rate and gene transcription" ***(2,3)***. Research into the formation of biofilms over the past two decades has shown that these are a significant factor in the resistance of infections to treatment and in the persistent contamination of medical devices. These problems carry over into the biopharmaceutical manufacturing world where the ability of biofilms to provide survival advantages in harsh environments such as purified water systems or recovery columns presents a major challenge to firms and regulators. Most current manufacturing processes are not designed to actively manage biofilm due primarily to limitations in detection strategies and methodology. The importance of improving our understanding and ability to control biofilms is extremely important. The direct and indirect impact of bioburden and biofilm (e.g., microbial counts, microorganism byproducts, toxins, enzymes) is a significant quality concern.

The task force includes experts in microbiology and engineering from industry and the U.S. FDA. The task force also includes European Pharmacopeia experts and is also consulting with European regulators for their input.

Five major sections will make up the technical report. Currently, the task force is in the process of defining effective microbial control program guidance encompassing product and process understanding as well as facility, equipment, process and personnel controls. These microbial control strategies will be based on the principles of risk management and will provide the foundation of the technical report. Design, prevention, detection and remediation will provide the four areas of emphasis on bioburden and biofilm understanding and management. The task force feels that this approach will provide the greatest practical guidance for individuals or firms engaged in the development of new processes or managing current production systems. Emphasis will be placed on biopharmaceutical manufacturing processes such as cell culture and fermentation, harvest, purification and formulation of bulk drug substance.

The introductory section will focus on the biology and mechanisms of biofilm formation. It will review the current understanding of bioburden and biofilm development in pharmaceutical processes. While these two terms can often convey the image of an absolute environment of planktonic ("free swimming") or sessile (attached) organisms, current evidence suggests that these are two ends in a continuum of growth modes and may not necessarily be the phenotypically distinct entities often reported ***(2)***.

The design section will discuss the overall strategy for a microbial control program including the interplay of facilities/utilities design, process design and the quality system including GMP and analytical controls. These design considerations must be included within a comprehensive quality management system to be successful and fulfill cGMP regulations and regulatory expectations. Effective microbial control cannot be achieved without robust training, risk management, change control, deviation, CAPA and documentation programs.

The prevention section will discuss considerations regarding the design of the facility, equipment, utilities, product process and cleaning process. Qualification and requalification activities, equipment maintenance and repair and an effective quality management system are critical for preventing ingress, proliferation and persistence of microorganisms and will also be described in the technical report.

The detection and control section will provide guidance on tools and technologies—including novel technologies—for monitoring bioburden and biofilm to assess the state of control of manufacturing operations. The development and application of detection

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Journal *Preview*

Improving Manufacturing

The May/June *PDA Journal of Pharmaceutical Science and Technology* brings a special commentary from FDA's **Janet Woodcock,** who examines what she says is the pharmaceutical industry's continued inability to meet high quality standards in manufacturing. Lagging adoption of advanced control technologies and inadequate quality systems are two of the culprits Woodcock points to. Drug shortages and compromised patient safety are but two of the symptoms brought on by poor quality. In end, she says, it is both the industry and the regulatory authorities' responsibility to overcome ongoing quality issues.

Editorial

Govind Rao, "Something Old, Something New"

Commentary

Janet Woodcock, "Reliable Drug Quality: An Unresolved Problem"

Research

Amit Kumar Aggarwal, Samarpreet Singh, "Fast-Dissolving and High-Drug-Loaded, Fatty Acid–Based Self-Emulsifying Solid Dispersions of Diacerein"

James F. Cooper, et al., "Alumina Depyrogenates F 18 Fludeoxyglucose Injection during Purification Processes"

Rong Zhou, et al., "Investigation of freeze/thaw-related quality attributes of a liquid biopharmaceutical formulation: role of saccharide excipient"

Rajendran Vijayakumar, et al., "Invitro antifungal Efficacy of Biguanides and Quaternary Ammonium compounds against Cleanroom Fungal Isolates"

Technology/Application

Kevin O'Donnell, et al., "Quality Risk Management: Putting GMP Controls First"

Harry Yang, et al., "Implementation of Parallelism Testing for Four-Parameter Logistic Model in Bioassays"

Review

James A. Melchore, Dan Berdovich, "Considerations for Design and Use of Container Challenge Sets for Qualification and Validation of Visible Particulate Inspection"

You can view the Journal at http://journal.pda.org/

In *Print*

Fouling/Biofouling: A Primer

Mark Fornalik, Industrial BioFouling Science

The following is excerpted from the chapter "Early Detection and Prevention of Biofilms in Process Equipment," which appears in the forthcoming PDA/DHI book, Biofilms: Preventing and Controlling Microbial Contamination in Pharmaceutical Production, *edited by* ***Lucia Clontz,*** *PhD, Biomanufacturing Training and Education Center, NC State University and* ***Carmen Wagner,*** *PhD, Strategic Compliance International. The book will be available later this year. Check the PDA Bookstore (www.pda.org/bookstore) for more information.*

The definition of biofilm is fairly straightforward, and was succinctly described by Characklis and Marshall ***(1)***:

- The unwanted adhesion of bacteria or other organisms onto surfaces of solution-handling systems
- Not necessarily uniform in time and space
- May contain significant amounts of inorganic materials held together by a polymeric matrix

This description accounts for seemingly random microbial contamination events in a process (i.e., "not necessarily uniform in time and space"). The organisms can occur in one particular area of a process and not appear upstream or downstream from that particular point. Further, the biofilm can grow and slough

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Tech *Trend*

Shrinking Carbon Footprints

Emily Hough, PDA

Pharmaceutical companies have become committed to shrinking their manufacturing footprint by consolidating operations and maximizing capacity to increase manufacturing efficiencies. Even companies supplying the industry are starting to develop similar practices.

In a sustainability report that was released in 2011 for the 2010 fiscal year, Pall reported that it had reduced its water and energy utilities by 11%, waste output by 26% and greenhouse gas emissions by 12%.

According to **Farsad Fotouhi,** Vice President, Global Environmental, Safety & Health, Pall set out to reduce its physical manufacturing footprint to consolidate operations into locations where it had excess capacity. This consolidation provided efficiencies in logistics, supply chain and inventory management.

Pall's smaller carbon footprint was enabled by a combination of many smaller efforts, for example, the addition of a

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strategies is an important need in the industry today.

The remediation section will discuss measures to investigate, identify and resolve bioburden and biofilm problems and assess effectiveness of corrective and preventive actions.

The technical report will end by presenting an overview of current regulations and guidelines. Additionally, real case studies will be presented to describe how bioburden and biofilm problems were resolved, how the effectiveness of CAPAs was assessed and what important lessons were learned and incorporated into the microbial control program.

The task force intends for this technical report to be a globally relevant document and will continue to seek input from interested regulators and expert organizations as the project progresses.

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Anastasia Lolas, President, Visionary Pharma Consulting, previously, was a Microbiologist in FDA/CDER's Division of Manufacturing and Product Quality and a Microbiology Reviewer with the New Drug Microbiology Staff in the Office of Pharmaceutical Science at CDER/FDA. Currently, Anastasia is a member of the *PDA Letter* Editorial Committee and serves on the Bioburden and Biofilm Task Force.

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Tech Trends continued from page 19

compressed air leak detection and repair system in its Cortland facility, and larger initiatives, such as the replacement of cooling towers at its Puerto Rico site. Fotouhi said that each facility is tasked with identifying and executing projects to help Pall meet its goals. "Pall has been working since 2006 to shrink our manufacturing footprint by consolidating our manufacturing activities. The overall result is a decrease in consumption of energy and other resources necessary to meet our growing customer and production demands." Pall also takes an annual greenhouse gas inventory that provides important baseline information that is used to make informed and effective policy decisions to reduce its carbon footprint.

Fotouhi said that Pall's sustainability strategies and programs are based on a disciplined process of setting clear objectives and measuring our progress. In addition, each manufacturing site at Pall has created "green teams" to help identify ways to further reduce waste. These groups generally meet each quarter to determine the needs and demands of each facility as well as to ascertain where energy can be saved in that facility.

The firm optimally would like to en-

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off from the surface over time. Trying to find and recover biofilm organisms from a complex process can be a maddening shell game, where it becomes difficult to see any pattern in the bioburden data.

The polymeric matrix that Characklis and Marshall refer to adds an entirely new dimension to microbial contamination. Even if the microbiologist recovers a biofilm from the manufacturing process, the biofilm may resist growth in the laboratory simply because the biofilm cells are still encased in a thick, protective polymer ***(2,3).*** Lack of growth in a Petri dish is not indicative of lack of viable cells, but may only indicate that the cells could not break free of the surrounding polymer to reach the nutrient media.

The biofilm and its protective polymeric matrix also have the ability to concentrate particles and metals from solution. It is not unusual to see a brownish haze on stainless steel pipe walls or even plastic vessels and containers. The brownish haze or stain is frequently a biofilm, with iron or manganese particles that were picked up and slowly concentrated from the low levels found in the product or water used in the process.

Biofouling is not the only event that happens on pipe walls, but rather just one of a number of events that can happen to pipe walls in a process. Bott has described the fouling of heat exchange surfaces. In fact, these fouling events are not limited to heat exchanger surfaces, but can happen with any man-made surface in contact with flowing solutions ***(4)***. Bott describes various types of wall fouling:

- Organic
- Inorganic
- Biological
- Particulate
- Crystallization
- Combination

When biofilms are involved, combination fouling is the most common, where two or more fouling types can be found in any particular process ***(4,5).*** This has large implications for Clean-In-Place (CIP) processes. Most design engineers, chemical engineers, and cleaning validations specialists andmake the assumption that they are cleaning residual product from the walls of a pipe. In fact, wall fouling may have little chemical similarity to the product running through the pipe ***(4),*** and may actually be insoluble in reagents that would dissolve the product transferred in the pipeline.

In all cases, the initial event in wall or surface fouling is the deposition of a conditioning or induction layer on the pipe wall. This conditioning layer can consist of proteins, glycoproteins, humic acids, or other surface-active organic material. These chemical species may be present in trace levels in the product formulation or process water system, but they will still be the first to adsorb to a pipe wall. This adsorption process is irreversible. Once the conditioning layer has formed, the pipe wall is no longer a bare stainless steel, polyvinylidene fluoride (PVDF), or polytetrafluoroethylene (PTFE) surface. Instead, the surface is coated with an organic "rug," and the inert, bare pipe surface is transformed into a welcoming environment to microbes. As stated earlier, once this conditioning layer forms, it becomes a constant nutrient source for organisms to find and feed on.

In spite of this, many systems have a stable conditioning layer that does not interact chemically or biologically with the product flowing through the pipeline. However, some systems can progress from conditioning or induction layer to rapid fouling (Figure 1), where chemical components of the formulation passing through the pipe begin to drop out of solution and form layers of material on the pipe wall. If this process is left unchecked or the chemical cleaning process isn't designed for this material, the layers will build up over time until the fouling layer reaches a steady state. Here, the fouling layer will physically (i.e., viscously) interact with the flowing solution, flaking off with high shear, redepositing and building up again during lower shear, and flaking off once more. Hopefully, downstream process filters can prevent these flakes and chunks from contaminating the final product.

More problematic, however, is how the wall fouling can interact chemically with the flowing product. This is particularly true for biofilms. Biofilms are not inert particles on the pipe wall. The biofilm organisms are harvesting nutrients and introducing waste in the form of surfactants, enzymes, and anionic species such as acetates, nitrates, nitrites, and formates. These organic and inorganic contaminants can potentially alter the purity, quality and shelf life or stability of a product, despite the fact that bioburden is not detected in product testing, using traditional microbiological methods.

The key point, though, is that microorganisms only attach after the conditioning layer has adsorbed to surfaces, and sometimes even after other layers have been deposited first. While microbiological techniques don't detect the conditioning layer on a surface, surface analytical techniques can detect this layer, even at the earliest stages of its formation.

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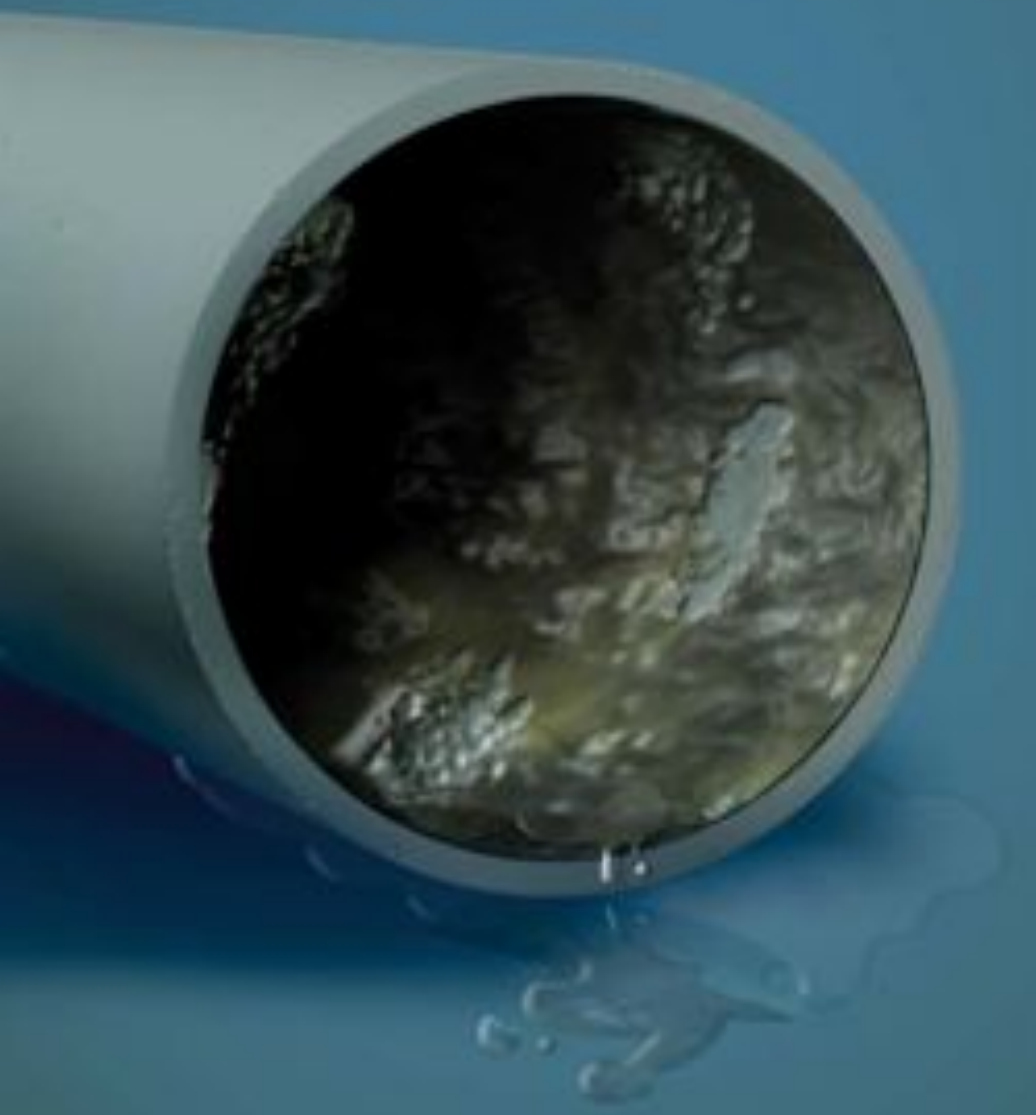
Considerations for Successful Design, Operation and Maintenance of an Ultrapure Water System

Morven McAlister, Pall

Water is undoubtedly the most fundamental requirement in the pharmaceutical manufacturing environment, but it is often an overlooked commodity in terms of maintenance and assurance of low bioburden levels. While multiple preventive measures are implemented into most water purification systems, contamination of the water by microorganisms remains a cause for concern.



While the most common source of microbial contamination of any given water system is typically bacterial related (usually due to Gram negative bacteria), the reasons for this are multiple and treatment to eradicate the bacteria can be a very complex process with varying levels of success. As a result, it is imperative that all components implemented into the pretreatment and polishing phases of a water system are well understood. In addition, the performance of the water system must be closely monitored, which can ultimately aid the end user with troubleshooting should a bacterial contamination issue arise in the future.

The purpose of this communication is to highlight some important items to consider in the design, operation and maintenance of high purity water systems to assure low bioburden levels.

Components Within a Water System

Most water purification systems used in the pharmaceutical industry are fed by municipal water and employ various steps to end up with bulk water that meets the compendial standards required (e.g., "purified water" or "water for injection") for the intended purposes. While purified water may be used for cleaning or used in nonparenteral preparations, water for injection represents the highest quality water and is used for parenteral applications ***(1).*** A well-designed system will typically operate without any bioburden issues. However, the items stated in this article should be considered for insurance of a bioburden-controlled water system.

Article at a Glance

- It is imperative that all components implemented into the pretreatment and polishing phases of a water system are well understood
- It is difficult to compare the occurrences of bacterial contamination in water systems due to the variation in methods employed
- It is advisable to sample as many locations of a water system as possible as part of a routine monitoring process to determine high risk "hot spots"

While there is no one universally accepted design for a water system, an example of typical stages included in a water system is indicated in **Figure 1**. Commonly employed pretreatment strategies include placement of multi-media ("particulate bed") filters and granulated carbon bed filters to remove chlorine prior to further treatment by reverse osmosis, though other pre-treatments may be suitable. Removal of chlorine is essential to prevent damage to the reverse osmosis membranes. After being treated by reverse osmosis, the water is usually collected into a storage tank.

Ideally, water in the storage tank should be circulated and can be ozonated to reduce bioburden levels. Any uncirculated water becomes a haven for bacterial proliferation partly due to the large surface area available for biofilm formation.

The process water may then go through ultraviolet irradiation at 185 nm (to reduce total oxidizable carbon), ion exchange, prefilters (0.45 µm rated to remove particulate matter), UV irradiation at 254 nm (to reduce microbial bioburden by DNA inactivation) and final point of use filtration through 0.2 µm or 0.1 µm sterilizing grade filters (as some waterborne bacteria can penetrate 0.2 µm rated filters) ***(2, 3)*** to remove bacteria before distribution to the final point of use or to distillation for conversion to water for injection.

Although many measures are taken to remove microorganisms from water systems, the potential for bacterial contamination is a constant threat. Any opportunity for stagnant water to exist should be eradicated. As such, careful evaluation should be made to ensure that no dead legs or pitting of the stainless steel exist within the water system, which can become the origin of a bacterial contamination event.

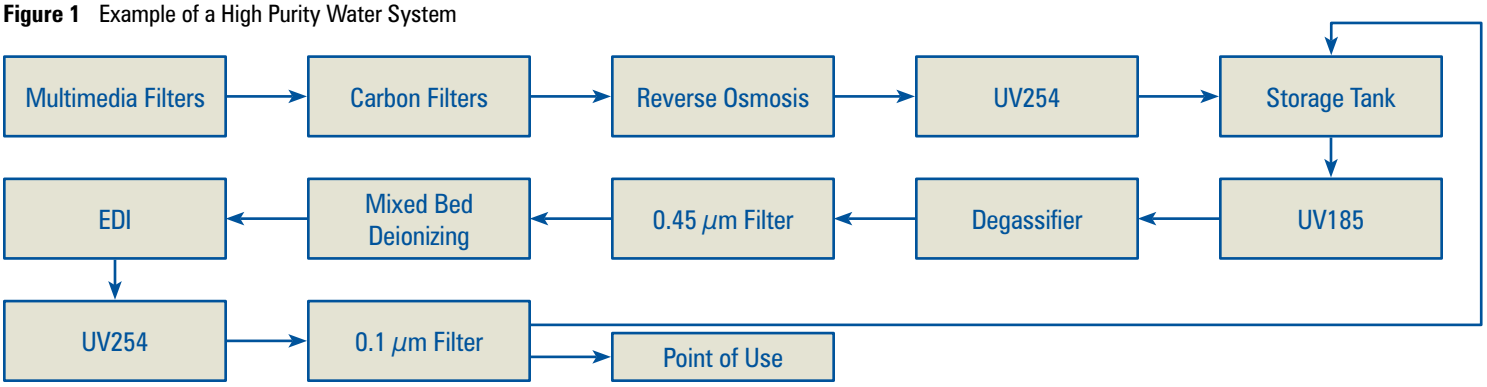
Biofilm Formation

It is commonly considered that bacteria in any aqueous system preferentially exist as sessile ("attached") colonies rather than planktonic ("free floating") cells ***(4).*** Any bacteria contaminating water will readily attach to available surfaces—typically the water/surface/air interface, which provides ideal conditions for biofilm formation. There are several advantages for bacteria attaching to a surface, including:

Structure: A biofilm can be regarded as a community of bacteria residing within a glycocalyx. The glycocalyx, often referred to as an extracellular polysaccharide, is a polysaccharide containing sticky material, which may contain microorganisms, polymers, nucleic acids, proteins and potentially any other substrate which comes into contact. It is held together by divalent cations contained within the sticky matrix ***(5)***. A biofilm is typically composed of 5-25% microbial cells with the remaining volume associated with the polymer network which itself contains a large percentage of water (70-95%) ***(6)***. The extracellular polysaccharide is an essential component of a biofilm due to its ability to concentrate nutrients from the flowing water stream, which serves to provide a nutrient source to the growing biofilm. In addition, the extracellular polysaccharide serves as a barrier to anti-microbial treatments due to the difficulties of many anti-microbial treatments (e.g., chemical agents, physical agents, antibiotics) to penetrate through the dense extracellular matrix ***(7, 8, 9, 10, 11, 12, 13).*** Further, due to the different physiological states of a biofilm (aerobic at the outside of a biofilm, potentially facultative anaerobic conditions towards the core of the biofilm), not all antimicrobial agents may be effective ***(14).*** In addition, by existing within the realms of the laminar boundary layer at the pipe wall, the bacteria are largely protected against removal by the shear stress of flowing water.

Quorum Sensing: In the early 2000's, studies showed the ability of bacteria to "talk" to each other ***(15, 16, 17).*** In essence, the research showed that once a Gram negative bacterial cell attaches to a surface, signals known as *N*-acyl homoserine lactone autoinducers are released which attract other bacteria to the specific area. The additional cells that follow and attach to the surface also emit these signals until the area is fully colonized. Further, the autoinducer cells induce cell division in the attached cells. Once a

Figure 1 Example of a High Purity Water System



critical density of the biofilm is reached, the specific signals are no longer emitted, preventing additional bacteria from being attracted to the area. The concentration of these signaling molecules may also trigger production of enzymes to dissolve the extracellular polysaccharide, releasing cells to flow downstream and colonize new surfaces. Therefore, it is feasible that the bacteria themselves may control the maximum level at which the biofilm can be sustained.

Genetic Exchange: The close proximity of bacteria in a biofilm means that there is a much greater potential for bacteria with resistant genes to transfer those genes to other bacteria via horizontal transfer. This could create a problem from the perspective of removing the biofilm where resistance to antimicrobial treatments could be a severe issue for sanitization of a contaminated water system.

Physiological Changes: Under the oligotrophic nutrient-poor conditions exerted by a water system, many bacteria can adapt their cell shape (especially Gram negative bacteria) to reduce their surface area. In addition, they may adapt the protein and lipid composition of their outer membrane to increase their ability to adhere to a surface.

Almost any surface can be the target of colonization. In addition to the quorum sensing mentioned above, bacteria come into contact with surfaces through a combination of Brownian motion, frictional drag, electrostatic attraction, gravitational forces and turbulent mixing ***(18).*** The microbial cells reversibly attach to the surface in the first instance ***(19).*** At this stage, they are easily removed. Once the cells produce copious quantities of extracellular polysaccharide, they become irreversibly attached and produce autoinducers and proliferate to produce a monolayer of cells. Next, these cells produce microcolonies ***(20)***, which are trapped within the extracellular polysaccharide network, and thus, a biofilm is created.

After reaching a critical threshold level, the biofilm become very difficult to remove. Some parts of the biofilm may be lost due to sloughing as a result of shear forces from the water system. In addition, some daughter cells are released from the biofilm, possibly colonizing other areas of the water system.

A schematic of the mechanisms involved in biofilm formation is shown in **Figure 2.**

Detecting Contamination

Most of the microorganisms associated as being "nuisance" microorganisms to water systems are bacterial and include *Ralstonia pickettii, Burkholderia cepacia, Bradyrhizobium* sp.***(21),*** *Sphingomonas paucimobilis, Stenotrophomonas maltophilia, Micrococcus luteus* ***(22)*** and *Pseudomonas* sp. ***(23).***

It is difficult to compare the occurrences of bacterial contamination in water systems due to the variation in methods employed. While many facilities rely on traditional plate counts, too often in-

appropriate growth media, incubation temperature and duration are used, potentially underestimating the true extent of bacterial activity in water system.

Due to the low concentration of available nutrients (particularly carbon), bacteria surviving in high purity water systems are often referred to as oligotrophs ("surviving under low nutrient conditions"), though this may be exhibited to various degrees ***(24).*** Bacteria residing in ultrapure water systems typically prefer lower nutrient conditions, a fundamental difference from their heterotrophic counterparts ***(25)***. Many oligotrophic bacteria have evolved a very broad substrate range and are able to grow using extremely low levels of nutrients (1-15 mg carbon/L), exhibit lower metabolism rates than hetrotrophic bacteria, have smaller cell sizes (thereby increasing their cell surface area) and increased adhesion to surfaces ***(26, 27).***

In view of the differences in growth requirements between truly hetrotrophic and oligotrophic microorganisms, it is natural to assume that in order to culture these microorganisms, different detection methods are also required.

There is a gap between selecting the right method and truly understanding the potential microbial loading of a water system. This is partly due to the challenges of balancing between selecting a recovery or detection method, that will provide timely results, and engaging the most robust and rigorous method, which would provide the end user with the information needed to understand the potential for microbiological activity at any given time.

If the microorganisms exist within a biofilm, what information does sampling of a given volume of a water system truly provide to the end user? The answer to this should be based on sampling a sufficiently large volume to try and capture as much information as possible at the time of sampling. In addition, it may be advantageous to sample water systems immediately after a period of minimal-activity (e.g., on a Monday for a facility operating largely on a Monday to Friday schedule), as well as sampling a high water flow rate to maximize the chances of catching any potential biofilm build up. Although bacterial biofilms do adhere strongly to surfaces, regular sampling of large volumes of water under worst-case conditions (e.g., high flow rate) to capture sloughing of a biofilm will provide the state of compliance of a water system. From this, trends can be analyzed based on past knowledge of the system. Continuous sampling can also be based on the same methodology.

Bacteriological growth media remains the most commonly applied technology used to detect bacterial contamination in water systems. In order to obtain meaningful data, use of dilute microbiological growth media, such as R2A, is imperative. Since the advent of

this growth medium ***(28)***, a plethora of studies have shown that when analyzing bacteria by plate counts, lower incubation temperatures (approximately 25°C) for prolonged durations (up to 14 days) yields higher recoveries and accounts for the slower-growing oligotrophic bacteria that may reside within a water system ***(29, 30).*** (Though an incubation period of 14 days may seriously impact operations within the facility.) For facilities relying on culture plate methods to monitor bacteriological activity within their water system, it is advised that several different incubation temperatures and durations are evaluated during the initial screening of the water system. This allows the user to understand the limits of each media type and culture conditions and potentially select a combination of methods to evaluate the system.

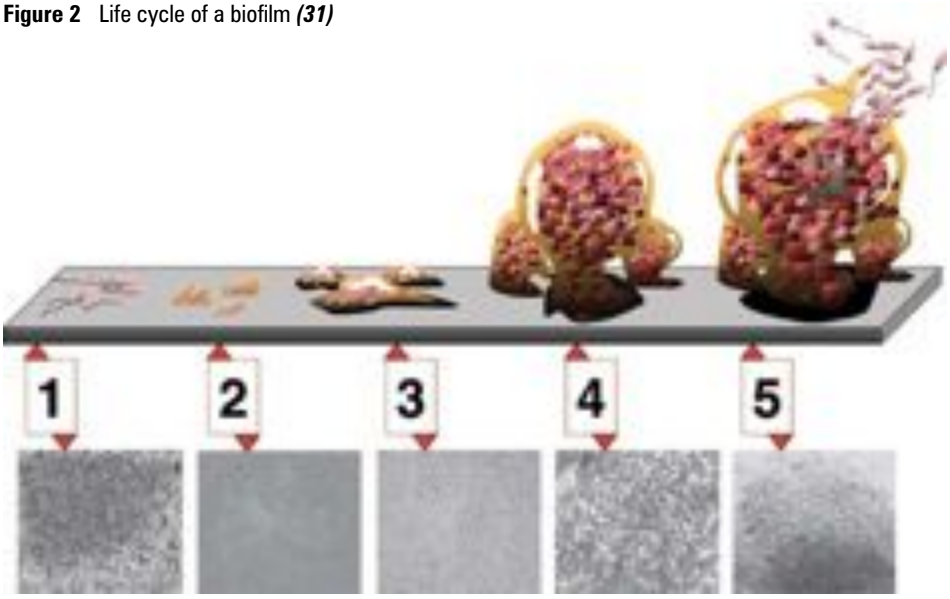
So, what other options are available? Other test methodologies do exist, such as quantification of adenosine triphosphate, epifluorescence microscopy and molecular-based methods like the polymerase chain reaction. These methods tend to require specialized equipment, trained operators to ensure correct sample preparation and data interpretation.

There may be merit in employing these methods as they typically will yield results significantly faster than the traditional plate count methods. These nonplating methods also find viable but not culturable bacteria in water systems. While the significance of viable but not culturable bacteria is frequently debated, there can be no doubt of the potential to underestimate contamination in water due to their presence or their ability to recontaminate a water system post sanitization ***(32).***

It is not unusual to find that several treatments may be required to overcome the resistance attributes often shown by waterborne bacteria

Implementation of rapid methods for microbial analysis still requires the end user to truly understand their water system. By performing a thorough qualification and validation of the water system prior to usage (qualitative and quantitative analysis), implementing as many preventative steps as possible within the water system and instituting alert and action levels based on real time performance data, it is possible that alternative methodologies may be appropriate for providing the end user with sufficient warning prior to a catastrophic contamination event.

Figure 2 Life cycle of a biofilm ***(31)***



5 stages of biofilm development: **Stage 1,** initial attachment; **Stage 2,** irreversible attachment; **Stage 3,** maturation I; **Stage 4,** maturation II; **Stage 5,** dispersion. Each stage of development in the diagram is paired with a photomicrograph of a developing Pseudomonas aeruginosa biofilm. All photomicrographs are shown to same scale

Removal of Biofilms

In the majority of water systems, sessile microorganisms significantly outnumber their planktonic counterparts. Since bacteria residing within a biofilm are protected to some extent from standard antimicrobial measures, how can a contaminated water system be sanitized so it can return to its normal state? Due to the difficulties of penetration through the dense extracellular polysaccharide and the different physiological states of the contaminating bacteria as well as potential resistance of the bacteria to a variety of chemical agents, a combination of treatments is often the only solution. Chlorination (bleach) is widely used to sanitize a water system with elevated levels of bacteria. Other chemical treatments such as ozonation can significantly reduce planktonic bioburden levels. It should be recognized that other steps should be used in conjunction with sanitization (such as high velocity water flushes, hot water and surface cleaning) to return the water system to a state of control.

In addition to chemical treatment, physical treatments involving the application of heat are typically involved. It is not unusual to find that several treatments may be required to overcome the resistance attributes often shown by waterborne bacteria. Further, since it is impossible to prove that a water system is sterile (and even more difficult to achieve), rapid recolonization of the bacteria to pretreatment levels can also occur. Therefore, it is essential that an adequate contact time be allowed for any given treatment to act on biofilms potentially present in order to achieve maximum results.

It is advisable to sample as many locations of a water system as possible as part of a routine monitoring process to determine high risk "hot spots." It has been previously shown that different locations within a water system can recover different populations of bacteria ***(33)***. For ➤

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example, carbon filters are a microbial haven, but research has indicated that post-UV254 exposure often shows increases too.

However, post-sanitization, this is of utmost importance. Typically, this will provide the end user with assurance that the contamination has been eradicated. In cases where the water system continues to show elevated levels of microorganisms, systematically sampling the entire water system will help determine the root cause of the contamination. Once the source of a biofilm can be determined, further appropriate actions can be taken to treat a specified area of a water system. Failure to sample each component may overlook the cause of the contamination, leading to much anguish for the water system controller.

Ultimately, if a water system continues to show elevated microbial contamination levels, the water should be sampled before and after each treatment. At this point, membrane filtration followed by direct culture onto R2A agar plates may indeed offer the best solution to determine the type of contamination encountered. As mentioned earlier, R2A agar is a dilute growth medium, which has been shown to recover significantly higher levels of waterborne bacteria than growth media more suited to nutrient rich environments (e.g., Tryptic Soy Agar)***(34).*** By knowing what is in the water system, specific treatments selective for the target organism may be the right choice.

Due to the opportunistic nature of bacteria, even the best designed water systems can rapidly become contaminated with biofilms. To minimize contamination, it is key to gain a deep understanding of the operation of the system, thorough qualification and validation of the system when operating and continuous monitoring of as many components of the water system as possible. While no one component can completely remove all bacteria, implementing the right tools in the right locations can serve to keep water systems trouble free.

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Biofilm Myths

The following was adapted from the presentation, "Design and Control Strategies to Minimize Biofilm Risk," given on April 17, 2012 at the 2012 PDA Annual Meeting *in Phoenix, Ariz. by* ***Mark Pasmore,*** *PhD, Baxter Healthcare Corporation. Pasmore serves on the newly formed PDA Bioburden and Biofilm Management Task Force.*

1) Bacterial cultures methods are representative of what is in your system

Often this is not true, because does not necessarily give you a clear picture (partly because of biofilm attachment).

2) All you need to control biofilms is high flow rates

High flow rate offers benefits, but other aspects of process must be considered to control biofilm as flow rate is not a control strategy.

3) It is lack of flow that makes dead legs a problem

Dead legs are really more of a cleaning issue.

4) You can't remediate a biofilm

The earlier found, the easier it is to remediate, but overall systems with bad cases can be brought back with diligence and remediation of the actual issues.

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Shipping Pallets: Taint as Clean as They Look

The scope of PDA T*echnical Report, No. 55, Detection and Mitigation of 2,4,6-Tribromoanisole and 2,4,6-Trichloroanisole Taints and Odors in the Pharmaceutical and Consumer Healthcare Industries* provides guidance on how to detect and mitigate 2,4,6-tribromoanisole and 2,4,6-trichloroanisole taints and odors from tribromophenol-treated wood pallets. It also provides a section on industry benchmarking and gives examples of encounters in the supply chain that have resulted in product tainting. The following is an excerpt from Section 4.0 of TR-55. The references for Table 4.1-1 are contained in the full technical report. PDA members have until May 31 to download a free copy of the TR at www.pda.org/bookstore.

4.1 Industry Examples of Encounters in Supply Chain That Resulted in Product Tainting

As noted previously, TCP, TCA, TBP and especially TBA have properties that increase the ability of these molecules to migrate into packaging materials, ingredients and products by leaching or diffusion (see **Table 4.1-1).** There are examples in the literature from the past 45 years of various materials that can absorb taints which include plastics, wood, adhesives, insulation, raw materials, foods, etc. **Table 4.1-1** provides examples of root causes and organohalogen-contaminated materials from the food, beverage and pharmaceutical industries and their probable sources of contamination.

Table 4.1-1 Representative Literature References to Organohalogen Taints in the Food, Beverage, Consumer Healthcare, Pharmaceutical Industries

Materials	Probable Cause of Taints	Reference(s)
Eggs and broilers	Chicken cage litter containing chlorophenol-treated wood shavings	*28, 29*
Dried fruit	Corrugate and wooden pallets treated with a chlorine-based spray with fungal biomethylation to form TCA.	*30*
Cocoa powder	Chlorophenols and chloroanisoles absorbed from packaging materials	*31*
Cheese	TCA from wooden pallets contaminated with TCP	*32*
Australian sparkling wine	Champagne corks shipped in polyethylene bags inside corrugate cartons tainted with TCA from a shipping container with TCP-treated wooden floor	*33*
Brazilian coffee	Tainting of coffee shipments due to TCA/TBA contamination	*34*
Fine wine	Corking of wine due to TCA/TBA contamination	*4, 15*
Tablets	TCA derived from packaging materials contaminated HDPE bottle tainted tablets	*35*
Canned beer	TCA absorbed into the internal lacquer of the cans during transportation in a shipping container	*36*
Water	TBA tainting of potable water	*37*
Sake	TCA tainting of Japanese rice wine	*38*
Milk	High density polyethylene resin used to make milk containers contaminated by halophenols during shipment	*2*
Calcium caseinate	Chemical tainting due to TBA derived from shipping containers	*39*

4.2 TBA and TCA Taint Examples from Food and Beverage Industries

As noted previously, TBA and TCA taints can migrate into packaging materials, ingredients and products by leaching or diffusion. Literature examples from the food and beverage industries indicate that porous materials such as wood, corrugate and plastic are susceptible to contamination with these taints. Likewise, food and beverage products are quite porous and can readily absorb these taints from contaminated materials. Consumers are more likely to notice contamination of food, beer, and wine because these taints can also produce unpleasant tastes that would more likely be noted during consumption because of their expectation of a pleasant sensory experience.

A dramatic food industry example was a case in which TBA diffused from corrugate dividers contaminated with TBA to the lacquer coating inside the beer can bodies. The TBA taint ultimately leached into the beer, which led to multiple consumer complaints and recalls. The levels of TBA in the beer were determined to be in the 1–40 ppt range. A thorough investigation indicated that the taint was not coming from the brewery but from a wood pallet transporting empty beer

can bodies from the supplier to the brewery. Both the wood pallet and corrugate dividers were contaminated with high levels of TBP and the resulting fungal metabolite TBA. As the wood pallets had not been treated with TBP, it was determined that the source of the TBP came from the wooden floor of the shipping container, which had very high levels of TBP (see **Table 4.2-1).** The beer can bodies had been sealed in the shipping container for 14 days under warm and humid conditions (>30 °C and >60% RH) that would encourage fungal growth.

Table 4.2-1 Concentration of Organohalogens in Beer and Packaging Materials

Sample	Beer A	Beer B, C & D	Pallet Timber	Local Paper	Local Divider	Imported Divider	Container Floor
TBA (ppt)	10–40 ppt	4–6 ppt	–	20–370	n/d–160 mean 40	3000	15 million
TBP (ppt)	–	–	260–17,300	9100	7500–28,200	8900	43 million

The Australian Food and Grocery Council recommends shipping containers be food-grade. If it is suspected that the containers have TBP-treated wooden floors, then dry cleaning is recommended in warm, humid climates and it is advised that plastic laminate foil sheets be placed between materials and the floor to minimize migration of TBP to materials ***(2).*** Many of the examples from the food industry cited in the literature are from Australia and New Zealand, as TBP has been known to be used as a wood preservative in other neighboring countries within this region. Apparently, the risk for TBA taint formation increases when goods are sealed in containers with TBP-treated wooden floors (or TBP-treated wood pallets) in warm, humid climates that can facilitate the growth of the fungi that converts TBP to TBA. Movement of goods from warm, humid climates to cooler climates also increases levels of moisture through condensation.

Another food industry example of diffusion and leaching was the transfer of taints from HDPE (high-density polyethylene) resin that was contaminated by diffusing halophenols during shipment. Ultimately these tainted HDPE resins were used to make milk containers. The milk held in the containers was contaminated via leaching of the taint from the plastics into the milk. The bottles of milk were recalled after consumer complaints. Although no haloanisoles were detected in the shipping container, the resin was held inside the container for 6 weeks. The resin supplier implemented several measures to prevent this problem from occurring in the future, which included the following: Rigorous inspection procedures of shipping containers; use of plastic laminate foil sheet to cover container floor; and adding a sensory testing method of in-coming resins.

Another good example from the New Zealand dairy industry also illustrates the processes of diffusion and leaching of these taints. Calcium caseinate, produced from skim milk and used as a food ingredient, was tainted with TBA ***(45).*** The wooden floor of the shipping container and the recycled plastic slip sheets used to move goods were both contaminated with TBP. Because the levels of TBP were higher in the slip sheets, these were believed to be the source of the TBA taint contamination; nevertheless, TBA was not detected in the recycled slip sheets. The TBA taint was not uniformly distributed throughout a single lot of calcium caseinate, indicating that absorption of the taint was not limited to just the outer surface of drums closest to the TBP-contaminated source. This necessitated the rejection of all lots of the ingredient from the suspect shipping container since the wooden floors were also contaminated with TBP. This dairy manufacturer now ships calcium caseinate on slip sheets made from virgin, food-grade plastic resins.

Multiple examples of TBA and TCA taint contamination have been noted in the wine industry. This industry has been particularly susceptible to these taints, as traditionally TBP and TCP have been used as fungicides to preserve cork wood. A

2004 survey of the industry indicated that 1–5% of corked wines are contaminated with TCA taints. Excessive use of hypochlorite-based disinfectants on wooden surfaces in wineries was reported to lead to the formation of TCP and the respective taint TCA. There have been examples in which the wooden kegs and wooden walls in wineries have been contaminated with TBA taints that originated from TBP-treated wooden containers. One strategy recommended to minimize cork taints is to avoid storing corks in high RH environments that would encourage fungal growth. Wineries have been advised to avoid the use of chlorine- (or bromine)-based disinfectants near wood materials. Interestingly, trade magazines serving the wine industry have recommended adding sheets of plastic to organohalogen-tainted wine to remove these chemical taints.

4.3 TBA and TCA Taint Examples from Pharmaceutical and Consumer Heatlhcare Industries

Table 4.3-1 provides examples of TBA and TCA taints in the pharmaceutical and consumer healthcare industries identified by company and year and highlights their common features. The first case evident in the literature was from Upjohn in 1990. The most recent cases from 2009 to 2011 are noted in this table. Details from some of these cases are provided below. During this time period there were 20 recalls from at least seven companies.

Table 4.3-1 Examples of TBA and TCA Taint Cases from Pharmaceutical and Consumer Healthcare Industries*

Company	Year/ No. Recalls	Source	Taint	Product/ Drug Action	Dosage Form	Packaging Component Material	Geographic Region (from/to)
Upjohn	1990/ literature report	Chlorinate phenols in wood pulp via bleaching	TCA, TeCA	Unnamed drug products	Tablets	HDPE plastic	Tropically located facility/US
J&J/ McNeil Consumer Healthcare	2009-2011/ 6 recalls	TBP-Treated Wood	TBA	Anti-histamine; OTC NSAID; OTC Aspirin; OTC Analgesic; OTC Antacid	Adult and/or Children: Tablets, gel caps, caplets, chewable	HDPE plastic	Puerto Rico, US**/ US, UAE, Caribbean Islands, Guatemala, Canada
Depomed	2010/ 1 recall	TBP-Treated Wood	TBA	Anti-hyper-glycemic for Type 2 Diabetes	Tablets	HDPE plastic	Puerto Rico/US
Pfizer	2010/ 4 recalls	TBP-Treated Wood	TBA	Lowers plasma cholesterol and lipoprotein	Tablets	HDPE plastic	Puerto Rico/ Ireland***/ US, Canada
BMS	2011/ 2 recalls	TBP-Treated Wood	TBA	Inhibitor of platelet aggregation	Tablets	HDPE plastic	Puerto Rico/US
J&J/Ortho-McNeil Neurologics	2011/ 3 recalls	TBP-Treated Wood	TBA	Anti-epileptic; Anti-psychotic	Tablets	HDPE plastic	Puerto Rico/US, Puerto Rico
J&J/ Janssen-Cilag	2011/ 1 recall	TBP-Treated Wood	TBA	Protease inhibitor for HIV	Tablets	HDPE plastic	Puerto Rico/ Europe, Canada
J&J/ Janssen & Patriot Units	2011/ 1 recall	TBP-Treated Wood	TBA	Anti-psychotic	Tablets	HDPE plastic	Puerto Rico/US
Dr. Reddy's Laboratories	2010 & 2011/ 2 recalls	Not in public domain	TBA, TCA, TBDMS	Cholesterol-lowering statin	Tablets	HDPE plastic	India/US

* This table represents recalls up to Sept. 5, 2011.

** Bottles manufactured in Puerto Rico packaged by and distributed from both Puerto Rico and US sites (linked to a series of recalls).

*** Bottles manufactured in Puerto Rico shipped to, packaged by, distributed from Ireland site.

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Although most of the examples in the literature for TBA and TCA taints come from the food and beverage industry, a review of the literature shows that up until 2009 there was only one case where such taints have affected pharmaceutical products. In 1990, the pharmaceutical company Upjohn detected musty odors in several unnamed oral solid pharmaceutical products in 1990, resulting primarily from TCA taint and secondarily from 2,3,4,6-tetrachloroanisole (TeCA) taint. The chloroanisoles were formed in corrugate shippers by fungal methylation of their respective chlorophenols. The probable source of the chlorophenols was chlorine bleaching of wood pulp used to produce the corrugate. The highly volatile, musty-smelling chloroanisoles contaminated the drug products by permeating the HDPE drug product containers. The article claimed that drug product tainting was eliminated by corrective actions in controlling humidity in the warehouse used to store packaging materials.

In 2010 and 2011, several pharmaceutical and consumer healthcare companies experienced issues with TBA taints. The TBA taints were evident in plastic packaging components and believed to be due to biomethylation of TBP, used as a preservative for lumber and to construct wood pallets. It is important to note that each of these cases have been linked to TBA taints entering into Puerto Rico facilities from lumber that have been treated with TBP. TBP is registered as a wood preservative in South America; thus, the risk of TBP entering the supply chain via wood pallets is higher for manufacturing sites based in Puerto Rico than the continental United States. In addition, the warm, humid environment in Puerto Rico increases the probability that the fungi that convert TBP to TBA will be present. Summaries for several of these industry cases are provided below.

In December 2009 and January 2010, J&J McNeil Consumer Healthcare voluntarily recalled multiple lots of over-the-counter products following an investigation of consumer complaints of an unusual moldy, musty, or mildew-like odor. The initial investigations focused on fungal growth on the products. Analysis by gas chromatography–mass spectrometry (GC–MS) indicated that the odor was due to the contaminant TBA. It was concluded that the probable root cause of the odor from the TBA taint was exposure of the product to packaging components that had been shipped to and stored at the pharmaceutical manufacturing site on TBP-treated wood pallets that had entered the supply chain. It was observed that the odor persisted in the open containers after tablets had been removed suggesting TBA resided in High Density Polyethylene (HDPE) containers and/or cap liners. In March 2010, the FDA, in response to these recalls, developed a Level 2 GMP Building and Facility Q&A Guidance to address the use of pallets to prevent risks from TBA taints.

In June 2010, Depomed recalled multiple lots of a diabetes drug due to the risk of exposure to TBA taints present in the packaging components used for the products that had been transported on TBP-treated wood pallets. In October 2010, Pfizer recalled multiple lots of a cholesterol drug due to the risk of exposure to TBA taints present in packaging components, yet both Pfizer and the packaging component supplier did not use TBP-treated wood pallets. Ultimately, it was discovered that the supplier's warehouse had been contaminated with TBA at some point (possibly from pallets constructed with TBP-treated lumber entering the facility) that was leading to the contamination of the plastic packaging components stored in the warehouse. Increasing ventilation in the warehouse did reduce the level of TBA in the packaging supplier's warehouse. In January 2011, Bristol-Myers Squibb recalled a cardiovascular drug due to the risk of exposure to TBA taints and complaints of musty, moldy odors in packages of medicines. In addition, several other recalls occurred from J&J's McNeil Consumer Healthcare and J&J's Janssen-Cilag in 2011 (see **Table 4.3-1).**

All of these cases indicate that pharmaceutical and consumer products are susceptible to contamination from haloanisole taints such as TBA and TCA. Thus, the intent of this technical report is to provide more guidance to industry on how to handle risk with these contaminants.

4.4 PDA TBA Industry Benchmarking Survey

The PDA TBA Task Force prepared a survey to benchmark knowledge of TBA/TCA risks and actions taken within industry to mitigate such risks. PDA distributed the survey to 27 pharmaceutical, consumer healthcare and biotechnology manufacturers, as well as the suppliers represented on the Task Force, to collect feedback from specific experts within these companies. The TBA Task Force requested that the responses reflect each organization's current position regarding how issues with these taints are handled so that the Task Force can publish general benchmarking information within the industry

The PDA TBA Task Force used the responses received from nineteen companies to develop solutions for industry via this Technical Report. To view detailed responses to this survey see the 2011 PDA publication *PDA Survey: Risk Mitigation of Tribromoanisole (TBA)/Trichloroanisole (TCA) Taints and Odors: A Pharmaceutical Industry Benchmarking Survey.*

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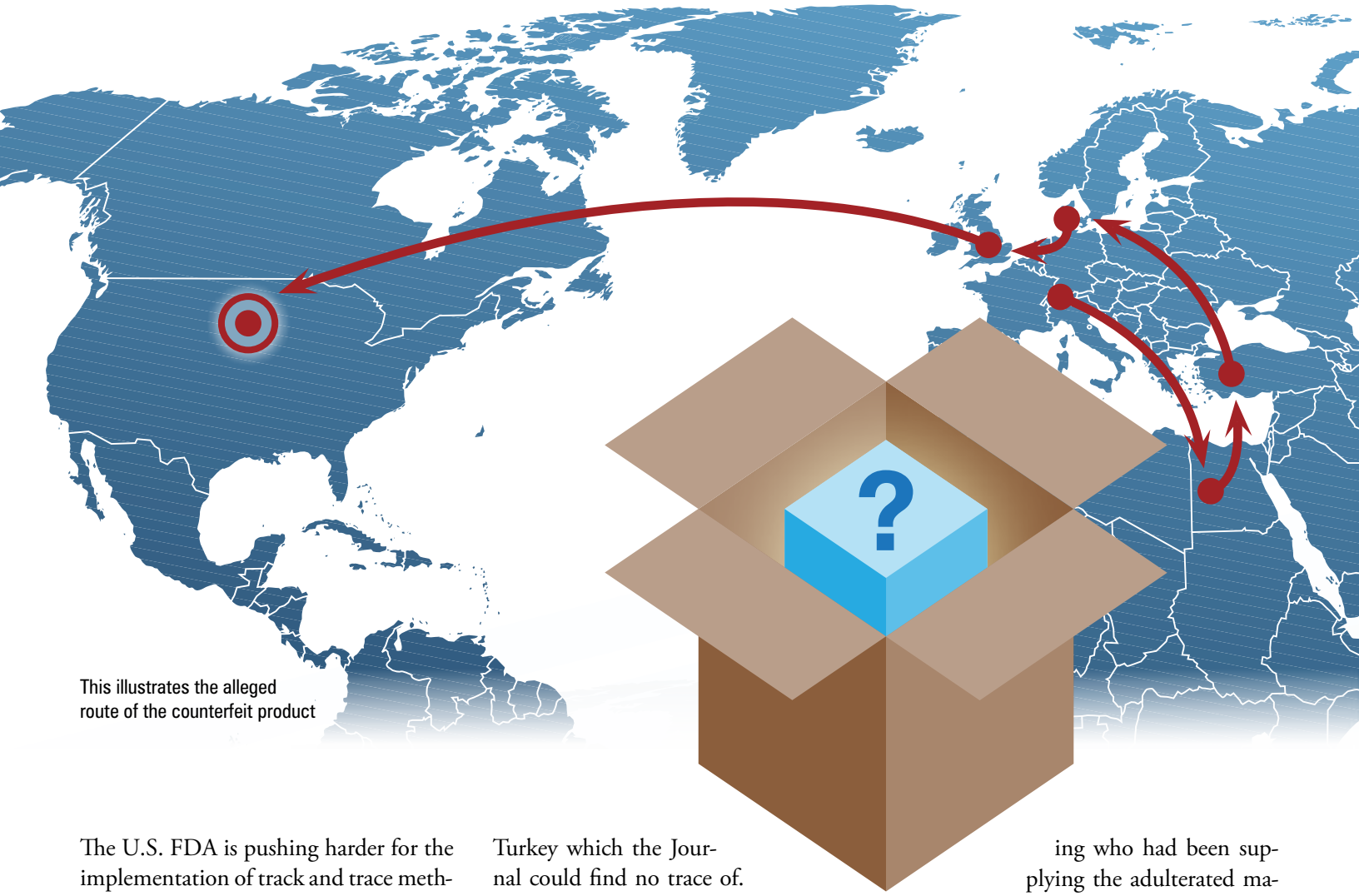
Recent Fakes Prompt New Regulatory/Legislative Reactions

Emily Hough with Walter Morris, PDA



This illustrates the alleged route of the counterfeit product

The U.S. FDA is pushing harder for the implementation of track and trace methods for drug products to protect patients from dangerous, low-quality fakes. Recent findings of counterfeit Avastin, a Roche anticancer drug, only heighten FDA's concern over the growing threat to patient safety in the United States.

The most recent incident of counterfeit Avastin surfaced in April, just two months after fakes of the drug were found in circulation. It isn't known where the phony intravenous drugs were made in either case.

Both incidents are very similar, with some of the same actors involved, according to a detailed article in the *Wall Street Journal* ***(1).*** Distribution of the counterfeits involved several wholesalers and middlemen in various countries, including one called Kirbaç Medikal in Turkey which the Journal could find no trace of. Another is an Egyptian company named Sawa. The point of departure to the United States was a group of Barbados and United Kingdom distributors operated by the same individual. A key cog in both incidents is Swiss wholesaler Hadicon**.**

At a Partnership for Safe Medicines Congressional briefing held on Mar. 15, **Connie Jung**, PhD, Acting Associate Director, Policy and Communications, U.S. FDA said, "We take these threats to our drug supply chain very seriously. Any substandard drug can be dangerous and, of course, harm public health."

She mentioned that if a universal track and trace system had been in place at the time of the Avastin incidents, the FDA would have had less difficulty determining who had been supplying the adulterated materials to the United States.

"From the regulator's perspective, having that visibility would be such a great tool for us to know who is really responsible for bringing those products in or trying to bring those substandard products in. We think that a track and trace system would be sort of a stop gap." Jung said that the Agency had been developing track and trace methods that involve identification, authentication and validation of drug products since 2007, and in 2010, it issued a recommendation to uniquely identify prescription drug packages. **[Editor's Note:** For a related article on track and trace systems, see "New Product Tracking Systems Soon Required," in the October 2011 *PDA Letter,* p. 34.**]**

One of the recommendations was for a barcode that could be read in both human-readable and machine-readable forms. This way, downstream distributors can quickly determine if the product code, lot number, expiration date and unique serial number are authenticate. If a product has a duplicate or invalid serial number, the product will be flagged and the counterfeit product should be reported immediately.

When the system is implemented, it can also be determined from the 2-D barcode from whom the product was received, how long the wholesaler had the product, when the wholesaler thought they were going to deliver it, if the product had been returned or if it had worked its way through the supply chain to the pharmacy.

should implement track and trace at the unit level from the start to avoid extra work in the future.

"We want to be cautions that whatever effort and investment that that we are putting forth is going to get us the benefit we are looking for," stated Jung. "We believe the track and trace system will be a very valuable tool to improve the integrity of the supply chain and protect it from substandard products."

Congress Considering Tougher Penalties for Counterfeiters

On Mar. 7, the U.S. Senate passed the Counterfeit Drug Penalty Enhancement Act of 2011 (S. 1886). If passed by the House of Representatives and signed by the President, S. 1886 will boost the maximum penalty for importing and marketing forged drugs in the United States from 10 years of imprisonment and a $2 mil. fine for individuals to 20 years and $4 mil. The potential fine will be doubled for repeat offenders.

The bill is now with the House Committee on the Judiciary and subcommittee on Crime, Terrorism, and Homeland Security. The bill was introduced by Sen. **Patrick Leahy** (D-Vt.), who cosponsored the bill with Senators **Michael Bennet** (D-Colo.), **Richard Blumenthal** (D-Conn.), **Charles Grassley** (R-Iowa), **Sheldon Whitehouse** (D-R.I.), **Dianne Feinstein** (D-Calif.), **Chris Coons** (D-Del.), **Jon Kyl** (R-Ariz.), **Amy Klobuchar** (D-Minn.) and **Robert Casey** (D-Pa.).

[Editor's Note: EU legislation to combat fake drugs was covered in "EU Directive to Thwart Noncompliant APIs"; see the April 2012 *PDA Letter* p. 30.]

IoM Report Offers 13 Recommendations for Regulators

On April 4, the Institute of Medicine presented its FDA sponsored report, *Ensuring Safe Foods and Medical Products Through Stronger Regulatory Systems Abroad.* The report identifies core elements of food, drug, medical product and biological regulatory systems in developing countries and pinpoints gaps in those systems. The report also designs a strategy that the FDA and other stakeholders can use to strengthen food and medical product regulatory systems abroad.

Thirteen recommendations are included in the report to improve product safety and public health around the world. (See box on following page for recommendations.) The full report can be downloaded at tinyurl.com/cvsw3ks.

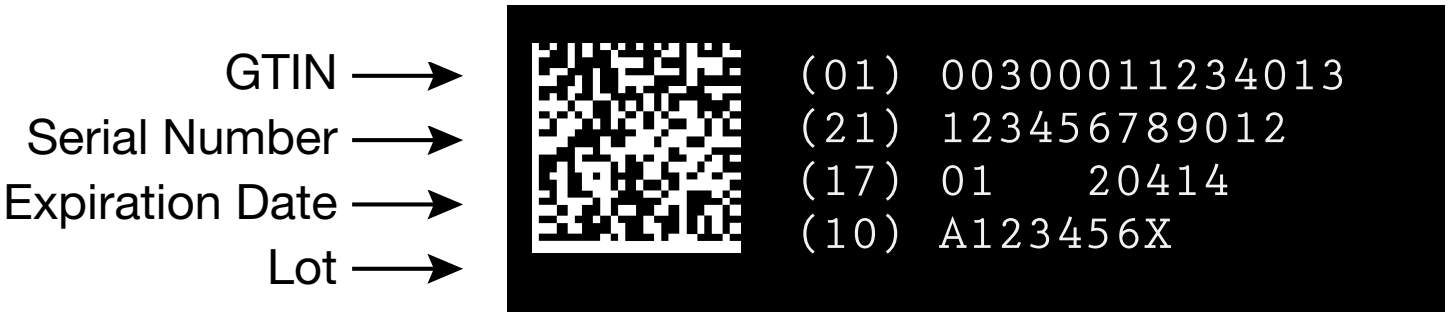
Rx-360 Audits Program Live

In April, Rx-360 announced that its Joint Audit Program was operational following a successful pilot phase. The program allows member companies to share the costs of audits with other companies, while reducing the number of audits suppliers need to host in a year. During the pilot, 19 audits were conducted in three regions of the world, including the United States, Europe, China, India and Japan. The scope of the pilots included raw materials, excipients, chromatography resins and APIs. Two audits have already been performed following the

We believe the track and trace system will be a very valuable tool to improve the integrity of the supply chain and protect it from substandard products

Shay Reid, Vice President, Operations, Pharmaceutical Distribution Security Alliance, agreed with Jung on the fundamentals of the track and trace system, but disagreed about how it should be implemented. Reid said that tracking the lot level as opposed to the unit level is more prudent. "We need to be careful about the level of technology that is introduced to the heavily regulated industry from the beginning." He said that as the track and trace technology evolved, the level of tracking would evolve to the unit level.

On the other hand, Jung believes firms



Regulators and industry agree that a 2–D barcode would improve the integrity of the supply chain

pilot, and there are currently 378 active audit requests.

Rx-360 also published a white paper that provides an overview of fundamental elements that can drive measurable and sustainable improvement of supply chain security practices. The paper, *A Comprehensive Supply Chain Security Management System*, can be accessed at: rx-360.org/LinkClick.aspx?fileticket=gn1NUQij6DU%3d&tabid=165

S. 1886 will boost the maximum penalty for importing and marketing forged drugs in the United States

Thirteen Recommendations to Improve Product Safety and Public Health

An Institute of Medicine report, *Ensuring Safe Foods and Medical Products Through Stronger Regulatory Systems Abroad,* sponsored by the U.S. FDA, offers thirteen recommendations to improve product safety and public health. The recommendations are divided by actions that can be taken domestically and abroad. To view the full report, visit tinyurl.com/cvsw3ks.

International Action

1: In the next 3 to 5 years, international and intergovernmental organizations should invest more in strengthening the capacity of regulatory systems in developing countries. The United States should work with interested countries to add it to the G20 agenda. Investments in international food and medical product safety should be a significant and explicitly tracked priority at development banks, regional economic communities and public health institutions. International organizations should provide assistance to achieve meaningful participation of developing country representatives at international harmonization and standardization meetings.

2: In emerging economies, national regulatory authorities, regulated industry and industry associations should engage in open and regular dialogue to exchange expert scientific and technical information before policies are written and after they are implemented. Starting in the next 3 to 5 years, these regulatory authorities should identify third parties, such as science academies, to convene the three pillars of a regulatory system—government, industry and academia—in ongoing discussion to advance regulatory science, policy and training.

3: Countries with stringent regulatory agencies should, within the next 18 months, convene a technical working group on sharing inspection reports with the longer-term goal of establishing a system for mutual recognition of inspection reports.

4: Industry associations should, over the next 3 years, define an acceptable protocol for sharing of internal inspection results among their members. After agreeing on the methods, they should regularly share their results among their members.

5: Starting in the next 5 years, USAID, FDA, CDC, and USDA should provide (both directly and through WHO and FAO) technical support for strengthening surveillance systems in developing countries. This technical support could include development of surveillance tools, protocols for foodborne disease surveillance and post-market surveillance of medical products, and training of national regulatory authority staff and national experts.

Domestic Action

6: The FDA should use enterprise risk management to inform its inspection, training, regulatory cooperation, and surveillance efforts. Enterprise risk management should apply to the Agency's entire operation, and it should incorporate a number of set criteria such as country of manufacture or production, volume and type of product, facility inspection history, and trends or data shared from other regulatory authorities.

7: The FDA should develop an information and informatics strategy that will allow it to do risk-based analysis, monitor performance metrics, and move toward paperless systems. In the next 3 to 5 years, the FDA should propose, in all its international harmonization activities, a standardized vocabulary, a minimum dataset to be collected, and the frequency of data collection.

8: The FDA should facilitate training for regulators in developing countries. The purpose is workforce training and professional development through an ongoing, standing regulatory science and policy curriculum. In the 3 to 5 years, the FDA should broaden the scope of FDA University to educate FDA staffers on international compliance with its regulations.

9: U.S. policy makers should integrate food and medical product safety objectives into their international economic development, trade, harmonization, and public health work. To this end, the FDA should lead in the development and adoption of international and harmonized standards for food and medical products.

10: The FDA, which currently requires one-up, one-back track and trace requirements for food, should, in the next year, hold a multi-sector, international, public workshop on applying it to medicines, biologics, and (when appropriate) to devices. ➤

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11: Starting in the next 2 years, the FDA and USDA should implement Cooperative Research and Development Agreements and other programs to encourage businesses and academia to research and develop innovations for low-cost, appropriate fraud prevention, intervention, tracking, and verification technologies along the supply chain.

12: FDA should ensure an adequate mix of incentives to importers of food and medical products that are confirmed to meet U.S. regulatory standards. One such promising initiative is the 2-year FDA Secure Supply Chain pilot program. The FDA should evaluate this program immediately after its pilot phase (scheduled to end in 2014). The program should be expanded, if successful, to include a greater number of importers and food.

13: Over the next 10 years, U.S. government agencies should work to strengthen the ability of those harmed by unsafe food and medical products to hold foreign producers and importers liable in civil lawsuits.

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About the Speakers

Connie Jung, RPh, PhD, Acting Association Director for Policy and Communications, Office of Drug Security, Integrity, and Recalls, U.S. Food and Drug Administration's Center for Drug Evaluation and Research, focuses on the development of policy and regulatory strategies to improve the security and integrity of the U.S. drug supply. She has worked on issues related to counterfeit and stolen drugs for several years in her previous position as Senior Advisor for Pharmacy Affairs in the Office of Policy, Office of the Commissioner and will continue these efforts in the new office.

Shay Reid, Vice President, Operations, AmerisourceBergen, is responsible for the implementation of technology and processes that help ensure patient safety, cost effectiveness and on time-delivery to more than 20,000 pharmacies and healthcare providers every day. Shay has been on the forefront of leading efforts for AmerisourceBergen to identify solutions for Florida pedigree, California track and trace. He has recently worked alongside his industry colleagues in the Prescription Drug Security Alliance to identify a national uniform solution for prescription drug traceability.

Considerations for Successful Design, Operation and Maintenance of an Ultrapure Water System continued from page 29

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About the Author

Morven McAlister, PhD, Sr. Technical Director, Microbiology, Pall Life Sciences, is responsible for providing global microbiology support. Since joining Pall in 2001, she has been responsible for biopharmaceutical customer support for sterile and virus filtration as well as the removal of microorganisms from water systems, including UPW, WFI and hospital water.

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North America

Counterfeit Drug Penalty Enhancement Act to Boost Penalty for Adulterated Drugs

A bill, S. 1886, which passed the Senate on March 6 will boost the maximum penalty for importing and marketing forged drugs in the U.S. from 10 years of imprisonment and a $2 million fine for individuals to $4 million and 20 years behind bars.

The Counterfeit Drug Penalty Enhancement Act of 2011, if passed, would hand out steeper fines to companies if they are implicated in counterfeiting crimes.

FDA Publishes Medical Device Guidance

The U.S. FDA has published a guidance, entitled, *Medical Device ISO 13485: 2003 Voluntary Audit Report Submission Pilot Program*.

This guidance is intended to provide information on the implementation of the FDA Amendments Act of 2007 with regard to how an establishment which was audited under one of the regulatory systems implemented by the Global Harmonization Task Force founding members using ISO 13485: 2003.

The guidance will be part of a two year pilot program beginning June 5. Following the completion of the pilot program, FDA will evaluate the results and report on the findings and any issues or suggested changes.

FDA Unveils Premarket Review Processes for Medical Devices in Guidance

The U.S. FDA has published a medical device guidance for manufacturers describing how the benefits and risks of certain medical devices are considered during pre-market review.

The guidance, *Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications,* includes a worksheet for device reviewers that incorporates the principal factors that influence benefit-risk determinations, such as the type, magnitude and duration of a risk or benefit, the probability that a patient will experience the risk, patient tolerance for risk, availability of alternative treatments, and the value the patient places on treatment.

Europe

EMA Reflection Paper Addresses Use of Starting Materials, Intermediates in Biological Medicinal Products

The European Medicines Agency has released a reflection paper on the use of starting materials and intermediates collected from different sources in the manufacturing of biological medicinal products. The document addresses to what extent any variability may be acceptable in the early manufacturing steps for biological medicinal products which contain active substance extracted from organs, tissues or fluids from living organisms and for which flexibility of sourcing in the biological starting materials may be needed to ensure product supply. This document also clarifies the definition of starting materials for these products. Advanced Therapy Medicinal Products are excluded from the scope of this document.

The consultation deadline is August 31.

EC to Update Volume II of EudraLex

The European Commission has announced it will update EudraLex - Volume II - Pharmaceutical Legislation, *Medicinal Products for Human Use.*

Volume II contains a list of regulatory guidelines related to procedural and regulatory requirements such as renewal procedures, dossier requirements for Type IA/IB variation notifications, summary of product characteristics, package information and classification for the supply, readability of the label and package leaflet requirements.

Key Regulatory Dates

Comments Due

August 31 — Use of Starting Materials, Intermediates in the Manufacturing of Biological Medicinal Products

Expanded Collaboration on EMA's GMP Inspections

The European Medicines Agency has announced it will expand its international collaboration on GMP inspections. The ongoing collaborative GMP inspections of active substance manufacturers by the EMA and international partners will be expanded to include the World Health Organization through its Prequalification of Medicines Program. Prior to the recent expansion, the program involved EU Member States, the European Directorate of the Quality of Medicines and Healthcare, the U.S. FDA and the Australian Therapeutic Goods Administration.

EMA Launches Electronic Application Form Pilot Program

The European Medicines Agency has launched an electronic application forms pilot program for submissions of centralized marketing authorization applications. The pilot will run until mid-July 2012 and allow pharmaceutical companies to apply for initial marketing authorization application for human medicines as well as for variation and renewal applications for human and vet medicines using an interactive PDF form to simplify and speed up the application process.

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Staying on Top of Training Issues

Bethesda, Md. • October 8-11 • www.pda.org/biennial2012

Rick Rogers, Genzyme

On behalf of the Biennial Training Conference Program Planning Committee and PDA, you are cordially invited to attend the 10th consecutive *PDA Biennial Training Conference* on October 8-9 in Bethesda, Md. This is the preeminent industry conference on training activities.

You do not want to miss this exciting opportunity to stay current on training related issues, enhance your skills, gain many new tools and network with your peers in the training arena. This year's focus is on improving performance in a regulated environment.

Recognizing the realities of our changing industry with common budgetary constraints and travel restrictions, this year's conference has packed as much as possible in this two-day event.

The conference will offer two plenary sessions featuring wide-scale training issues. One plenary session will be conducted by **Wendy A. Kouba**, Executive Director, Strategy Realization Office, Global Vaccines & Sterile Manufacturing, Merck. This session will offer the attendees the opportunity to learn how Merck's Vaccine Sterile Manufacturing division is leveraging learning to build capability and become a high performance organization—one where the hearts and minds of their employees are fully aligned with and seamlessly executing their goal to increase production, decrease cost-per-dose and provide life-saving vaccines to patients globally. Regulatory perspectives on pharmaceutical training will be given in the second plenary session.

In addition, twenty-seven concurrent sessions will be presented by practitioners from the industry, by trainers with years of experience making their living developing and delivering training for the organizations they represent. The presentations will cover the entire spectrum of training topics from presentations targeted at the relatively new trainer to those with years of experience. This year's concurrent sessions will be broken down in to three broad topic structures:

- From Training Programs to Learning Programs
- Training System Effectiveness
- From Theory to Practice

One of the most valuable aspects of the Biennial Training Conference is the opportunity the conference presents to attendees to meet and share information informally with others from the industry

Topics included in this year's concurrent sessions include measuring training effectiveness, preparing SMEs, instructional design, qualification processes and the globalization of training activities. These sessions were selected to offer the participants new skills and the tools to apply them in their organizations. There will be something for everyone who works in compliance training.

Attendees will also have the opportunity to attend three different round table discussions designed to give participants an opportunity to network with their peers on specific topics of interest to the group. This year's round tables include sessions devoted to what to do when training is *not* the solution, what to do when an employee passes their initial assessment, but does not apply the knowledge/skills on the job, and use of job aids. These moderated round table discussions provide the opportunity for participants to gather insight from the collective knowledge and experience of the group attending.

One of the most valuable aspects of the Biennial Training Conference is the opportunity the conference presents to attendees to meet and share information informally with others from the industry. The compliance training community in the industry is a relatively small group, numbering perhaps only several hundred. This conference typically attracts a very significant percentage of that number, including individuals in leadership positions with the several regional compliance trainer groups from across the country. The conference has numerous opportunities—both formal and informal—to provide attendees the opportunity to network with each other.

Those who work in our industry understand the importance of staying current with both technical and inspectional trends related to good manufacturing practices. Those who work in training are also looking for ways to constantly improve their craft. The PDA Biennial Training Conference offers anyone associated with training activities the opportunity to accomplish both of these things.

Following the *2012 PDA Biennial Training Conference,* TRI will be hosting three courses to complement the conference from October 10-11.

For more details about the conference, courses or to register, visit www.pda.org/biennial2012.

Everyday Microbiology–It's All About Control

Bethesda, Md. • October 22-26 • www.pda.org/microbiology2012

Ed Balkovic, PhD, Genzyme

The program planning committee would like to invite you to attend *PDA's 7th Annual Global Conference on Pharmaceutical Microbiology* from October 22-24 in Bethesda, Md. This year's conference will again offer an excellent opportunity to meet and interact with your fellow microbiologists, regulators, key product vendors and other global leaders in pharmaceutical microbiology.

The theme of the 2012 conference is *Everyday Microbiology-It's All About Control*. Our theme reflects two of the basic concepts of the quality by design approach to pharmaceutical microbiology: control of the microbiological aspects of the manufacturing process and control of the microbiological attributes of the product. These are not merely aspects to focus on once in a while, but are vital to the lifecycle of the product. To reinforce these concepts, the planning committee is shaping the conference agenda to include sessions dedicated to pyrogen control (including endotoxins), combating biofilms and rapid microbiology technologies.

The popular *Urban Myths, Future Leaders* sessions and *USP Updates* will also be on the program. Two new unique sessions this year address education and training of future pharmaceutical microbiologists and offer a hands-on tutorial of how to "do the math" as it relates to the practical aspects of the microbiological laboratory. In addition, we are working on a number of other sessions that will bring a truly unique selection of presentations to the conference. Finally, an excellent selection of poster abstracts has been received and will make for compelling viewing during our poster sessions in the Exhibit Area.

On the final day of the conference, we have expanded your opportunity to hear a presentation about microbiological control, risk management and modernization expectations from an invited FDA representative from the Center for Drug Evaluation and Research's Office of Compliance.

Our concluding session will be the annual *Ask the Regulators* round table composed of invited Center reviewers, compliance experts and field investigators who will be available to answer your questions and engage in a cross-panel discussion. This unique opportunity to interact with a diverse group of microbiological experts who regulate products from the Center for Drug Evaluation and Research, the Center for Biologics Evaluation & Research and the Center for Veterinary Medicine is sure to be an interesting and educational experience.

In addition, PDA's Training and Research Institute will be hosting five courses from October 25-26 to complement topics presented at this conference.

For detailed meeting information and registration, visit www.pda.org/microbiology2012.

Compliance Trends Presented at the ICH Q10 Workshop

Baltimore, Md. • September 12-13 • www.pda.org/Q102012

Jennifer Magnani and Anders Vinther, PhD, Genentech

The *2012 PDA ICH Q10 Workshop* is *the* workshop to attend if you in a span of just two days want to learn more about:

- Recent changes in regulatory compliance trends including warning letters and consent decrees
- Regulatory expectations for operations and executive management
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- Simplifying and strengthening your quality governance and business processes
- Identifying quality issues
- Selecting key performance indicators to drive the right behaviors
- Delivering a culture of accountable ➤

The Parenteral Drug Association presents the...

2012 PDA/FDA Joint Regulatory Conference

Compliance through Quality Systems: Implementing & Advancing a Sustainable Global Quality Culture

Register before June 29, 2012 – the first registration savings deadline!

September 10-12, 2012

Baltimore Marriott Waterfront Hotel | Baltimore, Maryland

"The 2011 PDA/FDA Joint Conference was excellent. I was impressed by the large number of participants which expanded my networking opportunities."
Lynn Collins, *BD*

The *2012 PDA/FDA Joint Regulatory Conference* offers the unique opportunity for you to join 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.

Also, on Wednesday morning we will host our popular Compliance and Center Initiative updates session. These sessions *always* play to a full house as FDA representatives provide the attendees with an update of hot topics from a compliance perspective and a summary of upcoming Center-led initiatives.

Topics include:

- Risk management and quality risk management systems
- Quality systems
- Quality by design (QbD)
- Science-based decision making
- Design space
- Innovation and collaboration with the goal of advancing the industry and impacting public health on a global scale

Immediately following:

- *PDA ICHQ10 Workshop: Expectations of Operations & Executive Management*. September 12-13
- PDA's Training and Research Institute (PDA TRI) will be hosting six stand alone training courses on-site on September 13-14

Be the first to know – Sign up to receive an email when more information is available about this event!
Visit www.pda.org/pdafda2012.

Visit **www.pda.org/pdafda2012** for more information.

Exhibition: September 10-11
Courses: September 13-14

leaders across the organization

ICH Q10 is the first time a regulatory guidance has significantly ventured into the area of expectations outside those of strictly meeting the GMPs. There are now clear expectations in place for management to sponsor continual improvement of the pharmaceutical quality system, allocating adequate resources, setting clear roles and responsibilities.

Quality is no longer just for the quality professionals. Quality must be owned by all across the technical disciplines in the company from the shop floor to the most senior executive.

This workshop is for you, if you are a decision maker at the senior level and looking for a workshop that will offer "everything quality in one package" as it relates to expectations of those in the operations area and executive leaders in our pharmaceutical and biopharmaceutical industry.

This is the perfect workshop if you are a decision maker at the senior level or a professional working onsite or at the corporate level in the following areas:

- Executive Management
- Senior Operations Management
- Quality Assurance leadership
- Operational Excellence leadership
- Quality Risk Management
- Senior Supply Chain Management
- Senior Procurement Management
- Pharmaceutical Development and CMC
- Regulatory Affairs
- Strategic Engineering Role
- Investor Relations

Discussing Vaccine Development

Bethesda, Md. • December 3-6 • www.pda.org/vaccines

Cochairs Norman Baylor, PhD, Biologics Consulting Group and Michael VanDerWerf, GlaxoSmithKline

We are excited about the opportunity to build off of the success of the inaugural PDA/FDA Vaccines conference in 2010.

The conference on December 3-4 in Bethesda, Md. will focus on the challenges and opportunities for providing vaccines to the world and will include industry, regulatory and vaccine experts from nongovernmental organizations such as the World Health Organization and Bill & Melinda Gates Foundation. This conference will provide a forum for discussion about vaccine development, manufacturing and regulatory issues.

Advances in science and technology are leading to research and development of a wide array of new vaccines and novel manufacturing approaches that may result in new and advanced tools for the prevention of emerging infectious diseases. Technical and regulatory challenges that the vaccine industry currently faces as these products are brought to various markets will be examined and discussed.

This event includes many information-packed sessions vital for today's vaccine professional, such as:

- Global Responsibilities and Challenges
- Global Regulatory Challenges Part I - Manufacturing in and for Developing Countries
- Cell Substrates
- Supply Chain - Part I/Part II
- Characterization and Analytical Technologies
- Bulk Manufacturing
- Quality by Design for Vaccines
- Rapid Test Methods
- Emerging Trends in Vaccine Manufacturing and Developments
- Standardization and Testing in a Global Environment
- Global Regulatory Challenges Part II – Seeking Regulatory Harmonization

This is a must-attend event for all involved in the manufacture and testing of vaccines for preventive and therapeutic purposes

This is a must-attend event for all involved in the manufacture and testing of vaccines for preventive and therapeutic purposes. Pharmaceutical and biopharmaceutical professionals with responsibilities in development, manufacturing, preclinical, quality assurance, quality control and regulatory affairs are encouraged to participate.

TRI will also hold two one-day courses on December 5 and 6.

Visit www.pda.org/vaccines for more information.

Solving Unmet Market Needs

Las Vegas, Nev. • October 15-19 • www.pda.org/prefilled2012

Georg Roessling, PhD, PDA and Brigitte Reutter-Haerle, Vetter Pharma International

"The best insurance policy for the future of an industry is research, which will help it foresee future lines of development, to solve its immediate problems and to improve and cheapen its products," according to the British chemist Sir Harold Hartley. While he may not have been speaking directly about our business of prefilled syringes and injection devices, he knew the inherent value of keeping abreast of the intricacies and advances of an industry.

Major changes have impacted and challenged our industry in just the last 12 months. Our industry continues to face challenges, especially as costs and regulatory demands continue to exert downward pressure on our ability to introduce devices that are safe and effective as patients and their needs continue to grow, while complex molecules and the demand for innovation continue to challenge our perspicacity.

Can we meet the challenge? Of course we can! And, we will! Find out how by interacting with your colleagues from around the world that have met the complexities challenging their innovation, imagination and tenacity. Their achievements are novel and many. Collectively, they have helped move our industry forward to a new level of previously unmet market needs while continuing to work on developments that will ensure the future successes of tomorrow. No wonder that the focus of our *2012 PDA Universe of Pre-Filled Syringes and Injection Devices* is about integrating the unmet market needs.

As in previous years, a variety of case histories, plenary and poster sessions, exhibitions combined with ample valuable networking time to interact with old and new colleagues will be your ticket to foresee the future of our industry.

A keynote will provide attendees with the opportunity of what it is like to be a patient struggling from a chronic disease and how using the tools of our industry have greatly affected the quality of their life. A number of compelling revelations of new methods and techniques from the "front lines" will show participants how to increase patient compliance and safety in difficult to treat patients. Novel technologies that are helping to meet the needs of the market by improving administration, compliance, safety, costs and accuracy will be presented.

Discussions and new advances in material construction, manufacturing processes and other improvements that ensure a dynamic future for the drug delivery arena in the future will also be given. Country-specific discussions on how combination products are being used differently in Europe versus the United States and what is being done to manage these differences will be held. A series of presentations on new and challenging guidelines from the various regulatory agencies that continue to challenge and demand new approaches from manufacturers will be organized. And, a first look will be given at how experimental designs are being used to gain a deeper understanding and offer optimal formulations and delivery systems for complex combinations of formulation parameters with differing syringe configurations.

Are you still not convinced that this conference is critical to your future and that of your company? Think again. It is important to be involved to better understand changes and the impacts on our business; therefore, we hope to have you at the *2012 PDA Universe of Pre-Filled Syringes and Injection Devices* conference. As with previous conferences, breakfast sessions will get your day started. Exciting presentations as well as panels of experts from around the world will also offer subjects of paramount interest during the day. And when you are not attending a session, visit the vast exhibit hall where current and future products of tomorrow are waiting to inspire you.

So mark your calendar now! You will not want to miss this year's conference. You certainly will leave with a plethora of information and a long list of new contacts and rekindled friendships. And as in previous years, the conference will be followed by a training courses. This year, the courses will take place from October 18-19.

Visit www.pda.org/prefilled2012 to learn more about the conference, courses or to register.

***It is important to be involved to better understand changes and the impacts on our business; therefore, we hope to have you at the* 2012 PDA Universe of Pre-Filled Syringes and Injection Devices Conference**

If you are in Operations or an Executive Leader in the Pharmaceutical/biopharmaceutical industry, this is the single most relevant conference for you as it relates to Health Authorities current Quality expectations of management and why some companies are struggling with GMP compliance.

The Parenteral Drug Association presents...

2012 PDA ICH Q10 Workshop:

Expectations of Operations & Executive Management

September 12-13, 2012

Baltimore Marriott Waterfront Hotel | Baltimore, Maryland

Has your company faced stock-outs due to quality problems in the past couple of years? Have you experienced different and stricter regulatory Health Authority dialog recently? Are you considering how deviations and failures in your operations can be reduced and how the product supply can become more reliable and predictable?

The *2012 PDA ICH Q10 Workshop: Expectations of Operations & Executive Management* is the event to attend if you want answers to these questions and you want to learn more about:

- Recent changes in regulatory compliance trends including warning letters and consent decrees
- How the Pharmaceutical Quality System (PQS) can be used to align your company across multiple sites and drive the right quality culture
- U.S. FDA's expectations for operations and executive management
- How ICH Q10 can be used as an efficient and powerful way to drive improvements within your company

This is the perfect conference if you are a decision maker at the senior level or professional working on site or corporate level in the following areas;

- Quality Assurance
- Manufacturing Operations and Engineering
- 6-sigma and Quality Risk Management
- Executive Management
- Senior Operations Management
- Senior Supply Chain Management
- Senior Procurement Management
- Pharmaceutical Development and CMC
- Regulatory Affairs

If you want 'everything quality in one package' as it relates to expectations of operations for executive leaders in the bio/pharmaceutical industry, then register for this workshop today!

Visit **www.pda.org/ICHQ10** for more information and to register.

Understanding Glass Containers and Associated Risks

Washington D.C. • June 4-7 • www.pda.org/glass2012

Diane Paskiet, West Pharmaceutical Services

The suitability of glass containers for use with drug products has come under increasing scrutiny because of multiple factors such as frequent occurrences of drug product recalls as a result of glass lamella, loss of product during manufacturing caused by container defects, interruption of supply caused by glass broken during shipping and most importantly, concerns regarding the impact of glass containers on patient safety.

The regulatory emphasis on risk management and continuous improvement efforts drive the need for a greater understanding of glass containers. It is no longer sufficient to pass compendia specifications to indicate the suitability of glass and rely on its long history of use. Careful consideration must be given to all materials used to manufacture and store drug products and glass is no exception. It is important to develop a better understanding of glass formulation characteristics and manufacturing processes that correlate to problems between drug product formulations and their containers.

Nearly a year has gone by since the PDA Glass Quality Conference and the Rx360 Glass Container Delamination Scientific Symposium brought together pharmaceutical scientists with regulators and glass experts to share experiences with the use and manufacture of glass. This set the stage for awareness of ongoing concerns and opportunities to share information, which led to a better understanding of critical issues. As time has passed, there have been more recalls associated with glass and concerns continue to mount. Trends toward novel products such as imaging for diagnostics, biomarkers, tissue engineering, nanocarriers and stem cell therapies can potentially bring a host of issues not yet discovered. The time to prepare to meet new challenges is now. Responsible decisions for the selection of containers in contact with drug products necessitate comprehensive knowledge of materials.

The *PDA 2012 Glass Quality Conference* on June 4 and 5 in Washington, D.C. will carry on the mission of continuous learning to understand the risks associated with glass containers and use with pharmaceutical and biopharmaceutical products. **David Jaworski**, Acting Branch Chief, Domestic Compliance Branch, Division of Domestic Drug Quality, U.S. FDA, has agreed to be the keynote speaker for the conference and speak about regulatory expectations. This conference will convey an in-depth understanding of glass materials, manufacturing, handling and strategies for qualification and control. Interactive sessions are planned to draw on experience from all who attend.

Future concepts for container handling in primary and secondary operations and improved container stability will be presented as well as distribution testing for package qualification

Topics include:

- Best practices to prevent and/or detect at-risk glass packaging
- Current expectations to help prevent recalls and help assure container closure integrity
- New methods for detection of lamella and actions taken by glass manufactures to address problems
- Identification of predictive and useful test methods specific to glass delamination
- New technologies developed for coating parenteral containers
- Methods for glass evaluation and insight on fracture analysis

The *2012 PDA Glass Quality Conference* will also present case studies providing insight into actions taken to reduce glass defect complaints and other external factors in the prevention of glass defects in sterile manufacturing and distribution operations. Extractables from glass and the potential for leachables will be discussed along with the new USP methodology for inorganic impurities and plans for standards. Future concepts for container handling in primary and secondary operations and improved container stability will be presented as well as distribution testing for package qualification. Participants will learn about risk and mitigation strategies from development to commercial manufacturing. This will benefit pharmaceutical sponsors, manufactures, suppliers, regulators and those involved in engineering, analytics, drug product stability and quality.

Following the conference, TRI will offer two-one day courses.

On June 6, "Technical Report 43: Identification and Classification of Nonconformities in Molded and Tubular Glass Containers for Pharmaceutical Manufacturing" will provide manufacturers and users of glass containers with valuable knowledge related to the quality of glass containers including the types of defects associated with glass manufacture, the development of standardized quality criteria and sampling plans for use in the quality decision-making process.

Through a series of lecture presentations accompanied by visual depictions of glass nonconformities, a review of cur-

rent best practices for identification and classification of visual nonconformities in glass containers will be provided. The course will also present criteria such as the development and use of appropriate sampling plans for incoming inspection of glass containers and the appropriate application of acceptable quality limits for accept/reject decisions.

The course will also cover how technical report 43 was developed.

On June 7, TRI will offer "Selection and Utilization of Glass Containers in Pharmaceutical Packaging." The objective of this course is to give a broad overview of the advantages and disadvantages of glass containers based on the interaction of glass with drug products.

The course will consist of both lecture and class discussions of case studies pertaining to the compatibility of glass with drug products, glass standards and regulatory requirements.

To learn more about the conference, courses or to register, visit www.pda.org/glass2012.

Securing the Supply Chain

Bethesda, Md. • November 12-14 • www.pda.org/supplychain2012

2012 Supply Chain Committee

The challenge of securing and protecting the integrity of the vast global pharmaceutical supply chain can be met through a variety of science- and risk-based approaches. New laws, regulations and guidances continue to evolve, helping to stimulate innovation toward enhancing good manufacturing, distribution and importation practices. Building on earlier PDA cosponsored conferences, the *2012 PDA/FDA Pharmaceutical Supply Chain Conference* will provide participants with a forum to further discuss innovative approaches aiming to prevent illicit acts such as counterfeiting, diversion and economic adulteration from threatening the safety of the drug supply.

The conference will feature speakers from: Abbott Laboratories, Amgen, Cisco Systems, Dunbee Investigations, the U.S. FDA, Genentech, GlaxoSmithKline, MHRA, OSO Biopharmaceuticals Manufacturing, Pfizer, Rx-360, Wal-Mart Stores and many others.

By attending this important conference, attendee's will be provided the opportunity to:

- Hear from U.S. FDA senior personnel and other regulatory agencies
- Share improvements in programs for supplier management and new technology
- Identify any barriers and associated actions to enable implementation of feasible solutions
- Learn about proven monitoring and testing methods as preventive measures
- Benchmark systems with leading pharmaceutical companies
- Discuss ways to minimize disruptions in the pharmaceutical supply chain–drug shortages
- Identify Global Initiatives from Europe and the United States
- Share ideas on how to derive maximal benefits from 3rd party audits and collaborative supplier-client relationships
- Investigate best practices of creating a secure supply chain by connecting industry, regulatory and national law enforcements

The program planning committee would like to encourage you to attend the *2012 PDA/FDA Pharmaceutical Supply Chain Conference* on November 13-14 in Bethesda, Md. and help in the development of initiatives to ensure the integrity of the global pharmaceutical supply chain.

For more information, please visit www.pda.org/supplychain2012.

On November 12, TRI will hold a course about developing a robust supplier management process. The course will

- Identify the primary steps in the supplier management process
- Apply the use of risk management tools in supplier management
- Identify critical elements to evaluate during on-site supplier audits
- Describe key metrics to use for supplier monitoring
- Develop an action plan to either enhance the supplier management process at their company

PDA Europe Conference

Parenterals 2012

Due to the fact that parenterals are gaining ever more importance, the 2012 conference will address the following topics:

- Technology updates, innovations in equipment and process technology
- Production environments and their control
- Facilities design and production planning
- Impact of recent regulatory guidances
- Component related quality impacts, testing and inspection
- Regulatory expectations and trends

Benefit from your early booking

6-7 November 2012

Hesperia Tower Hotel
Barcelona | Spain

CONFERENCE | EXHIBITION | TRAINING COURSE

Learn Aseptic Processing, Terminal Sterilization Practices

Chicago, Ill. • June 18–21 • www.pda.org/steriletechnology2012

Mike Sadowski, Baxter

Aseptic fill operations and terminal sterilization are considered special processes since the output of these processes, product sterility, cannot be fully verified by inspection or testing. Therefore, it is absolutely essential that these processes be properly developed, validated and controlled. The content for the *2012 PDA Innovation & Best Practices on Sterile Technology Conference* has been developed to summarize innovative and best demonstrated practices that have been recently developed and successfully employed to meet these objectives for the manufacture of sterile product with aseptic processing and terminal sterilization.

On behalf of the program planning committee, we would like to invite you to attend the *2012 PDA Innovation & Best Practices on Sterile Technology Conference* from June 18–19 in Chicago, Ill. In addition to the two-day-conference, PDA's Training and Research Institute will also be offering four exceptional sterilization courses from June 20-21 on moist heat sterilization, parametric release and dry heat sterilization, which has been designed to help you further strengthen your sterile product manufacturing program.

The foundation for the content of our conference has been developed to highlight contemporary approaches for sterile product manufacturing using case studies and personal experiences from recognized industry and regulatory agency experts.

Bring your current challenges and questions on aseptic processing and terminal sterilization to the conference and join industry and regulatory agency professionals

The conference will start with case studies on quality risk management for aseptic product manufacturing and also will include focus on the following sterile product manufacturing essentials:

- Risk-Based Approaches in Sterile Product Facility Design
- Contamination Control: Prevention, Detection and Eradication of Biofilm
- Novel Sterilization Science Approaches/Novel and Evolving Sterilization Technologies
- Summary of Regulatory Trends and Expectations for Submission Review and Field Inspections
- Summary of Critical Content of New PDA Technical Reports (Steam-In Place, Dry Heat Sterilization and Aseptic Process Simulation)

The conference will conclude with an *Ask the Experts* Session, which will feature a panel of distinguished experts that are not only recognized for their knowledge in the sterile product manufacture field, but are also equally recognized and respected for their willingness to address the tough issues that challenge our industry. In order to stimulate the most interactive and valuable discussion in this closing session, members of USP Expert Committees will open this session with updates on USP Chapters on Sterilization and Pharmaceutical Packaging Integrity.

We invite you join us in Chicago, Ill. for the *2012 PDA Innovation & Best Practices on Sterile Technology Conference.* Bring your current challenges and questions on aseptic processing and terminal sterilization to the conference and join industry and regulatory agency professionals. The value of the conference sessions, networking opportunities and the bonus of spectacular summertime weather in Chicago promise to make this an event that you will not want to miss.

Eye on TRI: Scott Lute, U.S. FDA

Scott Lute has been with the U.S. Food and Drug Administration since 2002 in the Bioprocessing laboratory in the Division of Monoclonal Antibodies. Over the past 10 years he has extensively studied viral clearance by biotech downstream processing associated with monoclonal antibody manufacturing, including: column resin lifetime studies, virus characterization studies, Q-PCR viral assay development and virus filter performance studies. He was an active member of the Virus Filter Task Force performing the lab-based studies leading to the nomenclature system outlined in *PDA Technical Report No. 41, Revised 2008, Virus Filtration*; thus, he is an ideal candidate to teach courses focusing on virus filtration.

Courses that you teach for PDA: "Virus Filtration" and "Preparation of Virus Spikes Used for Virus Clearance Studies"

How long have you been an instructor for PDA? This is my first year teaching for PDA

How long have you been involved with PDA and in what capacity? I have been involved with PDA since 2002. I have been an active participant of the PDA Virus Filter Task Force responsible for standardizing the nomenclature of both large and small pore size virus filters, performing the bulk of the lab-based development work. I have also given talks at the PDA/FDA Virus & TSE Safety Conferences related to virus-removal filters in Washington, D.C. and in Europe.

What are the challenges/problems that these courses identify and offer solutions to? Since biotechnological and biological therapeutic products are often manufactured using materials of animal or human origin and the risk of contamination by known or unknown pathogens exists, regulatory agencies worldwide require a demonstration of viral safety for these products, usually by spike/removal validation studies. Scale down virus filtration unit operations need to be representative of a large scale when validating an industrial bioprocess.

Since designing a robust and validated virus removal step is complex, and it is critical to carefully select virus filters and design the virus filtration process to ensure safe use of biological therapeutic products, the "Virus Filtration" course helps participants make these sound decisions.

In addition, it is critical to understand and control virus spike quality attributes to ensure that they do not perturb unit operation performance during these validation studies; otherwise, the study won't be representative of large scale. The "Preparation of Virus Spikes Used for Virus Clearance Studies" course helps participants understand the complexity and variability of virus spikes and teaches methods to further control the quality.

What makes these courses different than others which may be out there? Virus filtration and virus preparation are topics that have seen considerable interest in the past few years. Over the past decade, PDA has brought together industry, academia and government experts to write PDA *Technical Report No. 47, Preparation of Virus Spikes Used for Virus Clearance Studies* and TR-41 which provides advice on these topics. These courses will allow students to learn firsthand from members of the task forces responsible for publishing TR-41 and TR-47 and gain a thorough understanding of the documents and how to implement the recommendations into their own laboratories.

Why should people attend these courses over others? These courses will consist of both a classroom lecture complemented by a hands-on laboratory–based class. Participants will initially learn concepts behind virus filtration and virus preparation in the lecture section and will challenge themselves in the lab-based section by testing model virus preparations and performing lab-scale viral clearance studies using model bacteriophage.

What would you say to people considering taking a PDA course? You are about to increase your knowledge in specific and highly technical areas related to biotechnology viral safety that will benefit your company and your career. PDA courses are focused on areas of interest and are taught by instructors who have particularly strong expertise as well as knowledge and experience in a pharmaceutical manufacturing environment. PDA laboratory courses are held in well-equipped state-of-the-art laboratories designed to maximize the learning experience.

The 2012 Aseptic Processing Training Program is **SOLD OUT!** Visit **www.pda.org/aseptic** to sign up to receive an email notice when registration opens for the next session.

Parenteral Drug Association Training and Research Institute (PDA TRI)

Upcoming Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

July 2012

Quality Systems for Aseptic Processing

July 30 - August 3, 2012 | Bethesda, Maryland
www.pda.org/qsaseptic

August 2012

Filtration Week

August 27-31, 2012 | Bethesda, Maryland
www.pda.org/filtrationweek2012

- Filters and Filtration in the Biopharmaceutical Industry – Basics Course | August 27-28
- Filters and Filtration in the Biopharmaceutical Industry – Advanced Course | August 29-31

Fundamentals of an Environmental Monitoring Program – New Course

August 29-30, 2012 | Bethesda, Maryland
www.pda.org/environmental2012

September 2012

2012 PDA FDA Joint Regulatory Conference Course Series

September 13-14, 2012 | Baltimore Marriott Waterfront Hotel in Baltimore, Maryland
www.pda.org/pdafdacourses2012

- Biopharmaceutical QA/QC for Senior Management | September 13
- Application of a Quality Systems Approach to Pharmaceutical CGMPs | September 13-14
- Preparing for Regulatory Inspections for the FDA and EMA | September 13-14
- Application of Phase-Appropriate GMP to the Development of Protein Bulk Drug Substances | September 14 – New Course
- Development of Qualification and Validation Protocols – A Risk Management Approach | September 14
- Good Distribution Practices for the Pharmaceutical Supply Chain | September 14 – New Course

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

Laboratory Courses

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

The Faces of TRI

Bob Dana, PDA

If you are a regular reader of the *PDA Letter* and the monthly TRI section, you have recently heard about a number of our new and existing training opportunities, including: global and in-house training opportunities, our *Quality Systems for Aseptic Processing* course series and the training courses planned for PDA's *2012 Annual Meeting* in Phoenix, Ariz. in April.

In addition, our Eye on TRI column features some of our instructors and provides some background on the great volunteers who teach for us. **John Brecker** was featured in the January issue, and the March issue provided some background on **Carol Lampe**, who has returned as a faculty member after a few years off.

I'm sure you've also seen some of the ads for our courses as well. At least I hope you have! And of course, the PDA website contains lots of information about our upcoming training courses. All of these courses and training opportunities are our contribution to PDA's mission of *Connecting People, Science and Regulation*℠.

As I thought about writing this column for the May issue of the *PDA Letter*, it occurred to me that we provide plenty of information about our upcoming courses and we feature one of our instructors fairly regularly, but we never say much about our staff other than to acknowledge their contributions to our success. So, I thought this month I would take the opportunity to introduce them and give you some background on the folks you'll meet and work with when you take one of our courses.

We actually have a fairly small staff, especially given the diverse types and numbers of courses we provide. **James Wamsley** is the senior member of our staff, having joined PDA as the Assistant Coordinator, Laboratory Education in January 2004. He has a BS Degree in Biological Sciences, which has helped him in his work. James joined when TRI was still at the University of Maryland Baltimore County. James assumed his present position in 2007 and played a key role in the design, construction oversight and start-up of the current TRI facility in Bethesda, Md. in the same year. He is the man to see if there are any questions about the facility operations or any of the equipment we utilize in our laboratory courses.

TRI's staff: (l to r) Jeanine Resnick, James Wamsley, Bob Dana, Gerard Cornejo, Stephanie Ko

Stephanie Ko is the professional educator on our staff, holding a BA Degree in Biology and a Master's Degree in Education. She joined PDA in November 2007 as Manager, Lecture Education and was promoted to Senior Manager, Lecture Education in January 2010. Stephanie is responsible for ensuring all our programs in this area meet the rigorous the Accreditation Council for Pharmacy Education standards and for maintaining PDA's accreditation. In addition, she handles our instructor and student relationships for all of PDA's lecture courses at our United States conferences and at the TRI facility in Bethesda, Md.

Our newest staff member is **Gerard Cornejo** who joined TRI in March 2012. Gerard has Associate's Degrees in General Studies and Biotechnology and is currently pursuing a Bachelor's Degree in Biotechnology. He works closely with James and provides support for the various laboratory courses we run in Bethesda.

In addition to Gerard, **Jeanine Resnick** works closely with James and TRI instructors **Dave Matsuhiro** and **Hal Baseman** on a contract basis to provide support for our flagship *Aseptic Processing Training Program*. Jeanine has Bachelor's Degrees in Education and Business and enjoys working in the learning environment at TRI, where she has been since August 2010.

That leaves me, **Robert Dana**. I've been a PDA member since 1985, have been on the PDA staff since 2005 and have been responsible for TRI since January 2009. I have a B.S. in Pharmacy and have been in the pharmaceutical indus-

try since 1967. I've worked in R&D, manufacturing and QA/compliance in addition to working for a large multinational pharmaceutical firm and PDA. I also have owned and operated a consulting business for a period of time.

So that's who we are. Each and every one of us is committed to ensuring that PDA's training programs are of the highest quality and that the training experience our students receive both before and during their courses is second to none. We all truly believe that we do indeed provide intensive, hands-on, job-focused training our students can take home and apply immediately in their jobs. We look forward to meeting you at one of our courses soon.

PDA Who's Who

Hal Baseman, COO, ValSource

John Brecker, Senior Microbiologist, Quality Control, Fleet Laboratories

Carol Lampe, Sr. Consultant, Aseptic Processing, J.M. Hansen & Associates

Dave Matsuhiro, President, Clearoom Compliance

Tech Trends continued from page 20

hance its manufacturing processes to a point where it is consuming the minimum energy and resources necessary in order to meet its production and quality needs.

Collaboration and best practices among the global community of single-use system users is encouraged at Pall. Customer data shows that presterilized single-use systems can cut water and cleaning chemical consumption almost in half and enable drug manufacturers to cut their carbon footprint more than a third by reducing the consumption of water and energy needed to clean traditional systems.

Pall is gaining recognition for its efforts. The company has been included in the Cleantech Index ***(1)*** since 2006 and has been a constituent of the FTSE4Good Index ***(2)*** since 2001. Additionally, Pall was a partner in the U.S. Environmental Protection Agency's Climate Leaders program ***(3)*** and was ranked 69th out of 500 U.S. companies in *Newsweek's* 2011 Green Ranking listings ***(4)***.

References

1. Cleantech Index, www.cleantech.com/the-cleantech-index-ctius/
2. FTSE, www.ftse.com/Indices/FTSE4Good_Index_Series/index.jsp
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4. Newsweek Green Rankings, www.thedailybeast.com/topics/green-rankings.html

Editor's Message

It is Always the *Write* Time

What do *you* have to say? PDA's membership of over 9,000 professionals in quality, manufacturing, regulatory affairs, product development and more possesses boundless knowledge and expertise in areas crucial to the manufacture of life-saving and life-changing medicines. And we never tire of hearing from each and everyone of you!

There are many ways to make your voice heard, but none is as lasting as authoring a manuscript for the *PDA Journal of Pharmaceutical Science and Technology* or an article for the *PDA Letter*. The Journal accepts original research, new technology case studies, commentaries, and newly introduced technology briefs, which are designed for poster presenters to quickly get their posters peer-reviewed and published in a scientific journal.

The *PDA Letter* Editorial Committee works with the PDA editors to establish an annual schedule for feature articles. Currently, we are seeking articles on the U.S. FDA CDER's new compliance organization, biosimilars and targeted therapies. For those who secretly aspire to be a journalist, volunteers to write about the upcoming PDA/FDA Joint Regulatory Conference are always appreciated! Of course, the Letter departments (People, Science, Regulation, Programs and TRI) are open for content relevant to PDA. In the People department, Chapter updates, career and management tips (for Tools for Success), and other information pertaining to the human factor are welcome. In Science, the Letter accepts articles on research and technology, just not with the level of detail found in the PDA Journal. In addition, articles on task forces, interest groups, advisory boards, upcoming Journal editions and books can be found each issue in the Science Snapshot. The Regulatory department is open to discussion of regulatory trends, and, like the Science Snapshot, the Regulatory Snapshot keeps members informed of the activities under the PDA Regulatory Affairs and Quality Advisory Board. Programs and TRI are the departments reserved for conference chairs, course faculty and TRI staff to discuss the various events and educational offerings important to the membership.

For the truly ambitious author, consider writing or editing a PDA/DHI book or join a task force and help draft a PDA technical report or a regulatory response document.

We know PDA members are extremely busy and writing takes a lot of time. The editorial teams for the Letter, Journal and the technical books can help aspiring authors, and even well-established authors, develop their stories. Proposals for articles can be reviewed by the respective editorial committees, we can assist with outlines, and of course, we will provide editorial help with drafts.

Topics of interest to PDA include, but are not limited to: • Pharmaceutical/biopharmaceutical manufacturing • Sterile processing • Validation • Quality by design • Process analytical technologies/rapid microbial methods • Risk management • QA/QC • Regulatory science • Combination products • Glass • Prefilled syringes • Cleaning •Water systems • Filtration

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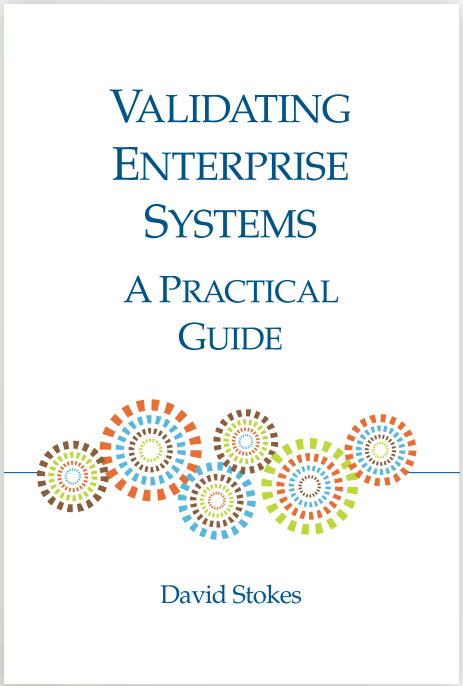

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