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PDA Letter

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www.pda.org/pdaletter

January 2010

In This Issue:

PDA Micro Conference Filters Fact from Myth

Walter Morris, PDA

While you won't find "urban myths" about pharmaceutical microbiology on any "top ten urban myths" websites (snopes.com fully indexes hundreds by subject matter, by the way), such myths do exist and some are well-engrained within the industry.

Let's forget for a moment the largest urban micro myth in the industry—that the classical sterility test is an effective and useful test, which is now more a punch line than myth—there are plenty of other practices that have mythical origins. Take, for example, microbial control in water systems. Think turbulent flow and high flow rates prevent microbial attachment and biofilm growth? Think again. Smooth, electropolished stainless steel surfaces reduce cell attachment and lessen biofilm development, right? Wrong. Or, look at sterilizing filters. One cannot properly challenge a sterilizing-grade filter with less than is 10^7 cfu/cm^2 because… why exactly? (See sidebar on page 17 for more on these.)

These and other micro "urban myths" were discussed at length during a highly rated session of *PDA's 4th Annual Pharmaceutical Microbiology Conference* in October in Bethesda, Md.

According to session moderator and conference planning committee member **Scott Sutton**, PhD, Principal Consultant, Microbiology Network, the session was highly anticipated by conference planners.

"We are here today to talk about urban myths, and we are very excited about this," Sutton said. "We are going to have an opportunity perhaps that we don't get a lot, and that is to take a step back and look at what we do, why we do it, might there be better ways to do it, or is there any point in doing it at all."

Sutton illustrated the power of myths on individuals by citing a research paper about monkeys, bananas and cold water sprinklers.* Whenever the monkeys tried to take the bananas, they were sprayed with the ice cold water. Over time, the monkeys learned not to touch the bananas. The researchers then substituted a "trained" monkey for a "naïve" monkey. When the naïve monkey went to the bananas, the other monkeys "beat him senseless," training it not to take the bananas. Eventually, all of the original monkeys were replaced by new monkeys, but for the training, none touched the bananas, though none knew why.

Sound familiar? As the three session speakers explained, many common practices

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PDA® Parenteral Drug Association

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2010 PDA Annual Meeting

Manufacturing Excellence

March 15-19, 2010
Gaylord Palms Resort & Convention Center
Orlando, Florida

Conference	I	March 15 - 17, 2010
Exhibition	I	March 15 - 16, 2010
Career Fair	I	March 15 - 16, 2010
Courses	I	March 18 - 19, 2010

PDA
Parenteral Drug Association

www.pda.org/annual2010

The *2010 PDA Annual Meeting* will explore an area of immense importance to the global bio/pharmaceutical industry – ***Manufacturing Excellence***. Join your industry and regulatory peers at this meeting to examine manufacturing best practices and strategies that can maximize your company's efficiency and productivity, while delivering safe and reliable drugs to patients. The program will address creating an environment of quality and operational excellence through properly planned and performed process design, validation, contamination control, testing, handling, product and supply chain security, and much more.

Complementing the conference are PDA Training and Research Institute (PDA TRI) courses, an exhibition featuring today's leading bio/pharmaceutical companies and service providers, PDA's 6th Annual Career Fair and enhanced networking opportunities that take advantage of all that Orlando and the exciting Gaylord Palms Resort and Convention Center have to offer.

Take your career to the next level with the knowledge, best practices and valuable contacts you will gain at the *2010 PDA Annual Meeting*.

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Cover art:
PDA's Pharmaceutical Microbiology Conference, now in its 4th year, helps the industry filter through Common Micro Myths

Coming Next Issue:
ICH: The Latest Document

2010 Starts with New Contribution to *PDA Letter*

We start 2010 with the first of four reports from Europe by PDA member **Barbara Jentges**, PhD. This month she looks at regulatory harmonization in the European Union, including rules for variations to marketing authorizations. Barbara is the Managing Director, Pharmaceutical Advice, Compliance & Training (PHACT), which specializes in Drug Regulatory Affairs. Her 19-year career in regulatory affairs includes time as an external assessor for the German Health Authority. We thank Barbara for committing to this and look forward to her reports throughout the year.

It is worth noting that the New Year brings a new policy for the way the European Medicines Agency refers to itself. Starting on December 8, 2009, the European Medicines Agency dropped the acronym "EMEA," due to confusion the acronym caused. The organization will now refer to itself solely as the European Medicines Agency or simply as the Agency. The Agency will use "EMA" for document references and its website and e-mail addresses. These changes will be implemented in the *PDA Letter* starting with this issue.

Finally, *PDA's 4th Annual Pharmaceutical Microbiology Conference* last October provided the fodder for this issue's feature stories. On the cover, I recap a session on microbiology myths which drew a packed house and ran-over thanks to the interesting discussions the three presentations elicited. The second feature is by PDA's **Emily Hough**; she reports on the proceedings of a session on mycoplasma. The "Tools for Success," and IG and Chapter contacts pages will return next issue.

Correction

The *PDA Letter* staff in the November/December issue mixed up the education information and join date in Christopher Smalley's Volunteer Spotlight (p. 32) with another volunteer's. It should have read: BSc, Pharmacy, Philadelphia College of Pharmacy; MS, Pharmaceutical Chemistry, Temple University College of Pharmacy; MBA, Temple University Fox School of Business; PhD, Healthcare Administration, LaSalle University. He joined PDA in 1984. We apologize to Christopher for the mistake. All Volunteer Spotlights are available online at www.pda.org/spotlight

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

PDA Europe
Adalbertstr. 9
16548 Glienicke/Berlin
Germany
Tel: +49 33056 43 6879
Fax: +49 33056 43 6884
Email: petzholdt@pda.org

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

CHAIR'S MESSAGE

Chair Maik Jornitz

Reflect Back – Going Forward

On behalf of the PDA staff and Board of Directors, I would like to wish all of you and your families a happy and prosperous new year. Yes, a new year already, and we are in the midst of planning our travels, projects and tasks for 2010.

However, let's briefly reflect on 2009, and in doing so, I would like to take the opportunity to sincerely thank **John Shabushnig**, the Immediate Past Chair, and **Bob Myers**, past President of PDA, for their tireless efforts and valuable contributions over the last years. They kept PDA, even under adverse economic conditions, sound and supportive to its membership with exceptional programs, far-sighted initiatives and commendable leadership.

In 2010, we start with a new team and, as we previously announced, are extremely pleased to have **Richard Johnson** as our new President. Richard and his team utilized the last quarter of 2009 to prepare for another successful year in PDA's history. For our Association, successful means continually improving our deliverables and ensuring they remain of interest to the membership. Successful, furthermore, means weathering an unprecedented economic downturn and coming out of it even stronger with a multitude of new programs, like an upcoming Biofilm and Parenteral Conference in Europe and a Vaccine Conference in the United States and Europe. In total, the PDA team has planned over 50 conferences in 2010. All topics derived from the input of the membership and current industry trends, and all programs supported by expert speakers from the industry and regulatory authorities.

As many of us have experienced, these conferences are essential networking settings that create a conversation ground with our peers and colleagues and inform us through lectures. One of the venues, the PDA Annual Meeting, March 15–17 in Orlando, Fla., with the theme "Examine manufacturing best practices and strategies to maximize your company's efficiency and productivity," centers on value creation, improvements and enhancements within our organizations. New manufacturing technologies and designs discussed during this meeting are a necessity for sustaining our industry and are safe and reliable for our patients. This venue is a must-attend for anybody who wants to learn about new trends in manufacturing science and technology.

To review the entire list of conferences planned by PDA, please visit our web site at www.pda.org. An important information tool to keep you up-to-date and inform you about newest trends and regulations is e-mail. We therefore would like to encourage you to keep your e-mail and contact data current. Otherwise, we do not have the ability to serve you appropriately as required.

Aside from the multitude of conferences, the Training and Research Institute (TRI) will expand its offerings to the membership and, if required, will bring the training to your site. This will save travel time and costs, without sacrificing high level training needs. The well-known, exceptional training programs of TRI are available at our members' discretion. Hands-on training courses, held within TRI, have been very successful, as our members realize it is better by far to make a mistake in a training setting than in a production setting. While there is no way to quantify this, I would imagine that TRI training courses have probably saved many batches, a service to you and the patients we all serve.

Another valuable, often used resource is the incomparable series of PDA Technical Reports. Multiple Technical Report revisions and newly defined reports will be published in 2010. These practical reports are created by volunteer task forces composed of experts from manufacturers, regulatory authorities and vendors and they are an essential read to stay current. PDA Technical Reports comprise a library of knowledge and indispensable support in our daily work.

The *PDA Journal of Pharmaceutical Science and Technology* is as well. It is now available in electronic format to create the ability to access this prestigious scientific publication via the Internet and readily

retrieve articles whenever necessary.

The list of membership services is too manifold to try to encompass within this message. Having said this, we,the Board, the President and the staff of PDA, will do our utmost best to enhance these services whenever possible and necessary. Your input is essential and asked for.

PDA has come a long way and become a vital part of our business life. PDA will continue to be a strong partner to its members, offering support when called upon. Over many years, PDA's support has primarily been possible, not only through the work of PDA's staff members, but by the effort of our volunteers. We would like to thank our volunteers for their hard work and efforts. Their time spent is invaluable for all of us. New volunteers are certainly most welcome.

As the new Chair of PDA, my prime ambition is to evaluate additional and improved member services. Continuous improvement, as we all strive for in our day-to-day work, is in effect within PDA. The long-term viability and excellence of PDA is of extreme importance to me. Long term means also a revision of PDA's strategic plan, a primary target of the Board. Our plan is to have by the end of 2010 a strategic plan in place that will direct and guide our organization over the subsequent five years. We are confident that the outcome will show that our members, as well as non-members, are able to continue to rely on the robust and vital support by the PDA, whether by training, networking venues, comment papers or scientific publications.

Additionally, we believe in an "open door" policy. Therefore, we encourage you to submit your comments and suggestions, either by e-mail or face-to-face at conferences. The PDA leadership and staff will appreciate your input.

Finally, I would like to thank again the many volunteers, exhibitors and sponsors for their support, which is the foundation that allows our organization to be the industry's "wingman." That is what we are to you. Our membership is our focus. Our desire is to serve you.

Deliver Safe and Effective Products to Patients' Hands

Technical Report No. 46, Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User Now Available at www.pda.org/bookstore

Managing shipments of product in the "last mile" to the point of patient administration can prove difficult, but PDA's Last Mile Task Force has sorted through the various distribution regulations in major markets to provide guidance on the proper handling of controlled-temperature medicinal products and devices along the final legs of the distribution chain. This follow-up document to Technical Report No. 39 on cold chain management is an invaluable tool to all involved in the "last mile."

Members download TR-46 for free until February 12

PDA members can access this technical report for free until February 12. Just go to the PDA bookstore and use your PDA ID and password when prompted.

2010 Board of Directors

Executive Committee

Congratulations to **Maik Jornitz**, Group Vice President, Product Management Filtration/Fermentation Technologies, Sartorius Stedim Biotech, who assumes the role of PDA Chair for the 2010-2011 cycle. He was voted Chair-Elect in 2007.

Anders Vinther, PhD, Vice President of Corporate Quality System & Support, Genentech was elected in 2009 to Chair-Elect for 2010-2011, and then, starting in 2012, will become PDA's next Chair. Anders was the PDA Treasurer in 2008 and 2009. **Harold Baseman**, Principal and Chief Operating Officer, ValSource, was elected to Treasurer in 2009. He previously served as a Director since 2008. **Rebecca Devine**, PhD, Regulatory Consultant was reelected in her position as Secretary. **John Shabushnig**, PhD, Sr. Manager/Team Leader, Quality Systems and Technical Services, Pfizer, moves into the Immediate Past Chair position for the next two years.

PDA would like to thank **Vincent Anicetti**, VP, Quality Biochem, Quality & Compliance, Genentech, for serving as PDA Chair in 2006-2007 and as Immediate Past Chair from 2008-2009. Prior to election to the Executive Committee, Vince served on the Board of Directors since 2000.

Directors

PDA congratulates and welcomes three new Directors, who were elected in 2009: **Gabriele Gori**, Global Head of Compliance, Novartis Vaccines & Diagnostics; **Zena Kaufman**, Divisional Vice President for Global Pharmaceutical Operations QA – US/Puerto Rico Region, Abbott; and **Lisa Skeens**, PhD, Vice President, Global Regulatory Affairs Pharmaceuticals, Baxter Healthcare Corporation. **Martin VanTrieste**, Vice President of Quality, Amgen, was reelected to the Board.

Gabriele is a co-founder, an officer and active member of PDA's Italy Chapter. He also has been a speaker and trainer for PDA on topics related to aseptic processing, GMP compliance and quality systems. He has represented PDA at important meetings with regulators, such as the December 2006 European Medicines Agency's Interested Parties meeting on the revision of Annex 1. In 2007, he received PDA's Distinguished Service Award.

Zena first became involved by attending Midwest Chapter dinner meetings. She then became involved with the Regulatory Affairs and Quality Committee (RAQC), which she chaired from 2006-2008. She was co-chair of the PDA/FDA Quality Systems conference series and the PDA commenting Task Force for FDA's GMPs for the 21st Century.

Lisa served on the PDA Board

Véronique Davoust,PhD
Pfizer

Gabriele Gori
Novartis Vaccines & Diagnostics

Lothar Hartmann,PhD
F. Hoffmann-La Roche

Zena G. Kaufman
Abbott Laboratories

Steven Mendivil
Amgen

Michael Sadowski
Baxter Healthcare

Junko Sasaki
Dainippan Sumitomo Pharma

Amy Scott-Billman
GlaxoSmithKline

Lisa Skeens, PhD
Baxter Healthcare

Christopher Smalley
Pfizer

Laura Thoma
PharmD, U. of Tennessee

Martin VanTrieste
Amgen

of Directors from 2000-2007, and was Secretary of the Board in 2006-2007. She sat on the RAQC from 1996-2006, serving as its Chair from 1999-2003. She participated in many planning committees for PDA, including chairing both the PDA/FDA Joint Conference and the PDA Annual Meeting.

PDA thanks **Stefan Köhler**, PhD, Director of Engineering, Maintenance and Utility – Sweden, AstraZeneca, and **Louise Johnson**, Vice President, Quality, Aptuit, for their service to PDA and its Board.

Experience With Supply Chain Auditing?

The Audit Guidance Advisory Board (AGAB) is preparing to update *PDA Technical Report No. 32, Revised, Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations* and are looking to establish an expert working group to expand and update TR–32 with volunteers and experience and supply chain auditing.

If you wish to participate in this effort, please submit your name and a brief background of your experience to the Audit Guidance Advisory Board for consideration to **Iris Rice** at rice@pda.org.

TRI Biotechnology Lab Dedicated to PDA Outstanding Scientist

PDA President **Richard Johnson** and members of PDA's Board of Directors honored **Theodore H. Meltzer**, PhD, on December 10 for his many contributions to PDA over his years as a member by dedicating a Training and Research Institute laboratory to him.

A placard hung outside the room states: "His contributions to PDA have been many, but none may be greater than his ability to assemble top thought leaders in his field to contribute to PDA's educational offerings."

Johnson said, "Ted was chosen for his long service and many contributions to PDA, especially in education." He continued, "Ted has long been a fixture at PDA, so now he'll actually be affixed to PDA."

In the span of his PDA membership, Meltzer has had over 20 manuscripts published in the *PDA Journal of Pharmaceutical Science and Technology*; served on the task forces responsible for *PDA Technical Report No. 40, Sterilizing Filtration of Gases, PDA Technical Report No. 26, Sterilizing Filtration of Liquids and PDA Technical Report No. 23, Industry Survey on Current Sterile Filtration Practices* and has co-published five PDA-DHI books in the Filtration handbook series. Additionally, his work as an expert in water preparation and filtration has significantly led to the success of the pharmaceutical/biopharmaceutical industries. As part of PDA's sixtieth anniversary celebration, Meltzer was named one of PDA's outstanding scientists.

Ted Meltzer watches as his placard is unveiled at a ceremony held at PDA's TRI facility

A very modest Meltzer said that he didn't think his performance warranted the honor presented to him.

In his typical humorous way, did make a request—he asked if future generations of students could take their shoes off before they enter his room.

(l-r) Maik Jornitz, Sartorius Stedim Biotech; Bob Dana, PDA; Ted Meltzer; John Shabushnig, Pfizer; Richard Johnson, PDA

Parenteral Drug Association Training and Research Institute (PDA TRI)

2010 ASEPTIC PROCESSING TRAINING PROGRAM

2010 SCHEDULE:

Session 1:
Week [SOLD OUT!] -29
Week [illegible]ary 22-26

Session 2:
Week 1: March 22-26
Week 2: April 19-23

Session 3:
Week 1: May 17-21
Week 2: June 14-18

Session 4:
Week 1: August 16-20
Week 2: September 20-24

Session 5:
Week 1: October 18-22
Week 2: November 8-12

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This ten-day, two week comprehensive training program, taught by 20 industry leading experts in their fields, with over 200 years of combined experience will give you and your personnel the training and information needed to properly evaluate and improve your aseptic processes to ensure sterile products. This program provides the perfect balance of hands-on laboratory and lecture training, equipping you with tools and actual experience you can bring home and apply immediately on the job.

BENEFITS OF ATTENDING:

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

LEARNING OBJECTIVES:

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

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

FOR MORE INFORMATION CONTACT:

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

LOCATION:

PDA Training and Research Institute
4350 East West Highway, Suite 150, Bethesda, MD 20814
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Science & Technology Snapshot

Advisory Board *Watch*

An Update on PDA's Three Scientific Advisory Boards

Iris Rice, PDA

PDA Audit Guidance Advisory Board

The Audit Guidance Advisory Board (AGAB) is comprised of 10 active members with experience in auditing, quality, validation and compliance. In 2009, **Steven Walter** joined AGAB as co-chair to assist Chair **Janis Olson.** Steven is a relatively new PDA member, joining in April 2009, and has already been active in the developing the agendas of all 2009 Advisory Board meetings.

One of the primary activities of the AGAB is the ongoing assessment of relevance and value of PDA Technical Report No. 32, *Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations* which was last revised in 2004. The goal of the revision process is to address changes in science, technology and regulatory policy that have occurred during the last 10 years and to introduce a new, "modularized" risk-based structure to the organization of TR-32.

Additionally, the AGAB will be monitoring the transition of the Audit Repository Center (ARC) from Syntegra to Intelaform, our new TR-32 process licensee. There is even discussion of expanding the scope of ARC to other areas, such as instrumentation, NIR and RAMAN, and RFID . To implement this expanded scope, the Advisory Board is seeking subject-matter experts in these areas too. Please contact Iris Rice at rice@pda.org if you wish to be considered for either of these opportunities.

PDA Biotechnology Advisory Board

The Biotechnology Advisory Board (BioAB) is comprised of 22 voting members with a diversity of experience in areas related to manufacturing, control and development of biopharmaceutical products. In 2009, the BioAB added **Michael VanDerWerf** as the Regulatory Affairs and Quality Control (RAQC) Liaison for the BioAB. Michael is responsible for keeping BioAB informed of RAQC's activities during the year and has served as an excellent liaison between the two groups. The BioAB also recommended the appointment of S**tephen Notarnicola,** as co-Chair of PDA's Biotechnology Interest Group. Stephen will work with BioAB member **Jill Myers,** to facilitate Interest Group meetings for PDA's Annual Meeting and the PDA/FDA Joint Regulatory Conference.

PDA Technical Report No. 15, (2009 Revision), Validation of Tangential Flow Filtration in Biopharmaceutical Applications was published in 2009 under the auspices of BioAB. Two of BioAB's members, **Hannelore Willkommen** and **Kurt Brorson** were proactive in facilitating the completion of an upcoming Technical Report on Preparation of Virus Spikes Used for Virus Clearance Studies. PDA anticipates publishing this report in early 2010. Other anticipated TRs under the auspice of BioAB for the years 2010–2011 are as follows:

- Points to Consider for Biotechnology Cleaning Validation
- Alternative Methods for Mycoplasma Testing
- Analytical Methods Development for Biotechnology Products
- Analytical Methods Validation for Biotechnology Products
- Reprocessing of Biopharmaceuticals
- Phase Appropriate Application of GMPs and Quality Practices to the Development of Biotechnological Bulk Drug Substance

In 2009, BioAB formed "Review and Comment Teams" to develop comments on behalf of the PDA membership to regulatory authorities. BioAB teams commented on the following guidances: • Note for Guidance on Minimizing the Risk of Transmitting Animal Spongiform, Encephalopathy Agents via Human and Veterinary Medicinal Products (European Medicines Agency) • Cell Substrates for the Production of Biological Products for Human Use (EU) • Monoclonal Antibodies for Human Use (EU) • Tests for Extraneous Agents in Biological Products (EU).

Barbara Potts, leader of PDA's Mycoplasma Task Force, introduced an organized conceptual methodology for assessing the progress current of PDA task force projects which uses a "bubble chart" to plot each team's progress. The chart is a visual portfolio of PDA's projects, including new task forces that are either forming or in development as well as tracking the new projects arising out of the Paradigm Change in Manufacturing Operations (PCMO) initiative. The chart plots developing task forces with an anticipated output of a

technical report or workshop; and mature task forces, with an anticipated output of a published technical report or upcoming Journal articles. This portfolio will help PDA better manage its technical report projects.

PDA Science Advisory Board

The Science Advisory Board (SAB) is comprised of 20 voting members with expertise in pharmaceutical sciences, technology and manufacturing processes. In 2009, Joyce Bloomfield of Merck and Co.joined the SAB. Each year, SAB reviews the progress on existing task forces, as well as vetting new and hot topics that have been proposed by members. One project nearing completion is the revision of PDA Technical Report No. 22, Process Simulation Testing for Aseptically Filled Products. This project, which focuses on media fills, has been expanded, and new teams will generate several additional technical reports designed to address several other aspects of aseptic processing.

In 2010, we expect to publish the following SAB sponsored technical reports, namely:

- Moist Heat Sterilizer Systems
- Parametric Release of Pharmaceutical Products and Medical Devices Terminally Sterilized by Moist Heat
- Validation of Dry Heat Processes Used for Sterilization and Depyrogenation
- Steam in Place
- Validation of Manual Aseptic Processes
- Fundamentals of Cleaning and Disinfection of Programs
- Evaluation, Validation and Implementation of New Microbiological Testing Methods
- Fundamentals of Environmental Monitoring

SAB provided valuable input to the development of Technical Report No. 46, Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User. **[Editor's Note:** For more information on TR-46 see p. 7.] And the SAB is committed to providing sound input on alternative work products. PDA recently published a white paper called "Using an Interactive Voice System or Interactive Web Technology to Manage IMP Retest Dates in Lieu of Placing Retest Data on IMP Labels."

All of the Advisory Boards are actively involved in PDA's new Paradigm Change in Manufacturing Operations (PCMO) strategic initiative. The goal of the PCMO Project is to drive the establishment of "best practice" documents and/or training events in order to assist pharmaceutical manufacturers in implementing the ICH guidelines on Pharmaceutical Development (Q8, Q11), Quality Risk Management (Q9) and Pharmaceutical Quality Systems (Q10).

We expect that this initiative will generate novel workshops, conferences and technical reports, all designed to facilitate communication and knowledge transfer among the experts from industry, university and regulators as well as experts from the respective ICH Expert Working Groups and Implementation Working Group

Task Force *Corner*

Size, Workload Distinguishes PDA's Mycoplasma TF

Emily Hough, PDA

PDA's Mycoplasma Task Force boasts an ambitious agenda of nine articles, three technical reports and a training workshop. Task Force leader **Barbara Potts** outlined the group's work at *PDA's 4th Annual Global Microbiology Meeting* in October.

The prolific workload is not the only reason this Task Force differs from others; the fact that it has grown from 22 members to close to 70 since 2006 makes the group unique.

The Task Force is divided into four subgroups that focus on specific areas of mycoplasma testing. When it meets, the Task Force alternates between meeting collectively and as subgroups to ensure that information and discussions of new technologies cross over to all of its members. At the start of face-to-face meetings, all members are seated together and share problems that their specific subgroups are facing. Next, the subgroups break out for topic-focused discussions. (See the box for subgroups by topic and leaders.)

If the amount of work that that the Task Force is putting out is any indicator, this arrangement is working well for the group. In early 2010, the Task Force is scheduled to publish nine articles in a special supplement to the journal *Biologicals*. The articles, which were authored by various task force members and co-edited by **Leonard Hayflick**, Professor of Anatomy, School of Medicine, University of California, and Potts, Senior Consultant, Biologics Consulting Group, Inc, touch upon a myriad of mycoplasma topics.

Three papers explore different studies of the validation of PCR assays and on the regulatory acceptance of a sensitive nucleic acid technology using a touch-down PCR amplification technique that can be completed within hours instead of days.

Another article is on A. laidlawii which has been known to survive over long periods of time in powdered components of cell culture media and bovine serum. The authors of this piece were asked to share their experience of this microbe.

The fifth and sixth papers cover the scope of mycoplasma contamination within the biopharmaceutical industry using the traditional detection methods and cross comparisons of new molecular biology detection methods for mycoplasma that includes PCR and electrospray ionization mass spectrometer.

The seventh article addresses a study for developing methods to influence Mycoplasma cell size and removal for filtration studies.

The final two articles are devoted to the biology of A. laidlawii and provide an in depth historical perspectives on mycoplasma research, Spiroplasmas and Phytoplasmas.

The Task Force is also developing three technical reports in various stages of completion. One of the three technical reports is about alternative methods for mycoplasma testing including nucleic acid detection and

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PDA Parenteral Drug Association — Connecting People, Science and Regulation®

PDA Europe Upcoming Workshops 2010

Stoppers & Elastomers

The workshop gives a comprehensive overview of elastomeric components relevant for parenteral pharmaceutical products:

- Manufacturing of elastomers: Chemical composition and process
- Chemical, physical and microbiological properties
- Processing of elastomeric components: Washing, siliconisation, packaging, transportation
- Processing in the pharmaceutical facility (bulk and ready to use): from Washing to visual inspection
- Container closure aspects
- Regulatory issues, e.g. change of stopper.

An update of the latest methods, technologies and processing will be presented. Case studies highlight the current best practice.

16-17 March 2010
Cologne, Germany

Siliconisation

– Silicon oil and its applications for parenteral products –

Silicon oil is an important processing aid in the pharmaceutical and biopharmaceutical industry. It is used for elastomeric components and for glass containers. E.g. Pre-filled syringes silicon oil is needed to move the plunger. Stoppers are siliconised to process properly in filling lines. This workshop gives an overview of all relevant aspects of the use of silicon oil including the following topics: Chemistry of silicon oils | Chemical, physical and microbiological properties | Test methods: Quantify silicon oil in bulk and on surfaces. Functionally testing. | Applications • *Siliconisation and testing of stoppers (How to do, what is the right amount)* • *Siliconisation and testing of pre-filled syringes* • *Processing issues in filling lines* • *Interaction of silicon oil with APIs and formulation, e.g. biopharmaceuticals* • *Visual inspection, droplet formation, surface changes leading to false rejects* • *Regulatory issues*
The workshop will give an update of the latest technologies and describes current best practice with case studies.

18 March 2010
Cologne, Germany

For other events see:
www.pda.org/europe

Task Force Corner, continued from page 13

is enzyme activity based. The purpose of this TR is to recommend procedures for validating against official methods, appropriate reference standards and potential applications for alternative mycoplasma testing. This Technical Report is in final review by representatives from the USP, the European Medicines Agency, Paul-Ehrlich-Institut (PEI), WHO and the Japanese regulatory agency.

The second Technical report is on the standardization of mycoplasma filters. Potts, at the PDA microbiology meeting, emphasized that the group is not trying to promote one kind of mycoplasma filter but is instead developing a consensus rating method so it can be used to evaluate all the different filters. In its research, the subgroup worked with vendors and users and started out with Acholeplasma laidlaii, five media and two methods using a .2 micron filter. The subgroup is currently looking for a challenge method to test and has narrowed the scope to two types of media. Once all the data has been collected, a technical report will be written and published for a standard challenge protocol.

The third report that the Task Force is currently working on is on peptones and complex media as a source of mycoplasma contamination. The objective of this report is to educate the end user on details about plant and animal-derived material that is being used in production, a review of the lifecycle the plant and animal-derived material all the way to the user, and an overview of the best practices throughout production and distribution which may minimize the risk of mycoplasma contaminations at the user site. Potts said, "You can do a risk analysis but if you don't have the knowledge, your risk analysis isn't very worthwhile and you need that knowledge."

And knowledge is what this group is providing.

In April 2010, the group will be participating in a Biofilm workshop, which includes topics on mycoplasma and bacteria and will sponsor a course on mycoplasma filtration.

Realizing that that there are no international standards for the Nucleic Acid Test for mycoplasma, the Task Force decided to help develop criteria and is currently collaborating with PDA, WHO, PEI and the National Institutes of Biological Standards in the United Kingdom. The Task Force plans on growing an organism to test early in 2010. The evaluation of this standard will be directed by the National Institute of Biological Standards and the PEI.

In 2008 and 2009, the Task Force surveyed its own membership to see what each member knows about the specialized areas within each subgroup. Using five questions from each subgroup, all members submitted their response. This survey was again used in 2009 in Berlin at *PDA's 3rd workshop on Mycoplasmas* with a wider audience.

The survey uncovered the prevalence of several myths regarding mycoplasma. For example, answers to a question asking about scientifically sound practices for mycoplasma testing regarding media fills, cleaning validation, disinfectant efficacy studies, environmental monitoring and peptone/complex media surprised and discouraged the group. Potts said that she and the Task Force were surprised that the answers to all of these weren't zero and that anyone who was a microbiologist would know to use standard microbiology assays for media fills, cleaning validation, disinfectant efficacy studies and environmental cleaning. According to Potts, "all of our Task Force co-leaders were on the floor weeping when they saw the result."

The Task Force is working on fixing the knowledge gap the exists between the "experts" and general public and in the future will be providing more focused education to attendees.

Be sure to keep your eye on this Task Force's upcoming technical reports and meetings. To volunteer with this Task Force or others, fill out the form at www.pda.org/getinvolved.

Subgroup Leaders

Alternate Methods for Mycoplasma Testing

David Asarnow
Kurt Brorson
Thomas Haemmerle

Emerging Mycoplasma Issues

Len Hayflick
Barbara Potts
Renate Rosengarten

Peptone and Complex Media as a Source of Mycoplasma Contamination

Ivar Kljavin
Chris Wilcox
Russ Nelson
Alison Smith
Hans Noordergraaf

Members of the Mycoplasma Task Force

Alison Armstrong
Alison Smith
Allen Burgenson
Ann Warford
Barbara Potts
Bob Kiss
Brandye Michaels
Carolyn Phillips
Catherine Milne
Christine Arbesser
Christine Mitchell-Logean
Christine Wright
Christopher Bussineau
Christopher Wilcox
Cynthia Romero-Arroyo
David Asarnow
David Onions
David Windsor
Dilip Ashtekar
Donna Chandler
Edward Balkovic
Emiliano Toso
Florence Bernard
Frances Browder
Frank Riske
Garry Takle
Hans Noordergraaf
Helena Windsor
Holger Bromm
Humberto Vega
Ivar Kljavin
Jean-PolCassart
Jerold Martin
Jill Mariano
John Duguid
John Geigert
Jonathan Blount
Kathleen Souza
Keith Hansen
Keith Richardson
Kerry Roche Lentine
Kurt Brorson,
Laura Okhio
Laurie Graham
Leesa McBurnie
Leonard Hayflick
Lin Chen
Linda Hendricks
Maik Jornitz
Marc Glogovsky
Mark Kaiser
Mark Trotter
Marshall Dinowitz
Martha Folmsbee
Mihaela Marian
Monica Cardona
Pierre Caloz
Pranhitha Reddy
Radhakrishna Tirumalai
Renate Rosengarten
Rich Levy
Robert Davis
Robert Maroney
Russell Nelson
Ruth Mantle
Sven Deutschmann
Terrell Kent Johnson
Thomas Haemmerle
Thomas Ihrig
Tim Coleman
Vladimir Chizhikov
Wang-Ting Hsieh
Yves Courties
Herbert Reichert
Vinayak Pawar
Bjorn Breth
Dmittriy Volokhov
Fabrizio Lecce
Barbara McManus
Scott Lute
Maureen Davidson

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PDA Micro Conference Filters Fact from Myth, continued from cover

within companies are rooted in some historical procedure, standard, scientific article or presentation and current personnel might have little to no idea what the rationale was.

Anatomy of a Myth

First off, what exactly is a myth and why do they exist?

Richard Levy, PhD, Senior Vice President of Scientific and Regulatory Affairs, PDA, answered these questions during his presentation, "Filter Sterilization of Liquids: Myths." According to the Merriam Webster Dictionary, a myth is a popular belief or tradition that has grown up around something or someone. According to Wikipedia (October 4, 2009), one of the foremost functions of myth is to establish models of behavior.

In his years with Millipore Corporation, Levy experienced a number of filtration myths that originated from various sources, including refereed and non-refereed sources, marketing campaigns and filter failure investigations. A common source at Millipore, he explained, was discussions within the company.

"I can tell you within my experience at Millipore, we had meetings and started talking about things that arose in the past, but we couldn't remember where they came from. Some people would make a statement, we used to call it 'Millilore.' There was Millilore going around about various things."

T.C. Soli, PhD, Soli Pharma Solutions, identified regulatory enforcement and industry benchmarking studies as two big sources of myth building. Soli, who serves on the USP Pharmaceutical Water Expert Committee and the PhRMA Water Quality Committee, presented "Pharmaceutical Water Mythology" following Levy's talk.

"I really do think the basic origin of most of the myths that exist, not just in water systems, but in our entire industry, is this: Regulation occurs because of the little cGMP, that is enforcement, not the big CGMP which is the regulation. Because the little cGMP is the interpretation. Now the interpretation comes from basically current practices in our industry and not from the promulgated law. And what happens is those expectations are a moving target. It is ever-tightening."

The problem doesn't originate with just the regulatory investigators, he explained. At times, companies will change practices or accept regulatory findings in order to move a product approval along. "Now there is an aversion to 483s, and we all know that 483s are just individual opinions of individual investigators that can be challenged, but the challenge involves delays, and with delays you could have lost revenue from delayed approvals and all kinds of other delays."

Regarding benchmarking, Soli said, "That is what we do when we come to these kinds of meetings, we find out what everybody else is doing, because if everyone else is doing it, it must be okay." In reality, he cautioned, benchmarking can stymie innovation. "It doesn't facilitate it, it actually stifles it, because innovation tends to be the driver for establishing new and tougher expectations that are then held for the whole industry."

Precedence can block scientific reasoning. Soli outlined a number of factors influencing precedence, including the following:

- Successful practices without understanding mechanisms
- Misperception of observed phenomena/mechanisms
- Unscientific opinions/edicts of managers
- Misinterpretation of standards/regulatory expectations
- Belief in antiquated concepts that have been revised/deleted

James Akers, PhD, Akers Kennedy & Associates, followed Soli with the presentation "Urban Myths in Pharmaceutical Microbiology – The 0 and 1 Myth."

Akers cited a number of regulatory documents and standards by the U.S.

Turbulent Flow and Flow Rate

- Turbulent flow (Reynolds # > ~4000) and high flow rates (> ~3 ft/sec) prevent microbial attachment and biofilm growth: WRONG
- Myth originated from microbial count differences between stagnant and recirculating systems. Actual cause:
  - "Fluffy," shearable biofilm forms in low-shear, stagnant water
  - Surface-hugging biofilm forms in high-shear flowing water
  - High-shear forces occur during sampling of both
  - More biofilm flocs sheared from "fluffy" vs tenacious biofilm = higher counts from stagnant water

— From T.C. Soli's Slides

Smooth/Hydrophobic Surfaces

- Smooth, electropolished SS surfaces claimed to reduce initial cell attachment and less biofilm development: WRONG
- Smooth, hydrophobic PVDF surfaces claimed to reduce initial cell attachment and less biofilm development: ALSO WRONG
- The delay in attachment and biofilm initiation is insignificant (minutes to a few hours)
- Once biofilm begins, it becomes the preferred attachment surface, regardless of MOC
- Questionably worth the high cost of EP-SS/PVDF for that purpose
- However, smooth surfaces are more easily cleaned of biofilm than conventional SS surface smoothness

— From T.C. Soli's Slides

10^7 CFU/CM^2–Unclear Origins?

- If there are 10 million pores per cm^2 of membrane area in a sterilizing grade filter, at least oversized pores would be challenged
- One bacterium per pore per unit surface of a sterilizing grade filter assuming 10^7 pores per cm^2
- Demonstrate the reduction of bioburden by a factor of 10^7 or 7 orders of magnitude per cm^2
- Maximum challenge level attainable by appropriate lower nutrient culturing methods
- Thermal sterilizations achieve fewer than one failure in a million–let's be higher since we cannot sample reliably

— From Richard Levy's Slides

FDA, the European Medicines Agency, the World Health Organization, ISO and others that promulgate the notion that every unit within a lot is sterile. The problem, he said, is that it is impossible to prove a negative. "Nevertheless, as the standards and guidance documents have evolved it seems quite clear that they have moved inexorably toward the expectation to at least approach an absolute proof of sterility." This conundrum is the source of myth making and misunderstanding.

In order to prove sterility, Akers asserted, an analytical procedure sensitive enough to differentiate between the absence of viable organisms (0) and the presence of not more than one viable (1) would have to exist. In addition to this unlikelihood, the method should be able to detect every viable organism virus up to multi-cellular parasites, as well as non-culturable organisms. Lastly, this unrealistic test "would need to evaluate every container produced in every lot, because to prove a negative absolute (sterility), we must test everything."

One of the real-life consequences of the belief that sterility can be proven is a ramping up of environmental sampling. In both isolators and ISO 5 aseptic rooms, Akers maintained, "we cannot come closer to sterility by simply looking harder." Regulators, however, favor "continuous monitoring and seem to believe that higher sampling intensity should equal better sterility assurance."

The focus of regulators and industry when evaluating aseptic processing, Akers stated, should be on patient safety instead of the "unreasonable" goal of sterility in the absolute. "Aseptically produced products manufactured in modern facilities are more than adequately safe and more testing or monitoring won't make them safer."

Akers has long advocated for efforts to eliminate personnel in aseptic processing and to curtail or eliminate interventions over efforts to increase monitoring and media fills.

Good Data Dispels Myths

In the end, good data is what is needed to counter myths. Levy concluded, "If significant myths exist, there is a need to step back and collect historical data, and for data that haven't been published, try to get those out there. We must pull together subject-matter experts, like we did with TR-26, and formulate strategies to generate the right data. This can lead to dispelling myths and creating harmonization."

Akers closed by saying, "The endless absolutist regulatory spiral in aseptic processing should be stopped immediately and replaced with better dialogue between industry and regulators/inspectors based upon sound analytical science. If we can do that, I think we can get off the merry-go-round that we currently find ourselves on."

Organizations like PDA exist, in part, to help the community of pharmaceutical professionals come together to share and develop best practices and contribute to regulations based on sound scientific principles.

All will agree with Levy's final words, "Good science-based decisions lead to the best practices and sound regulations."

*It is worth noting that this study about monkey behavior itself has reached urban "mythdom." After extensive research, the PDA Letter found that there was a study in the 1960s similar to Sutton's parable, but the object of desire was not bananas, naïve monkeys still played with the object when left alone with it, though at a reduced rate, and the trained monkeys did not physically harm the naïve monkeys. Nevertheless, the debates over this myth at snopes.com and other websites are no monkey business.

Mythical Processes

Most companies have processes and practices that have mythical origins and leave current employees scratching their heads. To those head scratchers, enjoy these anecdotes:

Grandma's Ham

A little girl is watching her mother prepare a ham for a family meal at grandma's house. As her mother prepares to put the ham into the oven, she takes a large knife and cuts the butt end off the ham, and then puts it on a tray and sticks it in the oven. The girl asks, "Why did you cut off the end of the ham?" To this the mother replies, "Because whenever my mother made a ham, she always cut off the butt end, and it was always the best, juiciest, most delicious ham I ever had. So I too cut off the butt end. You can ask grandma about her ham tonight."

So later that night at grandma's house, the little girl asks grandma, "Why did you cut off the end of the ham whenever you baked one?" To this the grandma replies, "Oh that is simple. You see, whenever I baked a ham, I had to cut off the end so it would fit in my baking dish."

— Paraphrased from T.C. Soli's presentation at PDA's 4th Annual Pharma. Micro Conference in October

Left Leaning in Synagogue

At a Bar Mitzvah celebration, the Rabbi is sitting with the family of the Mitzvah. After a few minutes of casual chatting, the aunt of the young man says, "There was something wrong with that ceremony. At our synagogue, whenever the Torah is taken out of the ark, we all lean to the left, and that is how we always do it to show reverence to the Torah. Today at the service, no one leaned to the left." To this the Rabbi says, "I'm sorry, but I never heard of that practice." The grandmother, who happened to live near the aunt, then spoke up. "Oh, honey, the reason we all lean left at synagogue whenever the Torah is removed from the ark has nothing to do with ritual. It is because at our old synagogue, there was a column that blocked our view, so we all had to lean left to see the Torah!"

— Overheard by the *PDA Letter* Editor at a recent Hanukkah celebration

Micro Session Previews USP Chapter, Case Study for Selecting RMM

Emily Hough and Walter Morris, PDA

The U.S. Pharmacopeia (USP) is moving forward with a general test chapter for mycoplasma testing that recommends the classic agar and broth method and indicator cell culture method. The USP previewed the Chapter, at *PDA's 4th Annual Global Conference* on Pharmaceutical Microbiology in October. This Chapter will be official in USP 33-NF28 (effective May 1, 2010). At the same session of the PDA Microbiology meeting, an expert from Genzyme presented a case study on the selection of a rapid method for mycoplasma testing.

USP <63> was developed by the USP Microbiology and Sterility Assurance (MSA) Committee of Experts with the assistance of the PDA Mycoplasma Task Force in response to requests for a reference standard from the biotech industry. (The Chapter was published as an in-process revision in the Jan-Feb 2009 Pharmacopeial Forum.) Official standards for mycoplasma testing are already delineated in both the European Pharmacopeia and the Japanese Pharmacopeia.

The Chapter stresses the necessity of testing for mycoplasma to assure uncontaminated biotech products and materials used to generate such products. It describes two procedures "to detect mycoplasma contamination of test articles, tissues and/or cell cultures used to produce test articles, digest broth or any other material in which mycoplasma contamination is suspected." The classic methods selected, agar and broth and indicator cell culture, both require up to 35 days to perform.

Like the guidance in the European Pharmacopeia, USP <63> states that newer rapid microbial methods such as Nucleic Acid Amplification Technique(NAT)-based procedures or an enzymatic activity based method may be used to detect mycoplasma, provided that the alternative methods are validated against both the agar and broth and indicator cell culture methods.

Anthony Cundell, PhD, Director, Pharmaceutical Sciences, Microbiology, Merck, who is a member of the MSA Committee of Experts, said that the U.S. FDA would accept alternative test methods for mycoplasma, but it would be easier on all parties if there was an existing standard in the USP. At this time, validation requirements for alternative methods are not addressed in this Chapter. Cundell said that "we just wanted a test with classical methods in place."

In his presentation at PDA's October Pharmaceutical Microbiology Conference, Cundell outlined a number of references to mycoplasma testing in regulatory guidances, regulations and official standards:

- 21 CFR 610.30 Subpart D Mycoplasma: This guideline uses classical plating techniques.
- Ph Eur 2.6.7 Mycoplasmas, 5.8 July 2007: This document states that nucleic acid amplification techniques can be used when a complimentary test is required or can be used as an alternative.
- FDA CBER Points to Consider in the Characterization of Cell Lines to Product Biologicals, May 1993: This document describes classical plating and broth culture methods.
- ICH Guideline for Biotechnological/ Biological Products: This guideline states that both the agar and broth media procedures as well as the indicator cell culture procedures are appropriate tests to run to test for contamination.

Cundell said industry experts estimate that mycoplasma contamination rates range from 15–30% in secondary cell cultures and 1% in primary cell cultures. Since only five species account for 95% of all mycoplasma contamination, any test method must excel at identifying those and also screen for a wider range of organisms. (See box.) He said that the effect of mycoplasma contamination is usually associated with host cell walls but may grow in nutrient-rich cell-free media with high counts without causing turbidity. They are resistant to penicillin and cephalosporin antibiotics as their cell walls lack peptidoglycans. They compete for nutrients, induce chromosomal abnormalities, interrupt metabolism and inhibit cell fusion of host cells.

95% of mycoplasma that is identified falls into the following five species:

Mycoplasma orale
Mycoplasma fermentans
Mycoplasma arginini
Mycoplasma hyorhinus
Acholeplasma laidlawii

Genzyme Selects RMM for Mycoplasma Testing

Following the discussion of the classic methods for mycoplasma detection, a case study on identifying and mitigating risks associated with implementing an advanced rapid microbial method was presented.

John Duguid, Staff Scientist II, Manufacturing Technical Services, discussed how Genzyme conducted a risk assessment in selecting from the various RMM tests that are commercially available. These include DNA/RNA methods, enzyme/antibody, immunofluorescence and oligonucleiotide genotyping-based techniques. Genzyme manufactures three autologous cell therapy products (the donor of the cells receives the final product). Generally, these products are assembled, shipped and used in less than a week. "So it doesn't take too much to do the math to realize that you are certainly [unable] to do a mycoplasma culture test in that period of time."

He said the first step of the risk-assessment involved surveying the available technologies. From the survey, Duguid and his team realized that Nucleic Acid Amplification Technique (NAT)-based procedures offered the sensitivity that his firm needed to replace the currently used culture method, which had a sensitivity level less than 10 cfu to be compliant with the European standard.

In the next step, Duguid and his team reviewed literature of 21 available mycoplasma test kits and identified eight "critical risk attributes" each kit was to be evaluated against: specificity, sensitivity, ease of use, lot release method, commercially available, no live mycoplasma controls, antibiotics okay and regulatory acceptance.

Duguid elaborated on the company's preferences regarding the various characteristics. For example, Genzyme wanted a method that could detect as many mycoplasmas as possible—"theoretically all the mycoplasmas that we could." They wanted to detect only viable organisms, and the test could not cross-react with bacteria. They preferred an instrumental method for a high-throughput QC environment. The results had to be obtained on a "same-day basis." Because Genzyme does not allow "live mycoplasma" to be brought into the facility, some of the validation experiments would need to be performed at contract laboratories.

For each kit, the attributes were given a ranking of 0, 1 or 2, with 0 meaning unacceptable, 1 may be acceptable, and 2 acceptable. The scores were multiplied together for each kit, and the kits were ranked from highest to lowest combined score. Duguid said "the nice thing" about this "simple ranking system" was that "anything that got a 0 wasn't going to work; no matter what you did about it, they dropped out." The team did not consider cost in the technical ranking.

After the top three kits were identified, detailed conversations were had with the kit manufacturers; one kit was immediately disqualified because it had a high false-positive rate. Duguid said that potentially it would be great for a screening tool but required more time than the company had for lot failure investigations of autologous cell therapy products. The other two kits that scored the highest used real-time PCR methods and had scored "relatively high on the ranking." Another real-time PCR method was brought in to replace the disqualified kit. The team evaluated the kits for sensitivity (serial dilutions of positive control down to extinction), selectivity (false negatives and false positives using spiked and unspiked samples, respectively), and cross-reactivity (spiked samples with three strains of bacteria).

During the hands-on evaluations, Duguid noticed varying results. Kits 1 and 2 detected a wide range of organisms, but kit 3 detected only eight. Kit 2 had Streptococcus pyogenes cross-reactivity and the vendor didn't quantify the positive control for the number of actual copies of DNA, which was "not terribly useful." Kit 3 also had stability issues.

Because molecular biology techniques were "kind of new to us," having very clear procedures was critical

When the kits were narrowed down to one, a Failure Mode and Effects Analysis (FMEA) was utilized "to find out what we were in for" and to identify items with the highest risk of failure to mitigate or lower the risk of those failures from happening. The failure modes were identified by dividing up the processes or designs into a number of steps and determining how each process or design step might fail.

Using a rating system, each item was rated according to the frequency, detectability and severity of a failure. These scores were multiplied together to produce a risk priority number (RPN).

In Duguid's system, a rating of 1 to 5 was used, with 5 being the worst. "The higher the number, the higher the RPN, the more risk." Duguid gave the following example, "a failure effect might be when a patient gets a cell culture infected with mycoplasma and dies. That would get a severity of five." He said that anything greater than a 41 required him and his team to mitigate and reduce the severity of those circumstances. The areas with the most risk were sample configuration and sample preparation.

Sample configuration was critical to choosing the right sample. According to Duguid, his team wanted "something that would include cellular material." Ideally, this sample should be taken prior to the trypsinization process, which can effect the mycoplasma recovery. , but might not pass regulatory muster. He chose to compromise and test a cellular sample of the final product in conditioned medium as an optimal sample configuration.

Because molecular biology techniques were "kind of new to us," having very clear procedures was critical. Duguid said what focused the team was having clear standard operating procedures and receiving feedback from regulatory agencies on their methods and finally on their validation plan. Duguid said that the U.S. FDA's Center for Biologics Evaluation and Research had valuable input on the organisms that his team used for validation of a previous RMM implementation. "I felt they were very collaborative. It took us five years, but I feel it would have taken longer had we not been talking to the Agency during the process."

Duguid said that the risk-based approach was a "useful tool for selecting a rapid mycoplasma test to take forward into validation." In closing he said, "We chose a test based on real-time PCR. The level of effort we put into this sort of analysis should be commensurate with the risk and ultimately the link to the safety of the product to the patients."

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Quality & Regulatory Snapshot

A Look Back and a Look Forward

Bob Dana and Jim Lyda, PDA

The Quality and Regulatory Affairs department is taking a cue from the Roman god Janus and is looking back to the past and ahead to the future

It's mid-December as we write this article for the January 2010 issue of the *PDA Letter*, and believe it or not, the "ought's" of the 21st Century are behind us. How is that possible? It hardly seems likes ten years ago we were worried about rolling from December 31, 1999 to January 1, 2000 ("Y2K"). What would happen to our computer systems—would they suddenly think we had gone back to January 1, 1900? Of course, as it turned out, the transition from 1999 to 2000 went pretty smoothly.

Fast forward to December 2009, and like the Roman god Janus, we'll take a look back at some of 2009's significant regulatory happenings and see if we can do a little prediction of what might happen in 2010 as well.

PDA's Regulatory Affairs and Quality Committee was very active in 2009. Over the course of the year, seven new members were added. We welcomed **Ruhi Ahmed, Jeff Broadfoot, Alan Burns, Robert Caunce, John Finkbohner, Siegfried Schmitt and Hongyan Xie** to RAQC membership. These new members significantly expanded both our geographical base and technical expertise and gave us a better balance of members from large and small pharma companies and consultants. With all the new members, RAQC recognized the need to improve its governance procedures and, following a long effort, an updated RAQC Commenting Procedure was finalized and a new RAQC handbook was implemented. These procedural controls will further strengthen RAQC's work in 2010.

Looking forward, RAQC will have new leadership in 2010. Mid-year, **Steve Mendivil** will complete two years as Chair of RAQC and **Stephan Roenninger** will assume the Chair's position. This will mark a first for RAQC as Stephan will be the first Europe-based Chair of the Committee. Sadly, as one door opens, another closes. **Zena Kaufman**, who has served PDA as an RAQC member, Chair and Immediate Past Chair will leave RAQC in 2010. We will miss Zena and her vision and many contributions, including being the champion of RAQC's first formal strategic plan.

With all this activity within RAQC, it was a busy year for the Committee. Under RAQC direction, PDA developed comments on eleven new regulatory initiatives. The full list can be seen on the PDA website at the Quality and Regulatory Affairs link (www.pda.org/regulatorycomments). Some of the more significant FDA initiatives we commented on include FDA's Process Validation draft guidance and their draft guidance on *Standards for Securing the Drug Supply Chain.*

In 2009, PDA members and volunteers helped prepare regulatory comments on the following European and International proposed guidances to the following agencies:

World Health Organization:

Draft guideline, *Recommendations for the Evaluation of Animal Cell Cultures as Substrates for the Manufacture of Biological Medicinal Products and for the Characterization of Cell Banks*

European Directorate for the Quality of Medicines:

Chapter 2031, *"Monoclonal Antibodies for Human Use"*

Chapter 2.6.16, *"Test for Extraneous Agents in Biological Products"*

Chapter 5.2.3, *"Cell Substrates for the Production of Biological Products"*

European Medicines Agency:

Revised GMP Annex 13, *Manufacture of Investigational Medicinal Products;*

Revised Guideline on *Use of Near Infrared Spectroscopy by the Pharmaceutical Industry and the Data Requirements for New Submissions and Variations*

Concept Paper on *The Revision of the EU Guideline on Good Distribution Practice*

Guidance on *Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents*

Speaking of new regulatory initiatives, several new one were proposed by the regulatory authorities in 2009. The U.S. FDA published the following new guidance documents in 2009:

- Q10, *Pharmaceutical Quality Systems*

- Q4B, *Regulatory Acceptance of Analytical Procedures and/or Acceptance Criteria*
- Q8(R1) and (R2); *Pharmaceutical Development*
- *ANDA's: Impurities in Drug Substances*
- *Pharmaceutical Components at Risk for Melamine Contamination*
- *Residual Solvents in Drug Products Marketed in the U.S.*
- *Positron Emission Tomography (PET) Drug Products–Current Good Manufacturing Practice (CGMP)*

In addition to the above proposals, FDA has announced a couple of new regulatory proposals which will extend into 2010. These include the proposed GMP's for Combination Products and the proposed FDA guidance on Postmarketing Safety Assessments for Combination Products. As we move into 2010, the European Medicines Agency has proposed revisions of Chapter 1, QMS, and Chapter 2, Personnel, of the EU GMP. There is much to look forward to and plenty for PDA members to focus on in 2010.

Of course, in the United States there is a new administration and a renewed focus on compliance-related issues on the part of FDA Commissioner **Margaret Hamburg**, MD, and her staff. In Europe, the European Medicines Agency announced reorganizations which eliminate the well known "EMEA" acronym, but did not propose a "user friendly" replacement.

So what is likely to happen in 2010? Beats us! Still, we are willing to suggest the following:

- FDA is likely to finalize their Process Validation Guidance.
- FDA will focus on supply chain integrity and associated issues. (PDA and FDA will be sponsoring a Workshop on this topic in 2010.)
- The European Medicines Agency will continue its evolution and enhanced collaboration with FDA.
- PDA will continue to remain active in these areas, and we will continue to represent our member's interests in these areas.

Stay tuned and check the PDA Regulatory and Quality website for new initiatives in 2010.

PDA's Who's Who

Ruhi Ahmed, PhD, Associate Director, Regulatory Affairs, BioMarin Pharmaceutical

Jeff Broadfoot, Director, Quality Assurance, Cangene

Alan Burns, VP, Global Quality, Global Quality Systems, Sartorius Stedim Biotech

Robert Caunce, Quality Project Manager, Quality Assurance, Hospira

John Finkbohner, Director, Regulatory Affairs, Vaccines, MedImmune

Zena Kaufman, Division Vice President, Global Pharmaceutical Operations, QA US/PR, Abbott

Steve Mendivil, Executive Director, Corporate Quality External Affairs, Amgen

Stephan Roenninger, PhD, Global Quality Manager, Global Quality, F. Hoffmann-La Roche

Siegfried Schmitt,PhD, Principal Consultant, Parexel Consulting

Hongyan Xie, Deputy General Manager, Regulatory Affairs, Qilu Pharmaceutical

Advisory Board *Watch*

RAQC Activities for 2009

Iris Rice, PDA

PDA's Regulatory Affairs and Quality Control Committee (RAQC) is comprised of 23 voting PDA members, with global representative delegations from the Asia Pacific, European and North American regions. RAQC members are experts in venues of Quality Management, Regulatory Affairs and Quality Assurance, Vaccines and Chemistry, Manufacturing and Controls issues.

In 2009, RAQC added seven members to their committee: **Ruhi Ahmed**, **Jeff Broadfoot**, **Alan Burns**, **Robert Caunce**, **John Finkbohner**, **Siegfried Schmitt** and **Hongyan Xie**. [**Editor's Note:** See article on previous page for more information.]

One of the primary goals of the RAQC is to develop and implement a new member handbook for its members. Completed and approved in December 2009, the handbook is a highly informative tool delineating the roles and responsibilities of RAQC.

RAQC developed in early 2009 a position paper on a "decision tree" that resembles the other PDA Advisory Boards portfolio with respect to task forces and project development. The decision tree was instrumental in identifying pressing "hot topics," which would allow task forces to determine which of these topics would be most beneficial to the PDA membership. The resulting deliverable would allow the task force to develop a particular position, and to enact that position through a conference, position paper, workshop or a training course. The decision tree was also key in determining which guidances from either the U.S. FDA or the European Medicines Agency would be most informative and beneficial to the PDA membership, and, as such, PDA should issue comments.

RAQC is the governing body within the infrastructure of PDA for submission of comments to regulatory authorities, globally. The group was involved in providing comments to various guidances in 2009 from the EDQM, U.S. FDA and WHO. [**Editor's Note:** See article on previous page for more information.]

RAQC helped to ratify a new PDA Interest Group on Supply Chain Management. This new group will be led by **Lucy Cabral**, Genentech, and will address the complexity of increasing substandard manufacturing, business, process controls and international counterfeiting practices.

Involved in PDA's Paradigm Change in Manufacturing Operations (PCMO) initiative, RAQC is also assuming a proactive role in the quality risk management arena and will be actively involved in the support processes of product and process improvement, change control, quality assurance and suppliers/subcontractors management.

PDA Parenteral Drug Association

Connecting People, Science and Regulation®

PDA Europe Upcoming Workshops 2010

Small Batch Production

- The technical Challenges of Producing Clinical Trial Materials and Small batches of Market Product -

The goal of the workshop is to give an update on the status of small batch production which includes ready to use components and the new machines to process small batches ranging from 100 to a few 10,000 containers. The main challenges are based on the request from pharma industry to produce clinical trial material more cost effectively under best GMP conditions. Additionally, future products are smaller in size because products are developed for specific and targeted – smaller - patient groups. This workshop presents the latest on ready to use vials and stoppers and new filling lines which were constructed to meet these special requests. Fully automated high tech machines with a minimum of cost for qualification and personnel.

23-24 February 2010
Berlin, Germany

Technical Report 22:

Process Simulation Testing for Aseptically Filled Products

The Task Force revising PDA's Technical Report 22 on Process Simulation exercises will present the current status of the document. Special attention will be given to the numerous comments received and how they will be addressed. Particularly the role of Process Simulation studies in the context of validating Aseptic Processes will be addressed. The workshop will cover inter alia how to

- challenge or demonstrate the aseptic process performance,
- demonstrate the capability of the process,
- include interventions (inherent and corrective),
- use risk based decisions for study design, change, and failure investigation.

25 February 2010
Berlin, Germany

For other events see:
www.pda.org/europe

Current Regulatory Harmonization Processes within the EU

Barbara Jentges, PhD, PhACT

Regulatory harmonization processes are ongoing within the European Union to overcome the regulatory hurdles, simplify the systems and reduce the workload for all parties involved.

In this article, three different topics are addressed where harmonization in the European Union is in process:

Variations to a Marketing Authorization: The new Variations Application 1234/2008 is not applicable to purely national procedures.

Submission Format—eCTD: European Medicines Agency mandates an electronic common technical document (eCTD) for electronic submissions for the centralized procedure, while some national competent authorities are still not ready for eCTD.

Clinical Trials: National assessment of clinical trial applications resulting in increased administrative costs and differing requirements by the concerned national competent authorities involving two national bodies.

Variations To A Marketing Authorization

In the European Union, a 3-steps approach has been taken to revise the regulatory framework on variations/changes. See Figure 1.

From January 1, 2010, the revised variations regulation 1234/2008 (step 1) applies to variations to a marketing authorization granted in a Mutual Recognition/Decentralized Procedure and to Community authorizations. The new variations regulation introduces a number of new features like annual reporting for minor type IA changes, type IB by default and implementing new procedures like "work-sharing" and "grouping of variations" aiming to reduce the workload for both competent authorities and applicants.

With the review of the variations regulations (new variations regulation 1234/2008 (1)) and the release of Directive 2009/53/EC (2) (step 2) for changing the legal basis of the variations regulation, the way towards the last major step 3 has been cleared for the harmonization of variations to purely national authorizations to Community law.

This third and last step will be taken by updating the variations regulation 1234/2008 to include variations to purely national marketing authorizations. A proposal for a revised variations regulations has been outlined in the public consultation paper, "Better Regulation of Pharmaceuticals: Towards a simpler, clearer and more flexible framework on variations." See Figure 2.

eCTD For Submission Dossier

Submissions are going paperless worldwide. However, regionally differing requirements transatlantic, as well as within the European Union make a good idea a complex matter. While the European Medicines Agency mandates the eCTD format in the centralized procedure for all electronic-only submissions for all applications (new and existing) and all submission types from January 1, 2010, not all European Union Member States are currently ready to accept eCTD formats. Applications via the centralized procedure are approximately 1% of the total applications annually within the European Union. The vast majority (approx 99%) of medicinal products are licensed according to national procedures. (5)

As revealed by the results of an "eCTD Implementation Survey Report," published in September 2009, only 15 National Competent Authorities or 47% of the Network were ready for an eCTD submission by the end of 2008. From those 17 authorities that were not ready, six planned to be ready within the target set at the end of 2009. However, there are still eight NCAs that did not know when they would be ready (5). As for national and Mutual Recognition Procedures (MRP)/Decentralized Application Procedures(DCP), it therefore becomes necessary to regularly check the relevant national requirements on electronic submissions as published on the Heads of Medicines Agency website.

Clinical Trial Applications

Requirements for the conduct of clinical trials in the EU are laid down in Directive 2001/20/EC ("Clinical Trials Directive"), (6) and Commission Directive 2005/28/EC ("Good Clinical Practices (GCP) Directive")(7) lays down principles and guidelines for good clinical practices and requirements for the authorization of the manufacture and importation of investigational medicinal products. Additional guidance is published in EudraLex Volume 10 and on the European Medicines Agency website ("Inspection procedures and guidance for GCP inspections conducted in the context of the Centralized

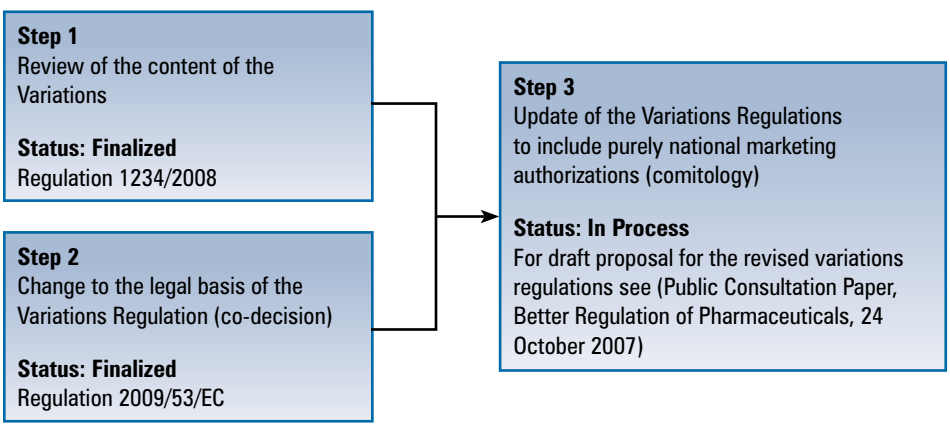

Figure 1: The 3-step approach towards a simpler, clearer and more flexible framework in variations ***(3,4).***

continued on page 28

2010 PDA Upcoming

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

JANUARY

25-29 **2010 Aseptic Processing Training Program—Session 1**
(Week 2: Fe[illegible])
Location: [illegible], Maryland
Website: www.pdatraining.org/aseptic
SOLD OUT

26-27 **PDA Conference on Investigational Medicinal Products: A Science and Risk Based Approach in Product Development**
Location: Paris, France
Website: www.pda.org/IMP2010

Web Seminars

January 14
Software Implementation in One Third of the Time and Cost
Time: 1:00 – 2:30 p.m. EST

For a full list of upcoming PDA Web Seminars please visit: www.pda.org/webseminars

FEBRUARY

9 **Interest Group Meeting: Filtration**
Location: Brussels, Belgium
Website: www.pda.org/europe

10-11 **Choosing the "Right" Microbial Identification Program for your Biopharmaceutical/Pharmaceutical Quality Control Laboratory**
Location: Bethesda, Maryland
Website: www.pdatraining.org/microID

22-24 **2010 San Diego Course Series**
Location: San Diego, California
Website: www.pdatraining.org/sandiego2010

23-24 **PDA Europe Conference on Pharmaceutical Microbiology**
Location: Berlin, Germany
Website: www.pda.org/europe

23-24 **PDA Workshop on Small Batch Production**
Location: Berlin, Germany
Website: www.pda.org/europe

25 **PDA Workshop on Technical Report 22: Process Simulation Testing for Aseptically Filled Products**
Location: Berlin, Germany
Website: www.pda.org/europe

Events

Save These Dates

MARCH

3-5 **Pharmaceutical Water System Microbiology Lab Course**
Location: Bethesda, Maryland
Website: www.pdatraining.org/watermicro

10-12 **Developing an Environmental Monitoring Program**
Location: Bethesda, Maryland
Website: www.pdatraining.org/DEMP

15-19 **2010 PDA Annual Meeting and Courses**
Location: Orlando, Florida
Website: www.pda.org/annual2010

16-17 **PDA Workshop on Stoppers & Elastomers**
Location: Cologne, Germany
Website: www.pda.org/europe

18 **PDA Workshop on Siliconisation**
Location: Cologne, Germany
Website: www.pda.org/europe

22-26 **2010 Aseptic Processing Training Program—Session 2**
(Week 2: April 19-23)
Location: Bethesda, Maryland
Website: www.pdatraining.org/aseptic

25 **Interest Group Meeting: Technology Transfer**
Location: Frankfurt, Germany
Website: www.pda.org/europe

APRIL

6-8 **2010 St. Louis Course Series**
Location: St. Louis, Missouri
Website: www.pdatraining.org/stlouis2010

7-9 **Cleaning Validation**
Location: Bethesda, Maryland
Website: www.pdatraining.org/cleaningval

12-15 **2010 PDA Pharmaceutical Cold Chain Management Conference and Course**
Location: Bethesda, Maryland
Website: www.pda.org/coldchain2010

13-14 **PDA Workshop on Filtration**
Location: Berlin, Germany
Website: www.pda.org/europe

15 **Interest Group Meeting: Pre-filled Syringes**
Location: Berlin, Germany
Website: www.pda.org/europe

20-21 **PDA Workshop on Bio-films**
Location: Frankfurt, Germany
Website: www.pda.org/europe

22 **Interest Group Meeting: Visual Inspection**
Location: Frankfurt, Germany
Website: www.pda.org/europe

22 **PDA Europe Workshop: Preparation of Virus Spikes used for Viral Clearance**
Location: Frankfurt, Germany
Website: www.pda.org/europe

26-28 **PDA/FDA Supply Chain Conference**
Location: Bethesda, Maryland
Website: www.pda.org/calendar

27-28 **Workshop on Container Closure Systems + Annex 1**
Location: Berlin, Germany
Website: www.pda.org/europe

28-30 **Development of Pre-Filled Syringes**
Location: Bethesda, Maryland
Website: www.pda.org/prefilled

For more information and to register, please visit **www.pda.org**

Current Regulatory Harmonization Processes within the EU, continued from page 25

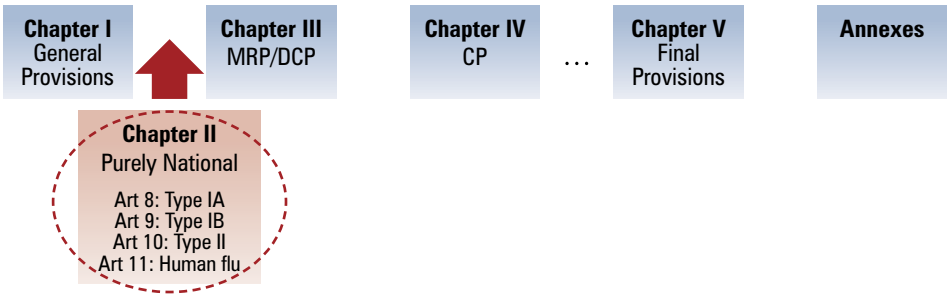

Figure 2: Proposal for an updated Version of variations regulations 1234/2008 to include "Chapter II Purely National"***(3,4)***.

Procedure" and "Scientific Guidelines"). Moreover, a Clinical Trials Facilitation Group has been established within the Heads of Medicines Agency in order to discuss ongoing technical issues.

One of the major regulatory challenges for companies sponsoring clinical trials within the European Union is the divergence between globalization of clinical trials on the one hand and national assessment of clinical trials within the European Union on the other hand. The national assessment of clinical trial applications involves two national bodies—the competent authority of the European Union Member State and the Ethics Committee.

The national assessment of clinical trial applications involves two national bodies

In the European Union/European Economic Area approximately 4000–6000 clinical trials per year are performed, with 64% being sponsored by the pharmaceutical industry. Approximately 25% of EU clinical trials are performed in more than one EU Member State and about 25% of all clinical trials performed in the European Union also involve at least a third of the country (8).

Based on its communication from December 10, 2008, the European Commission initiated an assessment of the application of the Clinical Trials Directive to "consider, in particular, various options for improving the functioning of the Clinical Trials Directive with a view to making legislative proposals, if appropriate, while taking the global dimension of clinical trials into account."

The major regulatory hurdles are addressed and summarized in five "key issues" in a commissions public consultation paper "assessment"(8) of the functioning of the "Clinical Trials Directive" 2001/20/EC:

1: Multiple and divergent assessments of clinical trials

2: Inconsistent implementation of the Clinical Trials Directive

3: Regulatory Framework not always adapted to the practical requirements

4: Adaption to peculiarities in trial participants and trial design

5: Ensuring compliance with Good Clinical Practices ("GCP") in clinical trials performed in third countries

The Commission's call for comments to this consultation paper ends on January 8, 2010. An evaluation of the comments and the proposal of a strategy to overcome the regulatory hurdles for clinical trials are awaited.

References

1. Commission Regulation (EC) No 1234/2008 of November 24, 2008 concerning the examination of variations to the terms of marketing authorizations for medicinal products for human use and veterinary medicinal products
2. Commission Directive 2009/53/EC of the European Parliament and of the Council of June 18, 2009 amending Directive 2001/82/EC and Directive 2001/83/EC, as regards variations to the terms of marketing authorizations for medicinal products
3. European Commission: Better Regulation of Pharmaceuticals: Towards a simpler, clearer and more flexible framework on variations; Public Consultation Paper–Version October 24, 2007
4. B. Friese, B. Jentges, U. Muazzam (editors). "Guide to Drug Regulatory Affairs," Edition Cantor Verlag GmbH, Germany, 2009
5. eCTD Implementation Survey Report (September 2009), published on the website of the "Heads of Medicines Agency," www.hma.eu
6. Directive 2001/20/EC of the European Parliament and of the council of April 4, 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use ("Clinical Trials Directive")
7. Commission Directive 2005/28/EC of April 8, 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorization of the manufacturing or importation of such products ("GCP Directive")
8. European Commission: Assessment of the Functioning of the "Clinical Trials Directive" 2001/20/EC; Public Consultation Paper (ENTR/F/2/DF D(2009) 32674 from October 09, 2009)

About the Author

Barbara Jentges, PhD, is Managing Director of Pharmaceutical Advice, Compliance & Training, which specializes in Drug Regulatory Affairs. She has more than 19 years experience in regulatory affairs. She has worked as an external assessor for the German Health Authority.

Starting in 2010, Barbara will be contributing regularly to the *PDA Letter* about European regulatory developments.

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CGMP Biotechnology Facility Design and Validation
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Implementing CGMPs in Biopharmaceutical Manufacturing
Review, at an advanced level, the current requirements for CGMP manufacturing of biopharmaceutical products and outline how to plan for CGMP implementation in your facility. Instructor: **Antonio Moreira**, PhD, Vice Provost for Academic Affairs, *University of Maryland Baltimore County.*

February 23
Sterilizing Filtration of Liquids – PDA Technical Report 26 (2008 Revision)
Discuss and analyze *PDA Technical Report No. 26, Sterilizing Filtration of Liquids, (2008 revision)*, which provides a systematic approach to selecting and validating the most appropriate filter for liquid-sterilizing filtration applications. Instructor: **Richard Levy**, PhD, Senior Vice President, Scientific and Regulatory Affairs, *PDA*; additional faculty to be named.

February 23-24
Biotechnology: Overview of Principles, Tools, Processes and Products
This course is designed to provide biotechnologists and non-biotechnologists with a basic understanding of the theory, principles, techniques and potential of biotechnology. Instructor: **Antonio Moreira**, PhD, Vice Provost for Academic Affairs, *University of Maryland Baltimore County.*

February 22
Virus Clearance
This program covers basic theory and practical applications for the removal / inactivation of virus contamination in biopharmaceuticals and biological materials. Instructor: **Sheri Dolan**, Product Manager, *Sartorius Stedim Biotech.*

For more information, please visit www.pdatraining.org/sandiego2010 or contact:
Stephanie Ko: Manager, Lecture Education
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Volunteer Spotlights

Stephan O. Krause, PhD, Principal Scientist, MedImmune

PDA Join Date: 2005

Areas of PDA Volunteerism: PDA/DHI Book Author (April 2007); PDA Task Force Chair of Analytical Method Validation (2007-present); PDA Task Force Member for Analytical Method Development (2008-present); PDA Task Force Chair for PCMO Initiative (IMP Manufacturing and Distribution) (2009-present); Speaker at several PDA conferences (2008-2009); Upcoming PDA TRI 2-Day Course Lecturer (Boston, 2010)

Interesting Fact about Yourself: My wife, Patricia, is French. I am German. Our (twin) children, Chloe and Connor are Americans.

Why did you join PDA and start to volunteer? I was encouraged to join and publish with PDA in 2005. I quickly realized that volunteering with PDA opened all kinds of doors, and I have since befriended many PDA members. Participating in task forces or other PDA groups provides insights on current and future best practices.

Of your PDA volunteer experiences, which stand out the most? I enjoyed presenting in front of larger and professional audiences. A formal presentation is still the most effective and satisfying communication platform for my work.

How has volunteering through PDA benefited you professionally? Actively participating in global task force teams has provided me with a better understanding of how much more practical guidance may be needed to make our industry more successful. I believe that finding the right balance of detail and scope for (practical) regulatory expectations is critical for future innovation and successful business models.

Which PDA event/training course is your favorite? At the PDA/FDA Joint Conference, I can ask many questions to the regulators who are right there in front of me. I usually get all of my questions answered.

What would you say to somebody considering PDA membership? Membership costs are low compared to the benefits. Being a member provides easy access to a very large and experienced global network group. This is probably the best career and learning investment I ever made.

Wenzel Novak, PhD, Director, Pharmaceutical Research and Development, Groninger & Co.

PDA Join Date: 2005

Areas of PDA Volunteerism: Speaker at numerous PDA conferences, organizing training sessions and hands-on courses on behalf of PDA; Universe of Syringe European interest group member (2007); Planning Committee member for the Universe of Syringe meeting (2008-2009)

Interesting Fact about Yourself: I'm always looking around the edge—hunting for new, better solutions—always questioning common meanings. Never accept something as given until it is proven in a "scientific" way. There is always a better way to do it!

Why did you join PDA and start to volunteer? To be in contact with enthusiastic people coming together to discuss the new ideas behind the scene of our industry; that was the initial driver to join PDA. A great mix of experts and open minded "beginners" creates an atmosphere of innovative thoughts. When Georg Roessling challenged me to speak openly about issues which can be overcome by sharing information, he pushed me into guiding people into developing the best product. It's fantastic to be part of such a giving community.

Of your PDA volunteer experiences, which stand out the most? Giving back the assistance I have received from experts at the start of my career to new colleagues. It should be a must for all of us.

How has volunteering through PDA benefited you professionally? By easily creating a network of professional helpers who at anytime are open-minded to assist. Gaining an understanding the needs of the industry, really down to the roots.

What would you say to somebody considering PDA membership? Doesn't matter how experienced you are, joining PDA will give you the input needed to be even ahead of the state-of-the-art level on technology, regulatory and practice. Just meet the really great people in this community.

PDA Volunteer Spotlights are available online:
www.pda.org/spotlight

Recipients of the 2008 Honor Awards

www.pda.org/2008honorawards

Service Appreciation Award

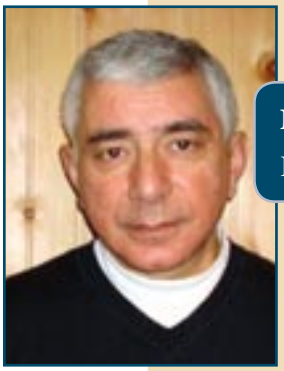
The Service Appreciation Award is presented annually for special acts, contributions or services that have contributed to the success and strength of PDA. The majority of the 2008 Service Appreciation Award recipients have received this award based on their work as the President of their respective PDA chapters, one recipient received the award based on his work as the Chairperson for the PDA Exhibit Advisory Board from 2006-2008.

Patrick Bronsard
Immediate Past President of the PDA Canadian Chapter

John Ferreira
Immediate Past President of the PDA West Coast Chapter

Frank Hallinan
Immediate Past President of the PDA Ireland Chapter

Sara Hendricks
Immediate Past President of the PDA Mountain States Chapter



Nate Manco
Immediate Past President of the PDA Metro Chapter

Art Vellutato, Jr.
Past Chairperson for the PDA Exhibit Advisory Board

The honor awards have been bestowed to esteemed PDA members since the first award was given in 1958. It is our intention to highlight the 2008 Honor Award Winners who were recognized at PDA's Annual Meeting banquet.

Please Welcome the Following Industry

Michael Abate, Amgen
Benjamin Adusei, Mataheko Pharmacy
Nadav Agian, Kyowa Hakko Kirin
Vipul Agrawal, Widener University
Nurguen Aktogu, Sanofi-Aventis
Pascal Albini, Debiopharm
Katherine Aldcroft, Genzyme
Justin Aldridge, Talecris
Pete Alegre, BioMarin
Veronica Algeo, Merck
Feras Al-Zubaidy, Delta Project Management
Maayan Anaf, Dexcel
Stephanie Anctil, Health Canada
Samuel Andrews, AstraZeneca
Jim Anthony, Enterey
Roberto Aquino, Bristol Myers Squibb
Marco Araya, Ben Venue Laboratories
Tamar Arkin, B. T. G.
Elie Arslan, Gilead Sciences
Hanna Ashh, Kamada
James Assini, Genzyme
Diana Baelly, Genentech
Derek Baker, Hospira
Bruno Baney, BD
Gabriela Barak, Biorest
Christopher Barnes, Eli Lilly
Jean-Luc Barnoux, IDD-Tech
Gary Barrera, Genentech
Lorena Barron, Amgen
Ryan Bartlett, Eurand
Tejinder Bawa, Genentech
Michael Beckloff, Beckloff Associates
Shannon Bellak, Terumo Medical
Hanna Ben-Artzi, B. T. G.
Yaniv Ben-lulu, Taro
Ramond Benoit, Sanofi Aventis
Chris Benson, United Therapeutics
David Bertsch, Pfizer
Barbara Bielska, Northampton Community College
James Bingham, MMG Biopharmaceutical Consulting
Lene Bjerregaard, NNE Pharmaplan
Carol Black, Intercell
Alisha Blalock, Eurand
Valerie Bobineau, Sanofi Aventis
Michael Boquet, Pfizer
Brent Borovskis, Proctor and Gamble
Annemiek Bosman, Pharmachemie
Belinda Bosu-Green, Eurand
Carrie Bracco, WL Gore
Scott Bramwell, BioReliance
Melina Bratton, Bayer Healthcare
Bill Brazier, Amgen
Bruce Breeden, TempSys
Tom Brieva, Celgene Cellular Therapeutics
Robert Briley, BD
Katja Brinkmann, Gerresheimer
Douglas Brown, Baxter Healthcare
Kimberly Buggs-Hill, Talecris Biotherapeutics
Todd Burdette, Particle Measuring Systems
Sara Burhans, Shire Pharmaceuticals
Beth Burke, Accugenix
Derek Bursey, MassBiologics
Frederik Buysse, Alcon
Kevin Cabral, VNUS Medical Technologies
Jeffrey Calloway, CSL Behring
Francisco Calvo, Scientific Protein Laboratories
Sheryl Cardona, Johnson & Johnson
Patrick Carmichael, Genentech
Jason Carter, Genzyme
Monika Cassani, Genentech
Anthony Castellazzo, Amicus Therapeutics
Kim Changil, Choongwae
Caroline Chardonnet, GlaxoSmithKline
Jie Chen, Genentech
Steve Chen, The Dunn Group
Bo Chi, FDA
Maccio Chiara, CTP Tecnologie Di Processo
Kathyrn Chieffo, Microtest Laboratories
Dawn Chien, ATCC
Kevin Chin, AstraZeneca
Jose Colmenares, Sartorius Stedim
Anna Corke, Genera Biosystems
James Correia, RxQual
Yves Courties, Millipore
Daryl Crouch, Eli Lilly
Bonifacio Cuenco, Ispen Biomeasure
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Naomi Grosman, Gal Pharma
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Weijun Gu, JPT Consulting
Mykola Gumeniuk, Uriafarm
Edward Gunzel, W. L. Gore & Associates

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Brandon Heritage, Ben Venue
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Takefumi Hoshikawa, Teikoku Seiyaku
Glenn Howard, Jr., ghconsultants
Scott Hughes, Chattem
Alfred Humm, F. Hoffmann – La Roche
Annette Husemann, NNE Pharmaplan
Wataru Ikebata, Shionogi
Kent Irby, OSI Pharmaceuticals
Douglas Irving, Roche
Shozo Ishizawa, Eisai
Gianpaolo Italiano, FIDIA Farmaceutici
Diane Jackson, DLJ Consulting
Thilo Jaeckel, F. Hoffmann – La Roche
Olivier Jankowitsch, Intercell AG
Larry Jeffers, GlaxoSmithKline
Maureen Jennings, 3M Drug Delivery Systems
Jerome Jennings, Baxter Healthcare
Xin-Ming Jiang, Abraxis BioScience
Steven Johnson, Baxter Healthcare
Jeffrey Johnson, New Age Industries
Mary Johnson, APP Pharamceuticals
Matthew Johnson, Chesapeake Biological Laboratories
David Jones, Rapid Micro Biosystems
Mangal Joshi, Biomerieux
Tobias Jungo, Rohner AG
Sandeep Kachhwaha, Aptuit
Kenji Kamada, Chugain Pharmaceutical
Noriteru Karasawa, Nitto Medic
Masahiko Katou, Takeda Pharmaceutical
Tabitha Kemp, Panther Expedited Services
Stephen Kennedy, Genzyme
Hiroyuki Kikukawa, Sumitomo 3M Limited
Ji Eun Kim, Hanmi Fine Chemical
Yoshiyuki Kimura, Senju Pharmaceutical
Erin Kingdom, Eurand
Laura Klewer, Amgen
Michael Koenig, Bayer
Allen Koesser, Takeda Pharmaceuticals
Fumie Kojima, Santen Pharmaceutical
Michael Kolf, NIH
Gary Konecnik, KRA
Toshifumi Koshiyama, Toyo Aerosol Industry
Keiichi Kotera
Shirley Kreutzfeldt, Abbott Laboratories
Wolfgang Kroemer, Biotest
Eran Kuratz, Kamada
Jun Kurihara, AstraZeneca
Yasuo Kurozumi, Tokiwa Engineering
Markus Kurz, Robert Bosch
Giorgio Kyriacatis, PTM Consulting
Paul LaBarre, Path
Mathieu Labedan, Sartorius Stedim
Karol Lacki, GE Healthcare
Jean LaDouceur, LaDouceur & Associates
Carol Lahti, Genentech
Rainer Lang, Intervet
Michelle Laraia, Sanofi Pasteur
Patrick Le Gal – Redon, BD
Jay Leversee, Bristol Myers Squibb
Sophia Levitskaya, MedImmune
Dennis Lew, AMAG Pharmaceuticals
Rebecca Lim, Lonza
Katrin Lindahl, AstraZeneca
Tim Lindis, Genzyme
Vicky Lioutas, CSL
Barry Liversidge, Tip-Top.Com
Julia London, Bayer
Patricia Lopez-Quispe, Advanced BioHealing
Helen Loughrey, Theratechnologies
Audrey Louie, Celldex Therapeutics
Drew Love, Revogenex
Philip Ludwig, ARCH Chemicals
Lyubov Lyubarskaya, Genentech
Alan Mac Neice, Alan Mac Neice
Geary MacQuiddy, Genzyme
Jin Maeda, Daiichi Sankyo
Holger Maegdefrau, Lohmann & Rauscher
Dror Magen, Taro
Hans Peter Maier, Fischer Soehne
Cynthia Maier, MedImmune
Anasuya Mallick
Kenneth Maltas, Tegrant Corporation
Melissa Maple, Alkermes
Thilde Marboe, Ferring Pharmaceuticals
Chris Marby, Genentech
Gerhard Marchon, Fischer Soehne
Arie Marom, Do-Coop
Jose Marquez, Bristol Myers Squibb
Lauren Martin, GlaxoSmithkline
Irene Martinez, Shire
Emmett Martz, Schering-Plough
Jerry Matacia, BioMarin
Jeff Mays, Bio Marin
Maryam Mazaheri, MedImmune
Kevin Maziarz, Ben Venue Laboratories
Paolo Mazzoni, PTM Consulting
Denise McDade, Amylin Pharmaceuticals
John McGinley, Onyx Pharmaceuticals
Brian McKenna, Merck
Brian McLoughlin, Shire Pharmaceuticals
Richard Mead, Amgen
Bhavin Mehta, Kilitch Drugs
Lee Meller
Antonella Mercado, Alcan Packaging
Lorraine Mercurio, Covidien
Yael Metz, Teva
Kristie Metz, Mallinckrodt Baker
J. Claude Miller, Fresenius Medical Care
Randy Miller, Fort Dodge Animal Health
Patrick Milliman, GlaxoSmithKline
Hideko Mine, Kyoto Red Cross Blood Center
Michelle Mintz, B. T. G.
Sahba Mirhashemi, Allergan
Toru Mizumura, Meiji Seika Kaisha
Karin Modler-Hauch, Novo Nordisk
Joseph Molon, Biogen Idec
Suri Monsef, Genentech
Bruce Moore, GlaxoSmithKline
Natasha Morales, Watson
Ismael Morales Ramos, Amgen
Mark Morimune, Bayer
Paul Andre Moritz, MCS
Brian Mowrer, Sanofi Pasteur
Robin Mroz, CSL Behring

Please Welcome the Following Industry

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Ronald Mueller, West
Martin Muellner, Boehringer Ingelheim
Katsushi Murai, Japanese Red Cross
Hiroko Muraoka, Kyowa Pharmaceutical Industry
Kevin Murphy, Merrimack Pharmaceuticals
Ronan Murphy, Schering-Plough
Lisa Musmanno, Talecris Biotherapeutics
Karyl Nat, Luitpold Pharmaceuticals
Hubert Nettelhoff, CSL Behring
Darrick Niccum, TSI
Hiroaki Nishii
Kazuhiko Nishii, Japan Tabacco
Mitsuhira Nishio, Senju Pharmaceutical
Heidi Nold, Bayer HealthCare
Jonas Norebring, SHL Group
Diana Nortey, Aeras Global TB Vaccine Foundation
Gregory Nowakowski, Covidien
Dan O`Mahony, Schering Plough
Patrick O`Meara, Forest Research Institute
Deborah O`Rourke, Watson
Martina O`Sullivan, Bioniche Pharma
Stephen O´Dwyer, Wyeth
Yutaka Ohkawa, Wyeth
Troy Ohmes, Aramar Cleanroom Services
Mitsuru Oka, Sanwa Kagaku Kenkyusho
Hiroya Okubo, Senju Pharmaceutical
Yasuhiro Okuno, AstraZeneca
Ashok Omray, USV
Kotono Ota, Rohto Pharmaceutical
Angela Overstreet, Mediatech
Judith Paltiel, B. T. G.
Paul Papali, Alkermes
Jeff Papi, BioMerieux
Julie Papp, Allergan
Joon-Seung Park, SamChun Dang Pharm.
Merry Parrish, Prometheus Laboratories
Judy Partch, Direct Relief International
Demil Pascale, GlaxoSmithKline
Suresh Patil, Genentech
Maria Lynn Pavco, NIH Clinical Center
Ayelet Peer, Teva
Toni Pfleegor, Millipore
Mark Pietropola, Great American Refrigerated Validated Logistics
Catherine Piton, Scientific Laboratory Services
Nicole Plumb, Halozyme Therapeutics Inc.
Ray Pocoroba, RHP Consulting
Sarah Potter, Novartis
James Powell, Biovigilant
David Pruchter, B. T. G.
Carol Pudlow, BioMarin
Kian Yong Puen, CCM Pharmaceuticals
Bill Puent, Lonza
Stefan Puller, Pluemat Packaging Systems
Annette Quinones, Dept of Health and Human Services
Noushin Rahimi, BD
Sushma Rajput, Orchid
Bradley Rank, Bayer
Nitin Rathore, Amgen
Swapnil Raut, Millennium
Ralph Reid, Baxter Healthcare
Pablo Reinoso, Merck
Anton Reschny, Octapharma
Merav Revach, IIBR
Brian Rhatigan, Catalent
Matthew Riccio, Safety Syringes
Gordon RIGG, Novartis Pharma
Richard Rigg, Allergan
Ralph Riggin, Marcadia Biotech
Natasha Rivas, Hospira
Ingrid Rodriguez, Abbott Laboratories
Donald Rogers, Genentech
Emilio Roman Castillo, Industrias Farmaceuticas Almirall
Rafael Rosario, Bristol Myers Squibb
Michael Rose, Steris
Shawna Rose, Biogen
Michael Royals, PharmaJet
Michael Ruane, Abraxis BioScience
Patrick Ruane, Johnson & Johnson Vision Care
Sandy Rubio, MicroWorks
Scott Rudge, RMC Pharmaceutical Solutions
Jens Rumsfeld, Sartorius Stedim Biotech
Natalia Rydberg, F. Hoffmann – La Roche
Natalie Ryther, Sinpex
Lotta Salmela, AstraZeneca
Ruth-Dinaz Sarkari, AgResearch
Shigekazu Sawada, Sanwa Kagaku Kenkyusho
Takao Sawai, Nippon Gohsei
Jean-Francois Schneider, Merck
Karin Schoenhammer, Novartis
Timothy Schofield, GlaxoSmithKline
Mathias Schroedter, IDT Biologika
Collyn Seeger, University of Connecticut
Mrinal Shah, InnoPharma
Monika Sharma, MedImmune
Christopher Shelhammer, Eli Lilly
Tomoko Shibayama, Bushu Pharmaceutical
Yukio Shinoduka, Kureha
Joshua Silverstone, Millipore
Balcar Singh, Dendreon
Maria Sjöberg, SentoClone
Przemyslaw Skoczen, ZF Polpharma
Dawna Smith, Millennium Pharmaceuticals
Glenn Smith, Genentech
Aaron Smith, Kimberly-Clark
Lauren Smith, Ben Venue Labs
Maria Smyth, Wyeth
Anna Sniezko, Shire Pharmaceutical
Doris Snow, DynPort Vaccine
Xu Song, Becton Dickinson
Jannette Soto, Bristol Myers Squibb
Shannon Southall, GlaxoSmithKline
Philip Albert Sparholt, Novo Nordisk
Bryan Spindler, Baxter Healthcare
Akundi Sriram, Biocon
Christoph Stahr, PEW Panasonic Electric Works
Len Steinborn, Steinborn Consulting
Jeffrey Stewart, Gnentech
Imme Stiebler, Procter & Gamble Pharmaceuticals
Bistra Strechkova, Novartis
Ian Striffler, Abbott Laboratories
Roman Strnad, Contipro
John Strokis, Baxter Healthcare
Fredrik Stromvall, SHL Group
Hsing-Yi Su, TTY Biopharm
Na Sughee, Choongwae
Hiroaki Sugiyama, Nichi-iko Pharmaceutical
Mary Sullivan Millipore
David Swartz, Baxter Healthcare
Lorie Swartz, BD
Jecky Szechtman, Steba Biotech
Hayato Takami, Senju Pharmaceutical
Kenta Takeshima, Teijin Pharma.
Anat Tal, B. T. G.
Andrew Talmadge, Merck
Jessica Tan, Amgen
Michael Tarle, NeurogesX

Leaders to the PDA Community

Dennis Taschek, Lonza
Kamilla Tasi, Gedeon Richter
Latercha Taylor, LT Biopharma Consulting
Kathleen Testaverde, Wyeth Pharmaceuticals
William Thomas, MassBiologics
Roy Thomas, AstraZeneca
James Thompson, West
Melody Timm, Baxter Healthcare
Maggie Tobin, Pfizer
Mario Tornari, Mylan
Gina Trimble, Wyeth
Maiko Tsutsui, Dainippon Sumitomo Pharma
David Turner, Cubist Pharmaceuticals
Keiko Uchimoto, Kringle Pharma
Kirsten Vadheim
Harish Vakil, Actavis
Juan Valdes, AstraZeneca
Linda Vanhoven, BioMerieux
Yakov VarShavchik, Mediwound
Torsten Vilkner, Boehringer Ingelheim
Jean-Christophe Voirin, Sanofi Aventis
Matthew VonEsch, United Therapeutics
Motohiro Wada, Terumo
Toru Wada, JCR Pharmaceuticals Co.,Ltd
Manpreet-Vick Wadhwa, Amgen
Mark Wagner, Bristol-Myers Squibb
Gwendolyn Wall, NNPII
Ignace Wallaert, Janssen Pharmaceutica
Bryan Waltrip, BioVigilant Systems
Deborah Warner, Novocol Pharmaceutical
Hajime Watanabe, AnGes MG
Kenneth Wenninger, Harris Group
Jennifer Wheatley, Eli Lilly
Karen Wheless, Food and Drug Administration
Paul Whyte, Future Injection Technologies
Matt Wiencek, Commissioning Agents
Samudra Wijeratne, Watson
Dennis Williamson, Genentech
Jessica Wine, Biotest
Jonathan Woodburn, LGM Pharma
Chiaki Yamada, Chugai Pharmaceutical
Shinichi Yamashita, Hisamitsu Pharmaceutical
Janet Yao, Bristol Myers Squibb
Kazuharu Yoshida, Nihon Generic
Xiang Zhuang, Life Technologies
Brenda Zimmerman, Eli Lilly
Terri Zolp, Perrigo
Laura Zurlinden, Sharp

If your information appears inaccurate in this list, please visit www.pda.org to update your profile or email changes to info@pda.org.

PDA's 4th Annual Global Conference on Pharmaceutical Microbiology

Dennis Guilfoyle, FDA; Richard Johnson, PDA

(l-r) John Duguid, Genzyme; Dennis Guilfoyle, FDA; Edwin van den Heuvel, Schering Plough; Geert Verdonk, Schering Plough; Michael Miller, Microbiology Consultants; Björn Breth, Greiner Bio-One

(l-r) James Akers, Akers, Kennedy & Associates; Rich Levy, PDA; Teri Soli, Soli Pharma Solutions

(l-r) David Shelep, Accugenix; David Molesh, GlaxoSmithKline; Robert Reagan, Pace Analytical Life; Alison Caballero, PDA

Dave Adams, Baxter Healthcare; Ash Khorzad, Baxter Healthcare

Rich Levy, PDA; Michael Dawson, Associates of Cape Cod

(l-r) Alison Caballero, PDA; Peter Pratt, BioScience International; Ramakrishnan Srikumar, Allergan; David Shelep, Accugenix

Anastasia Lolas, FDA; Michael Miller, Microbiology Consultants

(l-r back row) Bryan Riley, FDA; Edward Balkovic, Genzyme
(l-r front row) David Hussong, FDA; Tsuguo Sasaki, Pharmaceuticals and Medical Devices Agency, Japan; Radhakrishna Tirumalai, United States Pharmacopeia; James E. Akers, Akers Kennedy & Associates; Michael Sadowski, Baxter Healthcare

Workshop on FDA's New Guidance on Process Validation

(l-r) Chris Ames, Catalent Pharma Solutions; Bob Dana, PDA; Kelly Tunney, Merck

(l-r) Hal Baseman, ValSource; Rebecca Devine; Brian Hasselbalch, FDA; Scott Bozzone, Pfizer

An active dialogue followed at the conference

(l-r) John McShane, Genentech; Rich Levy, PDA; James Agalloco, Agalloco & Associates

Universe of Pre-filled Syringes and Injection Devices

(l-r) Fabio Nicoletti, International Commission on Glass; Georg Roessling, PDA

(l-r) Georg Roessling, PDA; Tom Nikolai, Abbott; Alexandra Winter, Boehringer Ingelheim

(l-r) Brigitte Reutter-Haerle, Vetter-Pharma-Fertigung GmbH & Co; Arno Fries, Geresheimer; Shawn Kinney, Hyaluron; Daniel MacDonald, Duoject Medical Systems; Rebecca Ingram, Wyeth BioPharma

Georg Roessling, PDA; Bob Myers, Beacon Pointe Group; Richard Johnson, PDA

2010 PDA Cold Chain Conference to Clarify Best Practices

Bethesda, Md. • April 12-15 • www.pda.org/coldchain2010

Chair Rafik H. Bishara, PhD

The importance of the proper handling, storing and shipping of temperature-sensitive pharmaceuticals is increasing as more new medicines belong to this class. Pharmaceutical and biopharmaceutical companies have been studying the supply chain and cooperating with all of its partners to ensure that the quality, integrity, efficacy and potency of the cold chain products are not compromised during distribution until they reach the end user, the patient.

During the last several years, global regulators have also recognized and paid more attention with new requirements, guidance and inspections to clarify and enforce compliance with good cold chain management practices. The regulators and the industry are actively engaged in conferences, round table discussions and panel sessions to share, exchange and learn about best practices. An effective venue that has been used by the regulators is sharing and trending their inspectional observations. These lessons learned have allowed supply chain partners, manufacturers and solution providers to focus on solving the cold chain management issues in an integrated supply chain.

In recent years, regulatory expectations for the distribution of temperature-sensitive pharmaceuticals have become clearer. It is now understood that Good Distribution Practice (GDP) is an extension of Good Manufacturing Practice. Individuals and organizations dealing with temperature-sensitive medicines have continued to work and share their knowledge, challenges and success stories to comply with the new requirements and ensure the patient safety.

One of the most active groups in leading the clarifications for the migration from cold chain to GDP, establishing industry best practices, cooperating with regulators, working with pharmacopeial experts and partnering with the cold chain visibility solution providers is the PDA's Pharmaceutical Cold Chain Interest Group (PCCIG). Among the first deliverables of the PCCIG is *PDA Technical Report No. 39, Guidance for Temperature-Controlled Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products through the Transportation Environment*. This will be followed shortly by the publication of *PDA Technical Report No. 46, Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User*. Several technical papers have been published by members of the PCCIG including such topics as Integration of Temperature Controlled Requirements into Pharmacy Practice ***(1)***, The Use of Mean Kinetic Temperature (MKT) in the Handling, Storage, and Distribution of Temperature Sensitive Pharmaceuticals ***(2)***,and A Distribution Batch Record Release System: Proposals for Improving the International Distribution of Medicines ***(3)***.

Another venue to consider for learning networking, sharing and debating about the migration from cold chain management to GDP within an integrated supply chain would be the *2010 PDA Pharmaceutical Cold Chain Management Conference* and Training Course, April 12-15, 2010, Bethesda, Md. It will focus on building efficient distribution processes and strategies to mitigate risk in navigating the global pharmaceutical and biopharmaceutical supply chain networks. Among the highlights of the program are:

- Security for the temperature-controlled pharmaceutical products while maintaining their integrity
- How are the wholesalers, as a major partner in the supply chain, managing the distribution of the temperature–sensitive medicines
- Discussing the energy input versus protein/biopharmaceutical issues (FDA's Compliance Policy Guide section 400.210) and the use of radio frequency
- Presenting the recently developed ISTA standards for temperature-controlled products
- Good cold chain distribution practice with focus on in-transit thermal mapping and airport authority cooperation
- Risk-based approaches to solve cold chain challenges with examples for blood components and ambient products.
- Green and environmentally responsible solutions

In summary, it is important to stay up-to-date, well informed and in tune with the latest GDP for temperature-controlled pharmaceuticals, biologics and devices. As there are continuous changing technologies and services that can improve the ability to store and transport, these medicines to their final destination, we are all encouraged to stay in touch and/or volunteer to identify the challenges and find solutions by becoming members of the PCCIG, participating in meetings such as the above-referenced conference and participating in developing best practice guidances.

References

1. Ziance, R., Chandler, C., and Bishara, R.H. "Integration of Temperature Controlled Requirements into Pharmacy Practice." Pharmacy Today, April 2009, pp. 36 – 44.

2. Seevers, R.H., Hofer, J., Harber, P., Ulrich, D. A., and Bishara, R. H.

"The Use of Mean Kinetic Temperature (MKT) in the Handling, Storage, and Distribution of Temperature Sensitive Pharmaceuticals." Pharmaceutical Outsourcing, May/June, 2009, pp. 30 – 38.

3. Holloway, I., and Bishara, R. H. "A Distribution Batch Record Release System: Proposals for Improving the International Distribution of Medicines." Pharmaceutical Outsourcing, May/June, 2009, pp. 50 – 52.

2010 PDA Annual Meeting, Workshop and TRI Courses

Orlando, Fla. • March 15-19 • www.pda.org/annual2010

Conference Chair Harold Baseman, ValSource

It is January, and it is time to consider which meetings and conferences you will attend this year. I want to suggest and to encourage you to attend the *2010 PDA Annual Meeting* in Orlando March 15-19, 2010. The conference portion of the meeting will be held on March 15-17, the post-conference workshop starts on March 17 and the PDA Training and Research Institute (TRI) courses will occur on March 18-19.

This conference has been carefully planned to be as beneficial to the attendee as possible to be uniquely interactive, stimulate thought and develop ideas, disseminate information and broaden knowledge, encourage networking and bring us together in an environment of informational sharing and camaraderie.

Here are some of the many reasons to attend the conference:

The Venue: The meeting will be held in Orlando, Fla., at the Gaylord Palms Resort and Convention Center. This location venue allows for easy access from major airports across North America, Europe and Latin America. Meeting space has been designed to provide efficient and attendee friendly access to exhibit areas, session and break-out rooms. The venue also offers unique opportunity to network and relax before, between and after conference sessions.

The Theme: The time is right to discuss the subject of manufacturing and operational excellence in the context of a science, quality and regulatory-based manufacturing environment. At times, some in our industry have considered quality, science, compliance and efficiency as different and mutually exclusive elements of our business. Today, we are realizing that this is not so. Operational excellence and efficient manufacturing should be synonymous with good manufacturing practices, product quality, patient benefit and sound science. The *2010 PDA Annual Meeting* in March will explore what we as an industry need to better make that connection.

The Keynote Speakers: Keynote and ending addresses will be given by leaders in our industry and by scientific and business leaders, including representatives from NASA, the Nobel Prize Selection Committee and elsewhere outside of the industry. Their objective will be to present areas of similarities, synergy and contrast and to stimulate thought on how we can improve and achieve operational excellence.

The Sessions: The meeting will include 24 sessions and 50 presentations covering topics of manufacturing process science, development science, quality science, process validation, microbiology, quality by design, rapid micro methods, process analytical technology and risk management. Each session is designed to encourage a high level of interaction between speakers and attendees. It is through this interaction and discourse that there is a good exchange of ideas and furthering of knowledge.

The Interest Group Meetings: The heart of any PDA interactive conference is the very informative Interest Groups. This year we will hold a record number of meetings–with over 15 Interest Groups holding sessions. No organization provides a better venue for recent industry developments and trends than the PDA Interest Groups. Select and attend as many of these informative sessions as you can. You will not be disappointed.

The Exhibitors: Over 100 of the industry's most talked about vendors will share innovative, new, and existing product lines—including focused presentations from the exhibit floor. The exhibit area and related activities are designed to provide unprecedented access to these products and direct contact with those most knowledgeable in their application and use.

The Workshop: In order to provide an even higher level of focus on *Manufacturing Excellence*–the PDA planning committee has asked a team of industry experts to conduct a dynamic and fast paced Lean Manufacturing Workshop on March 17 to explore the benefits, challenges, obstacles and implementation of processes for the improvement of drug product operations [see next page for more information.] Whether you are an expert in the field looking to interact with other leaders or a relative novice needing to know more about this important subject—this is a program you cannot afford to miss.

The PDA TRI Courses: Absolutely no one conducts better training courses than the PDA's Training and Research Institute. If you have taken one of our many courses in the past, then you know what I mean. If you have not, then you should attend! And this year, the TRI has scheduled 10 strategic one- and two- day courses related to scientific aspects of operations and manufacturing excellence at the end of the conference.

In conclusion, I wanted to reinforce that the *2010 PDA Annual Meeting* Planning Committee has planned a winning conference; one which every professional in our industry involved with the development, approval, validation, manufacture, testing, distribution, control and improvement of pharmaceutical, biopharmaceutical, diagnostics and medical device products in our industry must attend. This is a job well done for the committee and a great opportunity for the attendees. I am looking forward to seeing you in my home state of Florida this March–and leave your winter coat and gloves behind.

2010 PDA Annual Meeting: The State of Lean/Six Sigma in Pharma and Biotech

Orlando, Fla. • March 17 • www.pda.org/leanmanufacturing

Mike Long, LPD

As the recent publication of *ICH Q10: Pharmaceutical Quality System* tells us, our quality systems should not only promote the continual improvement of our products and processes but continually improve the robustness of the quality system itself. This continual improvement encouraged by Q10 carries us along the path towards *Manufacturing Excellence*, the aptly named title of the *2010 PDA Annual Meeting*.

The pharmaceutical industry is under significant cost constraints and must harness the tools of continual improvement while focusing on value added activities. It is important for the industry to have a venue to discuss methods in attaining this excellence while also discussing the hurdles and issues of implementing and sustaining continual improvement. PDA has created this arena with a workshop called, *What is the State of Lean/Six Sigma in Pharma and Biotech?* on March 17, which we expect to be a perfect bookend to the *2010 PDA Annual Meeting*.

This workshop has been designed to foster discussion. In fact, we endeavour to create an atmosphere that workshop co-lead **Jeff Baker**, PhD, calls a "power point free zone." Rather than a standard workshop with presentations, panel discussions and a Q&A, the agenda will be set around five topics with participants alternating between table and group discussions.

The five topics include:

1. How would you define the state of Lean/Six Sigma in the pharma and biopharma industries?

2. How do you measure value?

3. How would you evaluate your company's implementation of tools and management systems to analyze risk? What have been the potential pitfalls and unintended consequences?

4. If we as an industry know we need to improve the efficiency of our systems and operations, why has Six Sigma not become routine business practice in the pharma and biopharma industries? What are practical barriers? What are practical enablers?

5. How do you maintain a state of control of sustainability while always in a state of continual improvement?

We do not intend this workshop to be a Lean "revival." There are many who have not embraced Lean practices, and the workshop is not intended just for converts. True progress is only really synthesized through dialogue, and we trust this workshop will bring together the skeptics and the advocates for thought provoking debate. The guidance that Q10 brings to the industry is an excellent example of where we see the support for Lean/Six Sigma occasionally bifurcate and provides an expected topic of discussion for participants. Some see the tools and methods for Lean as solely belonging in the manufacturing domain with no express purpose or value in the overall context of quality systems. Some see its value holistically, while others still see it as the flavor of the month, a fad who will see its day eventually come to an end.

Whatever you position, we expect this meeting to bring together content experts and industry practitioners in a workshop environment to discuss the current state of Lean/Six Sigma in the industry and the barriers/hurdles to its implementation. This interactive workshop will capture the experiences of the participants, as well as sharing the experiences of leaders and facilitators to create process knowldge around the state of Lean/Six Sigma in our industry. We hope to see you there!

Visit www.pda.org/leanmanufacturing for more details about this unique workshop scheduled for March 17, 2010 in Orlando, Fla.

PDA's Who's Who

Jeff Baker, PhD, Senior Director, Manufacturing Science & Technology, MedImmune

Mike Long, LPD, Director and Principal, KPM International Associates; Faculty, Gordon Institute, Tuft's University; Faculty, Health Product Regulation Program, Regis College

Upcoming PDA Web Seminars Schedule

www.pda.org/webseminars

PDA Web Seminars are a cost-effective, high-quality training option for professionals wanting to gain the latest information about pharmaceutical/biopharmaceutical sciences and technology–with minimal impact on your time and budget. Accessible via your home, office or anywhere else you can access a computer, these live seminars provide detailed training right at your fingertips! All you need is a touch-tone telephone, computer and an internet connection to participate!

1/20/2010	Strategies for Implementation of a New Bioprocess Container in Commercial Biologics Manufacturing
1/21/2010	The Effect of Culture Media on Mycoplasma Retention by 0.2 μm Rated Filters
2/4/2010	ISNetworld-Supplier and Contractor Information Managements

Upcoming PDA Workshops to Discuss Vaccine Developments

Co-Chair Rebecca A. Devine, PhD

PDA is an organization devoted to advancing the science of pharmaceutical manufacturing; a perfect platform for leveraging the industry's experts to tackle issues surrounding the development, manufacture and quality control of vaccines, as well as to examine the opportunities for applying vaccines to new disease targets in the future. Recent events such as the H1N1 Influenza Pandemic, the threat of bioterrorism and the emergence of new diseases have underscored the importance of vaccines for protecting the public health. Advances in science and technology are leading to research and development of a wide array of new vaccines that are being applied in new areas of disease. The application of immunotherapy to diseases such as cancer, allergies and other chronic illnesses has also come to the forefront in recent years and is a rapidly emerging area. The industry should seek to advance these products with efficiency and quality to fully serve the public need.

While some vaccines can be manufactured using traditional production platforms, the manufacture and testing of many vaccines may also involve unique technologies that require highly specialized processes and control schemes. Coupled with the challenges associated with manufacture of live organisms (sometimes pathogenic), bulk aseptic processing steps, novel expression systems and the ever variable "bioassay," the manufacture and testing of vaccines requires knowledge and controls not often addressed in meetings targeting the "traditional" pharmaceutical industry. Many regulatory hurdles also impact the manufacture and testing of vaccines. PDA has had a long standing focus on issues facing the vaccine industry via its Vaccine Interest Group and has recognized that the area of vaccine manufacturing science and regulation deserves greater attention in broader forums sponsored by PDA.

Plans to develop a focused vaccine conference grew out of the feedback received from our PDA members at the Vaccine Interest Group conducted at the PDA Annual Meeting in April 2009. This has culminated in the planning of a two-and-a-half day vaccine conference in the United States and a one day conference in Europe focused on important topics in the area of vaccine science and regulation. These meetings will serve as the springboard for more vaccine-focused learning opportunities offered by PDA in the future.

Planning of both meetings (United States and Europe) is well underway and the U.S. Food and Drug Administration Center for Biologics Evaluation and Research will participate in the May 2010 vaccine meeting held in the United States. The focus of both meetings is to examine the technical and regulatory challenges currently being faced by the vaccine industry. The Bethesda, Md., meeting will address vaccine development primarily in the United States regulatory framework while the Berlin, Germany vaccine meeting will focus on development within the European regulatory framework. Both meetings will present information on the challenges and opportunities currently being experienced by manufacturers seeking and maintaining vaccine approval. Plenary and focused break-out sessions will include case studies to examine lessons learned including those from seasonal and pandemic flu manufacturing. These meetings will provide global coverage of the hottest vaccine topics and a chance for vaccine manufacturers to share knowledge and experiences.

We are all aware that new guidance documents including those implemented by the International Conference on Harmonisation (ICH) continue to be gen-

Are you in Europe? Join us for the PDA Vaccines Workshop in Berlin!

Berlin, Germany • June 16, 2010 • www.pda.org/europe

PDA Vaccines Workshop 2010: New Technologies for 21st Century:

- Applying New Vaccines Technology to old problems
- Cancer Vaccines
- New Developments in Conjugated Vaccines
- Cell Based Assays for Prediction of Vaccine Efficacy
- New developments with veterinary vaccines

Learn about the Following Vaccine Manufacturing Challenges at the Upcoming PDA Conference in Maryland:

2010 PDA Vaccine Conference • Bethesda, Md • May 17–19 • www.pda.org/vaccines2010

- Growth of live organisms (some pathogenic)
- Containment
- Facility design for multiuse
- Aseptic processing for bulk manufacture
- Adventitious agent contamination
- Removal of Host Cell DNA
- Adjuvants
- Bioassay development
- Potency measurement
- Inactivation/Clearance of live agents

erated by regulatory bodies, yet it is not always clear how these guidance documents impact vaccines. It is important for vaccine manufacturers to understand how to apply general guidance documents to their products. Many of these areas will be discussed at the meetings, such as the application of "Quality by Design" and the new FDA guidance on process validation. There are a wide range of vaccine technologies to which these principles should be applied. How will process design expectations be examined for technologies such as live agent vaccines, and what would the "design space" for various vaccine processes look like? How are other vaccine companies applying these principles, and what are the regulatory implications? How does this impact future manufacturing changes?

Preclinical testing has recently become more important for new vaccines. There is at least one vaccine specific FDA guidance document that addresses this, but what has the industry experience been with preclinical testing and what remains to be learned? What are the challenges associated with lack of relevant animal models? How is FDA viewing vaccines containing novel adjuvants? What are the current and evolving FDA expectations in general?

Changes to the product and process are inevitable during development, however the impact of such changes and the need for a robust process for which comparability and consistency can be demonstrated is no more evident than in the vaccine industry. Technical bridging of changes during development and how the use of comparability testing applies to vaccines is another "hot topic" for vaccine manufacturers. How are principles of "well characterized products" being applied to vaccines? How and when can sponsors best apply the comparability protocol tool to ensure optimal compliance and what will imminent changes to 21 CFR 601.12 imply?

All companies, including vaccine manufacturers, must meet good manufacturing practice expectations, but for many vaccine processes there are unique challenges that may originate from the technology in use. Understanding the expectations is important as a compliance strategy is implemented. The challenges for vaccine manufacturers are unique and sharing approaches is a good way to learn how the industry is addressing these issues. Of course, hearing what is expected directly from the regulators responsible for the products is also an excellent way to reach such understanding. Recent challenges for compliance and realizing satisfactory inspection status have been hot topics in the vaccine industry, and this forum will provide opportunity for sharing such experiences.

The quality control of vaccines involves a variety of analytical methods for assessing potency and other critical quality and stability indicating attributes. Many vaccines have animal tests or bioassays that are used to assess potency and consistency. Those with experience in this area are well aware of the challenges associated with the validation of these analytical methods, including minimizing the variability and the development of appropriate statistical tools to analyze the data. Sharing experiences with colleagues in this setting often leads to ideas that can be applied to your own situation, allowing you to develop solutions for your own assay problems.

Ensuring the continued supply of vaccines, including the maintenance of the "cold chain" for these highly vulnerable biological products has always been a challenge for the vaccine industry and will be another topic for discussion at this workshop.

The planning committee members for the PDA vaccine meetings fully recognize the challenges of vaccine manufacture as they are involved on a day-to-day basis in this pharmaceutical arena. It is our desire to provide a forum where these issues can be fully identified, discussed and recommendations for actions to address such challenges can be surfaced.

Attendees should leave the meetings with a better understanding of how to introduce and maintain high quality vaccines, manufactured efficiently that fulfill all regulatory expectations and ultimately serve the public and target new disease areas. So plan on joining us at one or both of these meetings and share your experiences with the rest of the PDA Vaccine Community. The United States conference will be held at the Marriott Bethesda North Hotel & Conference Center, May 17–19, 2010 and the Vaccines Meeting in Berlin, Germany is scheduled for June 16, 2010.

Extend your Time and Knowledge

Stay in Bethesda, Md., for one of the PDA Training and Research Institute (TRI) courses immediately following the United States Vaccines Conference. On May 19, TRI will be offering "Vaccines 101," a half-day course providing a solid foundation for those new to vaccine development and regulatory affairs or those wanting to expand their knowledge in these areas. In addition, on May 20, there will be two-half-day courses, one devoted to the application of modern science and technology concepts to vaccine manufacture and assay development.

Check the TRI website (www.pdatraining.org) for details and registration information for these courses. We look forward to seeing you there.

Managers Must Utilize Transitional Learning

Anita Pane Whiteford, PhD, Pennsylvania College of Technology

This article will explore the concept of transfer of learning, the transfer triangle, the importance of transfer of learning in the regulatory environment of pharmaceutical industry, transfer successes and failures and getting the transfer transitional.

Transfer of learning is one of the most critical elements of evaluation. Pharmaceutical-based companies will spend a large majority of their budgets on training and development for their workforce to gain the knowledge and skills in order to be competitive in a highly demanding pharmaceutical global market. The reality of this is that companies are making the investment of training and development in their workforce; however, companies are not following the investment through to make sure the knowledge and skills have made the journey from learning setting to work setting.

The Concept of Transfer of Learning

The concept of transfer of learning is to take the knowledge and skills participants learn in training programs back to the worksite and make application and integration into their work roles. Companies should be asking themselves the following questions: Did the employees learn the appropriate knowledge and skills in the training? Do the employees know how to take the knowledge and skills and make an application back to their work roles and department? Do the employees have ample support from the organization in order to make the transition? Did the organization see a positive impact on the organization with transfer of knowledge in a financial or non-financial return? The process of transfer of learning is not difficult or even time consuming, and yet many companies choose not to include this in their training and development practices. It is too common for a supervisor or manager to send an employee to an external training event and not connect with the employee pre- or post- training event. Many times the employee has been given the unspoken direction from management of attending the training to check the box and then return to work as if the training never occurred. In order to avoid such gaps in the training investment from the standpoint of manager and employee, an integration must take place between manager, employee and trainer.

Transfer Triangle

The transfer triangle must be intact initially before the training program occurs. The transfer triangle consists of the manager, trainee (employee) and trainer. Each of these three roles must be integrated and connected to one another to inspire the transfer of learning. The manager supports the trainee in participating in the training program and encourages the transfer to occur upon termination of the training program. The trainee understands the purpose and expectation of the training program. The trainer facilitates the training program to the trainee in which knowledge and skills are learned during the training experience. Without each of these three individuals working together cohesively, the transfer of learning will have a unlikely possibility of happening.

If any industry should view transfer of learning as crucial, it would be the pharmaceutical industry

Importance of Transfer of Learning in Pharmaceutical Industry

If any industry should view transfer of learning as crucial, it would be the pharmaceutical industry. The foundation of training in the pharmaceutical industry revolves around regulatory and compliance issues. It is extremely important that the skills and knowledge learned in these training programs are transferred back into the work area. The products made in the pharmaceutical industry are necessary for human existence. The U.S. FDA is particularly interested in how workers in the pharmaceutical industry transfers the knowledge and skills from regulatory training into the operational and research aspects of the industry.

Transfer Successes and Failures

There are clearly defined indicators that transfer of learning has either been successful due to the transfer taking place or failure due to a lack of transfer. The successful indicators are present due to the existence of the training triangle. In absence of the training triangle, transfer failures occur which contributes to ineffective training. These indicators are provided as follows:

Indicators of Successful Transfer

- The participant understood the content of the training program and has transferred the new skills back to the work area.
- The training content was applicable to the participant's job.
- The participant understood how the knowledge and skills learned in the training program was to be applied back to the work area.
- The participant had a clear vision for the purpose of the training and connection to work role in the organization.
- The organization is supportive of the training program and encourages participant for transfer.

Indicators of Transfer Failures

- The participant did not understand the content of the training and has difficulty transferring new skills back to the work area.
- The training was not applicable to the participant's job.

- The trainer did not make a connection during the training program of how the knowledge and skills were to be applied back in the work area.
- The participant did not have a clear vision for the purpose of the training as no explanation was given.
- The participant did not have defined expectations for attending the training and then post training.
- The organization is satisfied that the participant has once again checked the box for the training program.

Getting the Transfer Transitional

Companies need to be asking themselves the question what needs to occur in order for transfer of learning to occur? Getting the transfer transitional starts before the training program takes place, during the training program and then post training. Below are several guidelines that companies can utilize in getting the transfer transitional in integration with the training triangle.

Pre-Training

- Manager and participant discuss purpose of the training program and expectations for participant.
- Manager discusses with participant the outcomes of the training program and manager's outcomes for transfer of knowledge and skills.
- Manager has an understanding of the training program and the connection back to the participant's position.
- Participant has the basic knowledge and skills needed to be successful in the training program.
- Participant understands from manager how the training will connect back to his/her position and performance/developmental goals.

Training

- Trainer states the purpose and objectives of the training.
- Trainer provides participants with training materials that are relevant to the course.
- Trainer continuously makes connections during the training how the training will be beneficial to the participant's position.
- Trainer allows the participants to make application of the skills and knowledge learned in the training with interactive exercises.
- Trainer will test participants' knowledge and skill at the end of the training to measure learning with a post-test or demonstration.
- Trainer will work with management and participants to create an action plan to ensure post training transfer of learning.

Post-Training

- Manager will work with participant to discuss how to integrate skills and knowledge from training program to position in department—sharing in staff meetings, training the trainer and improving systems and processes.
- Manager must immediately meet with participant upon return from training program to start the transfer—it will not beneficial to wait a few weeks and then connect with participant.
- Manager will provide participant with the necessary tools and resources to support the transfer of learning.
- Manager will provide ample opportunities for participant to transfer the learning.
- Manager will continuously do a progress check with participant to discuss how the transfer of learning is occurring.

Transfer of learning is key in the training investment made by companies. Without transfer of learning the training investment and efforts will be wasted. The transfer triangle is the primary component in transfer of learning. The transfer triangle must be initiated and in existence from the moment that the manager identifies that the participant will be attending any training program. If transfer of learning is a success in the company then the return from the training investment will be profitable and beneficial.

Initiate "Transfer of Learning" With TRI's In-house Training Program

Stephanie Ko, PDA

With companies facing budget cuts that reduce or eliminate the funds allowing employees to travel for training opportunities, the Training & Research Institute (TRI) has literally brought the solution right to your doorstep. Accredited lecture and laboratory courses offered throughout the United States and around the world can be brought directly to your company, saving employees the time and expense of traveling to get the training they need.

The Training & Research Institute has many successes in delivering in-house training

TRI has had many successes in delivering in-house training. Whether you need one week of laboratory training in aseptic processing or a one-day lecture course on Media Fills, we will work closely with you to consider all options. We've even taken laboratory training overseas, so anything is possible.

The process is easy. To start, go to our website at www.pdatraining.org and browse through our 2010 online catalog for a general overview of available courses. We offer training in nine major areas: aseptic processing, biotechnology, environmental monitoring, filtration, microbiology, quality/regulatory affairs, training, validation and specialized courses, such as cold chain, supply chain and visual inspection. If you don't see what you need, we are happy to customize training by either designing a new course or modifying an existing one for the specific needs of your company.

Next, send us an email. You may contact

Robert Dana, Sr. Vice President, Regulatory Affairs and Training and Research Institute at dana@pda.org.

Please provide the following information:

- Training topic(s)
- Available Dates
- Number of individuals to be trained
- Number of days dedicated to training
- Training location
- Equipment available at your facility (only if requesting for laboratory training)

That's it! We'll do the rest in identifying an expert instructor and sending you a proposal. Our in-house services include course development, instructor travel arrangements and expenses, course notes for each participant, and the processing of Continuing Education Units for those who need it. We look forward to hearing from you soon.

2010 First Quarter Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

January 201025-29: 2010 Aseptic Processing Training Program–Session 1 (Week 2: Feb. 22-26)

February 201010–11: Choosing the "Right" Microbial Identification Program for Your Biopharmaceutical/Pharmaceutical Quality Control Laboratory

22-24: San Diego Course Series

March 20103-5: Pharmaceutical Water System–Microbiology Lab Course

10-12: Developing an Environmental

Monitoring Program

18-19: 2010 PDA Annual

Meeting Courses

22-26: 2010 Aseptic Processing Training Program–Session 2 (Week 2: April 19-23)

For an updated schedule of events please visit www.pda.org/calendar

Recession Creates Better Focus, Programs at TRI

James Wamsley, PDA

2009 was a difficult year for almost everyone and PDA's Training and Research Institute (TRI) was not immune to the same problems that many companies faced with reduced revenue. The good news is that the rough economy forced us to think along different paths and find innovative solutions that ultimately benefit you. In our aim to increase course registrations and facility utilization here at TRI, we've redirected our focus in ways that give you more opportunities and/or better access to our resources.

We have always strived to provide the widest variety of courses in the past, but we took a greater number of factors into consideration when selecting courses in 2010. Most specifically, we've condensed course selection to coincide with themes of PDA conferences and hand-picked courses specifically of interest to certain localities within the United States. To clarify the latter, we scheduled courses that would most benefit the employees of the companies surrounding that particular region, saving companies money on travel. In our efforts to give you the best selection, we've solicited our instructors to develop new training courses so that training can be delivered to a wider audience. In addition, we're updating courses that haven't been run in years so you can stay current. We'll actually have more than 20 new courses in 2010.

Eleven lecture course series will be offered in 2010, seven of which are in conjunction with PDA conferences and four "stand-alone" series in exciting cities spread across the US. The following is an abridged schedule with the location and focus of select course series:

February 22-24: San Diego Course Series–Five biotechnology courses

March 18-19: Nine courses aligned with the theme of PDA's Annual Meeting "Manufacturing Excellence"

April 6-8: St. Louis Course Series—Five courses selected in response to a survey conducted by PDA's Midwest Chapter reflecting customer preference

May 24-26: Boston Course Series—Five more biotechnology courses

September 16: Six Quality/Regulatory themed courses held immediately after the PDA/FDA Joint Regulatory Conference in Washington, D.C.

October 14-15: Four training courses following PDA's Biennial Training Conference in Baltimore, Md

For the complete lecture series schedule, please visit our website at www.pdatraining.org.

We have a well-equipped laboratory facility where many different research projects can be performed

We are continuing to offer courses at our facility in Bethesda, Md., which is conveniently located near three airports and easily accessed by public transportation. We currently have 23 laboratory courses, including 5 *Aseptic Processing Training Program* sessions and 18 other courses ranging from two to five days each and covering a wide variety of topics from cleaning validation to fungal identification. We also have scheduled nine lecture courses at our facility covering basic and advanced topics.

One of our big successes in 2009 will continue to be a focus in 2010. We worked with multiple companies last year to provide in-house training at their facilities, including laboratory training. These training courses have been well received by the attendees and instructors alike. It allows companies to send multiple employees to a training course without the burden of travel costs for 10, 15 or even 30 people. Another added benefit is the course can be tailored to fit your specific needs. (See related article on TRI's training on page 45 of this issue.)

One of the original intentions for TRI is found right in the name! TRI was designed not only to serve as a facility for laboratory training but also to be utilized by the community for research that would benefit the industry. We have a well-equipped laboratory facility where many different research projects can be performed. Since our facility does not produce product, there may be opportunities for types of research which cannot be done elsewhere. Already one research project was successfully completed at our facility and we're ready throughout the year for others. If you have something you would like to study, just give us a call!

As we rebound from 2009, we've worked to be creative and proactive in 2010, but we don't claim to know everything. We've planned a focus session at the *2010 PDA Annual Meeting* in Orlando to receive feedback from you. Keep an eye on our website and your inbox for details on this upcoming focus session. We'd like to hear from you directly, what your needs are, and how we can best address those needs.

Maybe 2009 was a blessing in disguise! We are more determined than ever to deliver you the best training and research opportunities possible.

Workshop To Address Impact of Biofilms on Bio/Pharma Manufacturing

Frankfurt, Germany • April 20-21 • www.pda.org/europe

Marc Mittelman, Harvard University

Biological contamination of various fluid handling systems continues to present significant challenges to the pharmaceutical, biotechnology and medical device industries. Bacteria, in particular, are well adapted to survival in purified water and media formulation systems. Their presence leads to the contamination of process equipment, raw materials and in some cases product adulteration leading to recalls. Effective control of bioburden requires an understanding of those factors that promote microbial growth and biofilm formation. The presence of biofilms associated with wet surfaces gives rise to both bioburden and associated endotoxin (pyrogen) contamination.

Mycoplasma, for example, may form biofilm complexes during peptone manufacturing that protect them from heat. These heat resistant biofilms then lead to contamination of peptones and other media formulations.

The 2010 PDA *Workshop on Biofilms: The Impact of Biofilms on Pharmaceutical and Biopharmaceutical Manufacturing* will focus on the genesis, detection, prevention and treatment of biofilms in pharmaceutical and biopharmaceutical fluid-handling systems.

In addition, the workshop will feature invited lectures by leading experts in the field on original scientific presentations ranging from topics such as mycoplasma biofilm formation to the impact of surface properties on biofilm formation to novel treatment modalities. Information on workshop registration, invited speakers and workshop topic areas may be found at www.pda.org/europe.

For information on presenting at this PDA workshop, please refer to the abstract submission instructions on the PDA website. The abstract submission deadline is January 29, 2010. For further information, please contact **Ailyn Kandora** at kandora@pda.org.

PDA Workshop To Discuss Aseptic Process Simulation Exercises

Berlin, Germany • February 25, 2010 • www.pda.org/europe

Volker Eck, PhD, PDA

During a workshop on validating Aseptic Processes held on December 1 and 2, in Milan, Italy, **Ian Symonds**, Director, Aseptic Quality Assurance, Global Quality, GlaxoSmithKline, was presenting an interesting overview on "Regulatory Expectations for Aseptically Produced Parenterals." During his talk, he touched on the most challenging issues practitioners are confronted with when striving for compliance with current guidelines, rules and regulations.

The first challenge to the professional is to find a way through what he called the "regulatory maze." There are a multitude of documents issued by bodies like the U.S. FDA, the European Commission, WHO, the diverse Pharmacopoeias, industry associations and many more making it a difficult task to stay updated on trends and expectations. As the guidelines are quite general in nature, it becomes vital to have some regulatory intelligence at hand to get a current interpretation of those documents.

Ian then highlighted some key changes to the Annex 1 of the EU Guidelines on GMPs, such as:

- Media fill limits are harmonized with the U.S. FDA 2004 guidance on Sterile Drug Products produced by aseptic processing.
- More guidance on investigation is given for contamination incidents during media simulation runs.
- The limit for 5 micron particles in Grade A zones at rest and in dynamic conditions is increased to not more than 20 particles per cubic meter.
- Sampling of air quality in clean rooms and clean air devices should be based on data obtained during qualification and a formal risk analysis.

These changes and the related wordings had other hidden consequences as, for example, in paragraph nine. It states that "The Grade A zone should be monitored at such a frequency and with suitable sample size that all interventions, transient events and any system deterioration would be captured and alarms triggered if alert limits are exceeded." To comply with this requirement of transient events and any deterioration, continuous monitoring becomes mandatory although it is not explicitly requested.

Another issue within this document are contradictory requisites, for example, the requirement in paragraph 34 states that "prior to the the completion of stoppering, transfer of partially closed containers, as used in freeze drying, should be done either in a Grade A environment with Grade B background or in sealed transfer trays in a Grade B environment" is not aligned with paragraph 116. "Partially stoppered freeze drying vials should be maintained under Grade A conditions at all times until the stopper is fully inserted." These and other examples he gave underlined the need of assisted interpretation for this document in order to become and/or remain compliant.

Continuing with the U.S. Code of Federal Regulations (CFR), Ian pointed to the obvious but not outspoken harmonization of expectations, for example, the revised CFR Section 211.67(a) requires that equipment and utensils be cleaned, maintained and, as appropriate for the nature of

Table 1: Typical Upper Respiratory Flora

Bacterium	Nose	Pharynx	Mouth
Staphylococcus epidermidis	++	++	++
Staphylococcus aureus*	+	+	+
Streptococcus mitis		+	++
Streptococcus salivarius		++	++
Streptococcus mutans*		+	++
Streptococcus pneumoniae*	+/-	+	+
Streptococcus pyogenes		+	+
Neisseria sp,	+	++	+
Neisseria meningitidis	+	+	+
Proteus sp.	+	+	+
Haemophilus influenzae*	+	+	+
Lactobacillus sp.		+	++
Corynebacteria	++	+	+
Actinomycetes		+	+
Spirochetes		+	++
Mycoplasmas		+	+

Will grow on TSA/TSB

May grow on TSA/TSB

Will Not* grow on TSA/TSB

* Under typical incubation conditions

the drug, sanitized "and/or sterilized" at appropriate intervals to prevent malfunction or contamination. This change recognizes that for sterile drug products, sterilization (sometimes in addition to sanitization) is appropriate. This comes very close to the European position where terminal sterilization is the first choice and any deviation from this expectation needs to be justified.

Another example is CFR Section 211.84(d)(6), that requires microbiological tests before use of each lot of a component, drug product container or closure "with potential for microbiological contamination" that is objectionable in view of its intended use. This is consistent with the long-standing agency interpretation and ICH Q9 requirements that ask for a risk assessment and rationale to support a testing regimen.

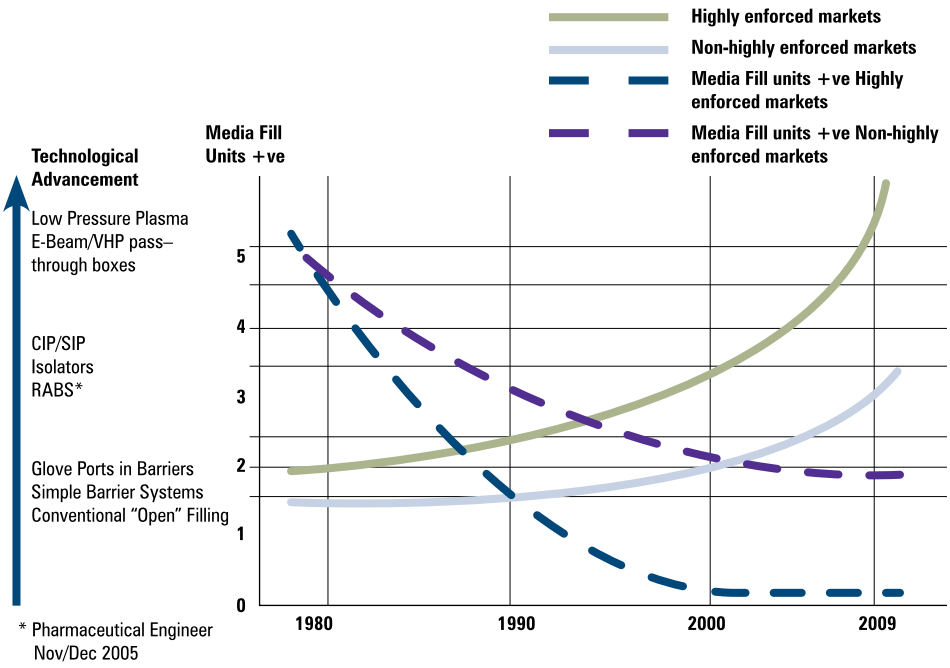
Symonds said, in essence, there is no change in practical terms as many companies follow the published requirements. The significance is that these requirements have moved from guidance (which is not directly legally enforceable) to law which is legally enforceable! "The bottom line is," he pointed out, "FDA can take more drastic action if any one of these requirements is not met. Previously FDA had to find evidence that deviation from guidance could result in an "adulterated product" but now non-compliance with the CFR default state constitutes already the adulterated product state."

Symonds illustrated the effect of this trend with an exemplifying graphic. (See Figure 1):

The graph shows empirical data correlating technology advancement and "found positive units (+ve)" per aseptic process simulation run, respectively, over the time period from the 1970's to today for both highly enforced and non-highly enforced markets. One possible interpretation could be that enforcement has a positive impact on the quality of the products manufactured, as industry is investing into advanced technologies to avoid any compliance issues.

At the end of his talk, he turned to

Figure 1: Standards Gap



environmental monitoring issues. **[Editor's Note:** See Table 1 on previous page.] By a simple comparison of the monitored fraction of air (0.005% by active air sampling, 0.02% by continuous particle monitoring) and surface (0.42% by contact plates and 0.42% by swabbing) for a filling machine within a RABS system, he concluded that:

- Only a small fraction of the air and surfaces that can have an influence on product can be tested.
- Monitoring techniques have low recovery efficiency.
- A limited range of organisms can be isolated using common media and incubation conditions.
- A positive isolate is a significant event.
- A negative result may be misleading.

As the table demonstrates, there is a risk that some bacteria potentially present in human respiratory flora and hence a potential contaminant of a product are not growing on the standard TSA/TSB medium used to test for microbial contamination.

Having said this, Symonds summarized:

- Assurance of sterility is achieved through good design and operation of facilities and equipment.
- Process understanding and capability control is paramount (much of this is achieved at the design and qualification stage).
- Aseptic process simulation runs and environmental monitoring data is there to support a well designed and operated facility, not to defend poor practice.

To identify and avoid poor practices, PDA Europe will organize a workshop on Aseptic Process Simulation to be held on February 25, 2010 in Berlin, Germany. Keeping in mind that correct and current interpretation of guidelines is essential. To avoid compliance issues in your daily practice, we invite professionals involved in media fill studies to participate. The workshop will enable attendees to avoid common pitfalls and develop robust aseptic process simulation plans.

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February 2010

10 -11: Choosing the "Right" Microbial Identification Program for Your Biopharmaceutical/Pharmaceutical Quality Control Laboratory
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The PDA Training and Research Institute is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education.

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3-5: Pharmaceutical Water System Microbiology Lab Course
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www.pdatraining.org/watermicro

10-12: Developing an Environmental Monitoring Program
Bethesda, Maryland
www.pdatraining.org/DEMP

18-19: 2010 PDA Annual Meeting Courses
Orlando, Florida
www.pdaannualmeeting.org/courses

Courses Include:

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- Bioprocess Validation - New Course
- Change Control: A Practical Workshop
- Clean Room Design, Contamination Control, & Environmental Monitoring for Controlled Environments
- Fundamentals of Lyophilization
- Isolators: From Concept through Qualification - New Course
- Risk Mitigation Solutions: The Response to Risk Assessment - New Course
- Role of the Quality Professional in the 21st Century
- Use of HACCP for Microbiological Control in Pharmaceutical Manufacturing

22-26: 2010 Aseptic Processing Training Program - Session 2
(Week 2: April 19-23)
Bethesda, Maryland
www.pdatraining.org/aseptic

April 2010

6-8: Saint Louis Course Series
Saint Louis, Missouri
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- Managing Quality Systems
- Process Validation for Pharmaceuticals: Current and Future Trends with Emphasis on Implementation of the New FDA Guide
- Risk Management for Aseptic Processing
- Single-Use Technologies in Downstream Processing: A Blueprint for Implementation – New Course

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14-15: Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems
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28-30: Development of Pre-filled Syringes
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www.pdatraining.org/prefilled

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Stop seeking...
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When to identify ?

"Sequencing of the 16S ribosomal RNA gene to identify the class, order and genus of a microorganism is now an integral part of the approach to microbial taxonomy, but this gene is not useful for identifying many microbes at the species level."

Source: RECONCILING MICROBIAL SYSTEMATICS AND GENOMICS - ASM REPORT 2004

"With many isolates phenotypic identification is completely adequate and the added expense of using a genotypic identification system is not justified."

Source: PDA JOURNAL OF PHARMACEUTICAL SCIENCE AND TECHNOLOGY 2008

VITEK 2 compact

When to investigate ?

"...it may be necessary to employ sensitive typing techniques to demonstrate that a microorganism isolated from the product test is identical to a microorganism isolated from the test materials and/or the testing environment."

Source: EP 5.1.3

diversilab Strain typing

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