People • Science • Regulation

PDA Letter

Volume XLVII • Issue #1 www.pda.org/pdaletter January 2011

Protective Packaging Choices Challenge Packaging Engineers

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The Parenteral Drug Association presents...

2011 PDA ANNUAL MEETING

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

1946 65TH ANNIVERSARY 2011

April 11-15, 2011

JW MARRIOTT SAN ANTONIO HILL COUNTRY | SAN ANTONIO, TEXAS

www.pda.org/annual2011

Welcome to your meeting! PDA is pleased to invite you to attend the *2011 PDA Annual Meeting*.

The Opening Keynote addresses include:

- **EMA Perspective: Knowledge Management**

Piotr Krauze, Scientific Administrator/Compliance and Inspection Sector, *European Medicines Agency*

- **Fostering Academic-Industry Collaboration for Product Development**

M. Lynn Crimson, Dean, School of Pharmacy, *University of Texas*

Janet Walkow, PhD, Director, Drug Dynamics Institute, *University of Texas*

Join more than 50 speakers in over 45 presentations in sessions that will discuss:

- Quality Science
- Development Science
- Manufacturing/Process Science
- Outsourcing/Supply Chain
- **New in 2011 is the Fundamentals Track** – This track is designed for those who are new to the pharmaceutical/biopharmaceutical industry or have recently changed jobs with a change in focus.

Additional Educational and Training Opportunities!

- Attend the **PDA Process Validation Post Conference Workshop** to learn about US and international regulations, technology transfer, documentation strategies, post approval reporting and more!
- **PDA's Training and Research Institute (PDA TRI) is offering seven courses** in conjunction with this meeting – covering topics such as GMP regulations, Rapid Micro Methods, six sigma in process validation, cleanroom management and more!

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MEETING April 11-13 | **EXHIBITION & CAREER FAIR** April 11-12

PDA/FDA PROCESS VALIDATION POST CONFERENCE WORKSHOP April 13-14 | **COURSES** April 14-15

The Parenteral Drug Association presents...

2011 US Exhibition and Sponsorship Opportunities!

Exhibit at PDA events to gain on-site exposure and connect with industry experts from manufacturing, operations, quality assurance, compliance, engineering, packaging, research and development, logistics and supply chain as well as representatives from regulatory agencies. In addition, PDA's comprehensive sponsorship packages provide your company the opportunity to strengthen brand image, increase visibility and reinforce its commitment to the pharmaceutical and biotech manufacturing industry.

2011 PDA Pharmaceutical Cold Chain Management Conference
March 1-2 | Bethesda North Marriott Hotel | Bethesda, Maryland | www.pda.org/coldchain2011

2011 PDA/FDA Atypical Actives Workshop
March 9-10 | Hyatt Regency Bethesda | Bethesda, Maryland | www.pda.org/atypicalactives2011

2011 PDA Annual Meeting
April 11-12 | JW Marriott San Antonio Hill Country | San Antonio, Texas | www.pda.org/annual2011

PDA Container Closure/Glass Defects Workshop – *More Information to Come!*
May 2011

2011 PDA Pharmaceutical Supply Chain Workshop – *More Information to Come!*
June 2011 | Chicago, Illinois

PDA Single Use Systems Workshop
June 29-30 | Montreal, Canada

PDA Analytical Methods & Validation Technical Report Workshop – *More Information to Come!*
July 2011

2011 PDA/FDA Joint Regulatory Conference
September 19-20 | Renaissance Hotel | Washington, D.C. | www.pda.org/pdafda2011

2011 PDA Visual Inspection Forum
October 3-4 | Hyatt Regency Bethesda | Bethesda, Maryland | www.pda.org/visualinspection2011

PDA's 6th Annual Global Conference on Pharmaceutical Microbiology
October 17-18 | Bethesda North Marriott Hotel | Bethesda, Maryland

Adventitious Virus/Cell Substrate Workshop – *More Information to Come!*
November 2011

The above dates indicate exhibition dates.

For more information please contact:

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PDA Letter

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Cover Art Illustrated by Katja Yount

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Features

PDA's New Strategic Plan Unveiled

Anders Vinther, Genentech

The PDA Board of Directors approved a new strategic plan at their December 2010 meeting. The plan outlines where PDA will focus its activities in the areas of manufacturing science, quality and innovation over the next four years.

In summary, the plan ensures that we will continue to operate and serve members globally with publications, conferences, training and other activities, as well as continue to serve as the foremost organization for membership networking and sharing of best practices among colleagues in industry, regulatory agencies and academia.

In times of challenges for our industry it is even more important that we maintain a scientifically and technically sound approach to areas within our scope and that we collectively advance science and regulation of safe medicine to patients worldwide. We trust that our strategy will help achieve this objective with the help of active members. A key factor in our strategy is to further engage members and build on their experiences and ideas to achieve the objectives.

If you are interested in being more involved in any of the strategic elements please contact the PDA office.

Thank you to all of you who have contributed to the PDA Strategic Plan. ➤

PDA's "Mid-Term" Elections Result in Three New Board Members

Members have chosen three new Directors for the Board and favored the return of one Director.

PDA welcomes **Jette Christensen**, **Susan Schniepp**, and **Glenn Wright** as newly elected Directors and congratulates **Michael Sadowski** for being selected for a new term.

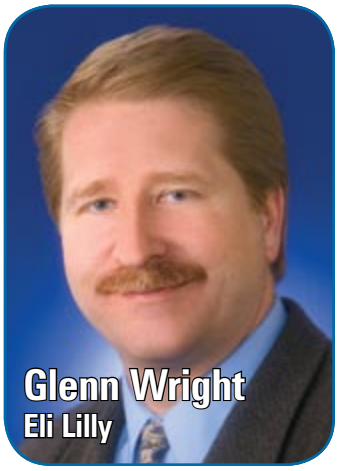
Jette's involvement in PDA began in 1998, and in recent years she has helped plan conferences on microbiology both in the United States and Europe, served on the task force revising PDA Technical Report No. 13, and served on the task force that commented on Annex 1.

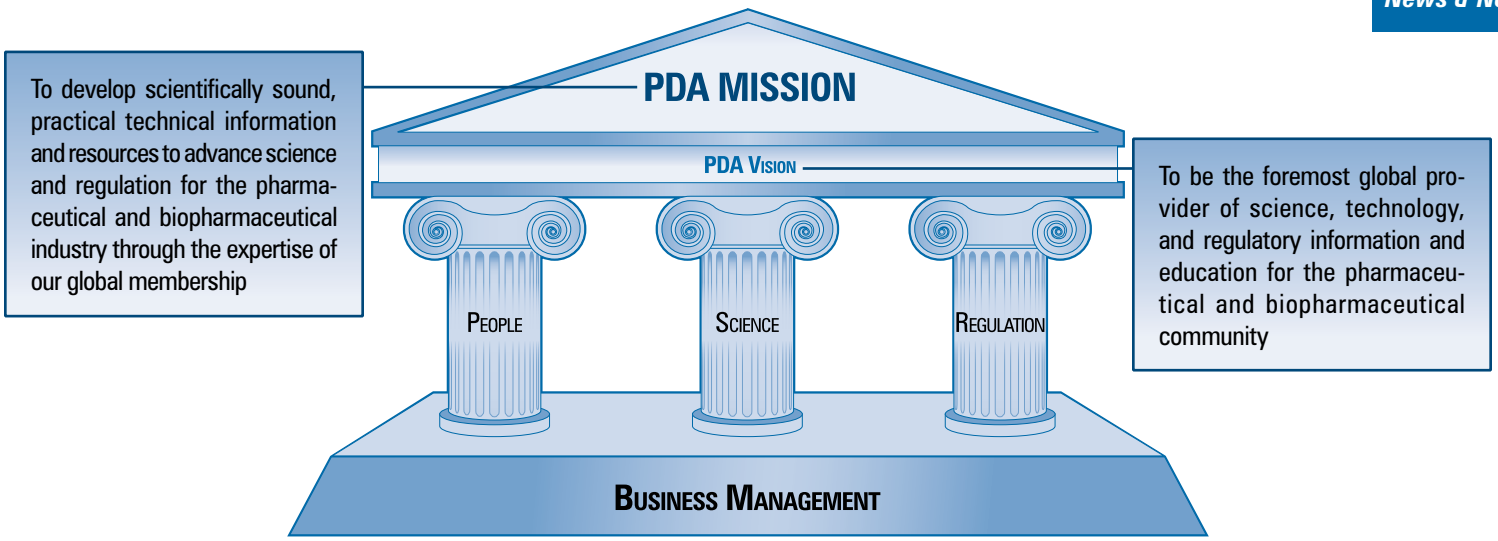
Sue sits on a number of PDA committees, including the Regulatory and Quality Advisory Board (formerly Regulatory Affairs and Quality Committee), the *PDA Letter* Editorial Committee, and the PDA/FDA Joint Regulatory Conference planning committee (chair in 2007 and 2010), is the winner of the 2009 PDA Gordon R. Personeus Award, and has written articles and spoken at many conferences for PDA.

Glenn actually served as a PDA Director from 1998 to 2003, winning the 2003 PDA Frederick J. Carleton Award for his service and has been involved in numerous PDA activities since joining PDA over two decades ago.

PDA wants to thank outgoing Director's **Laura Thoma**, University of Tennessee, **Véronique Davoust**, PhD, Pfizer, and **Lothar Hartmann**, PhD, F. Hoffmann-La Roche for their service and look forward to their future contributions.

[Editor's Note: We are calling the 2010 Board of Directors election a "mid-term" election, not just to play off of the dramatic vote in the United States last November, but because the election really is a mid-term. The PDA Officers are elected for two-year terms beginning every even year; on the odd years, four of the 12 Director positions are open to new candidates.**]**





PEOPLE — *Enhance the Value of the PDA Membership*

Chairs: Richard Johnson, PDA and Maik Jornitz, Sartorius Stedim Biotech/ PDA Chair

1. Hold Scientific, Quality and Regulatory conferences based on current industry focus, if needed with the support of other organizations or regulators
2. Develop a core and standardized curriculum for Education and continually improve training and education programs
3. Focus on global membership expansion
4. Actively create networking opportunities and use rewards and recognition mechanisms to attract and retain volunteers

SCIENCE — *Be recognized as a leading organization for manufacturing science, quality and innovation*

Chairs: Rich Levy, PDA, and John Shabushnig, Pfizer/PDA Immediate Past Chair

1. PDA's technology focus is Pharmaceutical Manufacturing and Quality including: Aseptic Processing and Sterile Manufacturing; API, Non-Sterile and Combination Product Manufacturing; Quality Management, regulatory compliance and process validation; and Pharmaceutical and biopharmaceutical Supply Chain
2. Ensure the most current information about technical topics are published through the PDA Technical Reports, PDA Journal, *PDA Letter*, PDA Conferences and PDA Website
3. PDA will assure that current and upcoming technical and scientific topics within PDA's core competencies will be addressed timely, with high quality and distributed by PDA Task Forces, PDA Interest Groups, PDA TRI and PDA Focus Meetings
4. Implement a research strategy and utilize TRI to promote science in PDA's strategic areas

REGULATION — *Our regulatory activities are scientifically and technically focused, and current information is communicated to our members*

Chairs: Georg Roessling, PDA, and Steven Mendivil, Amgen/PDA Board member

1. Provide science and technology based input on regulations and guidelines related to PDA strategic areas, utilizing PDA's volunteer and membership base
2. Bring sound scientific and technical information to the regulatory process, maintain valuable and effective relationships with global regulators, and educate members on current expectations
3. Engage in activities, for example training and education, in BRIC countries when we can benefit the general membership
4. Engage regulatory agencies in the development and adoption of PDA TRs

BUSINESS MANAGEMENT — *Enhance business processes to provide a solid foundation and organization to sustain PDA's people, science and regulation strategies*

Chairs: Craig Elliott, PDA and Hal Baseman, ValSource/PDA Treasurer

1. Maintain reserve to a minimum of 12 months of Global Operating Expense
2. Establish a five year rolling financial and marketing plan to sustain and balance major revenue streams
3. Leverage staff and volunteer resources by aligning programs, TRs and other PDA activities
4. Maximize the use of the TRI facility and other PDA products as reliable and constant revenue stream, for further investments into the support of PDA's membership

PDA Retains Member Experience by Forming PDA Board Alumni

As it is so often, the phrase "out of sight, out of mind" is also applicable to PDA's former board members. Most often when board members have completed their tenure, certain exhaustion sets in and their active participation within PDA slows down. However, years of active membership and experiences as a former board member are an essential support for PDA's activities and leadership requirements.

"Former board members have a wealth of information and experiences which PDA wants to tap in to" explains **Maik Jornitz**, current Chair of the Board. "As an organization of volunteers, we cannot afford to lose this knowledge base, as well as leadership potential, for example, for task forces or interest groups."

For this reason, PDA has formed the PDA Board Alumni, a group for former board members. The Board Alumni leader is **Vincent Anicetti**, a former Chair of the Board and long-term active member of PDA.

"I am excited about the Board Alumni, as it will create a great opportunity to draw upon the extensive experience of the board alumni and seek their input whenever possible. Maintaining a link to prior generations of PDA leadership is an important thread in our legacy and a valuable resource to future PDA leaders," says Anicetti. "This group will be an additional asset to PDA's development. Former board members, who are active members of PDA, will be contacted shortly to learn about the charter and next steps within this activity."

PDA is very pleased to have this opportunity of experience exchange and active communication and encourages all former board members to join the Board Alumni.

The PDA Board Alumni, headed by Vincent Anicetti, will help future generations of PDA Leaders maintain a link to the past

Dinner with a Dash of Mycoplasma & a Day of Process Val at Lilly

Emily Hough, PDA

October was a busy month for PDA's national and European conferences, but for those members who could not commit the time or resources to make long trips, two Chapters hosted shorter, more intimate affairs. I was fortunate for the opportunity to attend both and enjoyed the hospitality provided to me by the Chapter leaders!

At the Capital Area Chapter dinner meeting in Gaithersburg, Md., on October 6, I spent the networking time mingling with chapter officers, **Allen Burgenson**, **Barry Friedman** and other PDA members. Afterwards, I enjoyed a lovely meal with my fellow attendees. What an excellent way to kick-start a meeting and a "validated" method by a chapter known for its dinner affairs!

The night's marquee talk was by **Christine Wright**, who discussed mycoplasma detection and products her company, EMD Millipore, has developed for it.

When evaluating a system for use, she said it was important to:

- Consider the type of technology being utilized versus the type of microbiological test being performed
- Initial system and routine costs
- If the system can handle the type of products that are being manufactured, filterability, sample size and if the detection limits are appropriate for the test

Acknowledging that mycoplasma is one of the most difficult contaminants to prevent and detect, she presented new products by Millipore to aid in this task: the Milliprobe System, the Milliflex Quantum system and the Milliflex Quantum Fluorescence Reader.

Lilly Hosts Midwest Chapter Event

A week later, I traveled to the Eli Lilly headquarters in Indianapolis, Ind. to attend a full-day Midwest Chapter event on process validation. But before I could even board the airplane, I came face-to-face with how TSA employs its quality systems in the airport and gained first-hand experience with a body scan, which hopefully had been validated!

The next morning, I met chapter officers **Scott Hartman** and **Peter Noverini**, who graciously met with me to make sure I had everything I needed for the meeting. After the morning networking period, **Jeff Boatman** provided an in-depth review of the draft U.S. FDA Process Validation guidance and what industry should expect from the Agency when it is finalized. He told the audience that three batches will no longer be automatically acceptable, and instead, the guidance will recommend that the number of validation batches to be derived statistically.

The process validation guidance will be dependent mainly on good science as opposed to set standards.

Kelly Davis presented, "Process Validation – Incorporating Quality Design and and Risk Management." Her talk highlighted some problems the firm encountered when transferring an existing product to a new filling line and how it solved the problems using sound design principles. During the validation of the new process, two of the six validation batches had out-of-trend reject rates because of silicon particle contamination. An investigation found that silicon tubing used on the line was faulty because it was not long enough for its intended use and had variable wall thickness. Operators were stretching the tubing to make the connections, resulting in the silicon particle contamination. The firm launched a design study of various tubing sources to solve the problem, and evaluated factors like wall thickness. Ultimately, the firm settled on a new source of silicon tubing and successfully validated the new line. As part of its risk management solution, the firm implemented an enhanced in-process

testing regime to monitor for the particulate contamination.

The next speaker, **Susanne Resatz** gave a series of case studies involving the process development for a lyophilized vial from the first lab trial to the validation strategy of the product. With trial and error, Susanne said at she learned that rushing to validate large-scale manufacturing may in the end cost more time and money than if useful studies were performed in the laboratory prior to up scaling.

Following an hour-long luncheon that gave attendees additional time to network, **Janet Bowen** took the stage and spoke about the ASTM E2500, a standard guide for specification, design and verification of pharmaceutical and biopharmaceutical systems and equipment, and how it relates to the FDA's process validation guidance. Janet gave an example of how the ASTM E2500 standard and FDA draft guidance posed similar documentation requirements, with some minor differences in nomenclature. Missing from both documents, she said, is language on the structuring of the design review, inspection and test programs.

Steven Ensign spoke next on regulating the stability batches of a biologic drug product that was costly and in short supply. He said. in this case, it was of the utmost importance to understand all aspects of the process, as his team had to figure out potential problems and equipment modifications using a drug product substitute.

The speakers participated in a panel discussion to close out the meeting. The key point was that the process validation guidance will be mainly dependent on good

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Membership Milestone: Frank Kohn Now a 40 Year Member

Frank has reached the 40 year membership milestone, joining a select, but growing group of longtime members. Over the years, Frank has made his mark within the microbiology, quality and manufacturing sectors of PDA.

PDA: Frank, thanks for sitting with us today. This year marks your fortieth year as a PDA member. You are now joining elite company. How did you get involved with PDA in the first place?

Frank: One of the past presidents, **Nate Kirsch** from Schering Plough Corporation encouraged people who were working within Schering to join PDA.

PDA: You hold graduate degrees in environmental microbiology and operations management. In addition, you hold the title of Specialist Microbiologist by the National Registry of Certified Microbiology (American Academy of Microbiology) and you are registered as a Specialist Microbiologist by the American Society of Clinical Pathology Board of Registry and the Canadian College of Microbiology. Why are you so fascinated with microbiology?

Frank: That's a good question. I really became interested in microbiology interestingly enough as a junior in high school. At that time, I was working part time in a local hospital lab washing their test tubes and the equipment they had used. I was able to get a part-time job after school in the hospital. I'd walk down the street after class and walk to the hospital. I started washing laboratory glassware. Then there was a science fair in my high school, and I talked to the pathologist who ran the hospital lab. He told me that he would let me work in the microbiology lab and show me how to handle cultures and grow microorganisms. Ever since then I've been interested in the area of microbiology.

PDA: How has PDA changed or evolved over the last 40 years?

Frank: It has been a huge change. Originally, at the annual PDA meeting, all attendees' sat in one room—primarily all men, and a few women. We sat in one large room at the annual meeting, and everyone had a suit on and listened to the various lectures, as well as to the U.S. FDA. The presentations were very formal.

PDA: And how has it changed since then?

Frank: Structurally, it changed in that today we break up in different sections. There are many more people who attend the annual meeting. Originally, the annual meeting was always in the city of Philadelphia. Again, I think it is much more diverse and much more international today.

PDA: What do you like best about being a member of PDA?

Frank: The opportunity to stay current in your field. The opportunity to interact with colleagues and to see new technologies as they're being presented by the various companies.

PDA: How did your membership in PDA parallel your career? You must have been a member for most of your career.

Frank: Initially, I started out as a research scientist with Schering. At that time it was a way to get exposed to the pharmaceutical industry, because coming out of school you don't normally think of the drug industry for employment. Prior to that, I was working in the N.J. Dept of Health. I changed from working in the health department to working for Schering as a research scientist. So the PDA was a way for finding out about the pharmaceutical industry in general. As time went on, I moved into manufacturing, and I was the head of manufacturing operations for Schering in Madison, Wisconsin. At that time in my career, it was more important to hear what was going on with the Food and Drug Administration, as well as the other regulators, and become more involved in learning what was going on in the industry as new technologies evolved.

Later in my career, PDA became very important as I headed up the vaccine interest group. We used to have breakfast meetings before we had interest groups at round tables, and I started heading up some of those discussions. Later on, I ended up as the Chair for the Vaccines Interest Group. I also began speaking more at various meetings within PDA.

Frank Kohn, PhD, will be awarded his 40 year membership pin at the 2011 Annual Meeting in San Antonio, Texas

In the later part of my career as a consultant, I've been doing more teaching as well as continuing with the vaccine interest group.

PDA: So you pretty much volunteered for every position possible at PDA?

Frank: I've been on the planning committee meetings at different times. Also, I participated at the first PDA/FDA meeting in Washington on the seminar, "Team Biological Inspections," several years ago. I've also participated in other interest group meetings and as an instructor at the TRI for PDA.

PDA: You're the president of your own consulting company. How long have you been a consultant?

Frank: Eight years.

PDA: Is belonging to an Association like PDA important as a consultant? How does it help your business?

Frank: It constantly exposes you to people, so it has given me an opportunity to be able to talk to clients and to meet with friends at various meetings. Sometimes, I use a meeting as an opportunity to either meet with client or reestablish a relationship with a past client.

PDA: What have you learned during your career that you apply to your TRI courses?

Frank: I've been teaching classes on various topics related to microbiology, quality

and manufacturing. I believe that you get a lot of different views from both participating and teaching classes. As a consultant, you get the opportunity to see your clients' problems and issues from a very practical scientific quality standard. By using these experiences, I've been able to integrate this practical experience and my discussions with people into my classes, case studies.

PDA: Do you learn from your students?

Frank: Yes, working with students you learn as much information as you give. You learn an equal amount from their review. I often like my students to bring their problems to the class discussion, and I encourage them to do that. By them doing that, that gives them a chance to say 'I have the same problem' or 'We had the same problem and this is how we solved it.' This sometimes gives me a new view to solve the problem or different way to solve a regulatory problem or offer a clarification. You take away an awful lot from working with students. For several years, I've been interested in teaching because I feel it is a responsibility of a professional person who has had a lot of opportunities to work with a number of people who have served as mentors to me. I always feel it is very important to give back to that mentoring and support in the industry, and I've felt that way for the last 15 or 20 years. I see that as a way of giving back to your profession.

Later in my career, PDA became very important as I headed up the vaccine interest group

PDA: What are your plans for the next forty years with PDA?

Frank: Attending every meeting for the next forty years.

PDA: The PDA would like to present you with a special forty year member pin, and we appreciate your loyalty to PDA.

Is there anything else you want to say about PDA? Are you happy you are a 40 year member?

Frank: I have mixed emotions. PDA has really offered me a huge opportunity to expand some of my skills and an opportunity to stay current in the industry and to be involved and watch new technologies actually evolve into actual practical things.

About the Member

Frank Kohn, PhD, is the President of FSK Associates, an international consulting company providing services to the pharmaceutical, biotechnology, and vaccine industry. He has more than thirty years of industry experience working for Schering Plough, Armour Pharmaceutical, Sanofi and Wyeth Vaccines. Frank is the chair of the PDA Vaccine Interest Groups and teaches several courses for TRI.

Volunteer

Berit Reinmüller, PhD, Senior Researcher, KTH Royal Institute of Technology

PDA Join Date: 1992

Areas of PDA Volunteerism: I attended my first PDA course in 1989 in Frankfurt, Germany with Fred Carlton as one of the teachers, and later PDA courses in the United States. Since 1992, I've been a PDA member and have worked in cooperation between R³-Nordic and PDA and have arranged three joint PDA/R³-Nordic conferences in Stockholm. In addition, I have participated in program committees and arranged around 30 PDA courses in Stockholm. I've participated as a speaker and teacher at several PDA conferences and at PDA courses in Europe, the United States and Japan.

Interesting Fact about You: With more than 30 years in the pharmaceutical manufacturing field and having specialized in the areas of contamination control, environmental monitoring and microbiological risk assessment, I enjoy challenges and am interested in the development of new technology. In cooperation with Bengt Ljungqvist, I published my first paper in the *PDA Journal of Pharmaceutical Science and Technology* in 1991. Over the years there have been several joint papers.

I try to look at risk assessment and microbiological monitoring in a scientific way. For example, microorganisms in the air are and behave like particles; small particles follow the air movements and large particles settle. It is very satisfying to teach that there is nothing magic in the methods used to monitor and do risk assessments. I'm also active in the international standardization work on clean rooms. When I'm not working, I like to spend time with family and friends, travel and enjoy life.

Why did you join PDA and start to volunteer? R³-Nordic needed international contacts for the benefit of their members, and PDA represented the biopharma and pharma industries in the United States. During Ed Fry's leadership, PDA became a strong presence to the world. To participate in the cooperation between PDA and R³-Nordic has over the years has been very rewarding. I'm one of the two R³-Nordic international liaisons with PDA, the Pharmaceutical and Healthcare Sciences Society (PHSS), A_3P, and the International Confederation of Contamination Control Societies (ICCCS).

Of your PDA volunteer experiences, which stand out the most? To attend the first European PDA International Conference in Basel in 1992 as a speaker was exceptional. Attending my first PDA Annual Meeting in the United States in 1992 was a great event to go to. The success of the joint PDA/FDA/R³-Nordic conference in Stockholm in June 1996 was the reward of a lot of hard work. The Annual Meetings in Anaheim 2006 and in Colorado Springs 2008 are very special to me, since I was appointed "Outstanding PDA Scientist" at the former and was awarded "PDA Honorary Membership" at the latter.

How has volunteering through PDA benefited you professionally? PDA has always been well connected with the U.S. FDA, and my contacts to FDA have been through PDA. To meet and establish contact with very knowledgeable people from the industry and from authorities have been very useful in my work. I also appreciate all friends that I have met through PDA.

Which PDA event/training course is your favorite? The PDA training courses held in Stockholm with attendees from the whole of Europe and teachers such as James Akers, Anne Marie Dixon, Ted Meltzer, and Irving Pflug, to mention only a few of outstanding teachers who have come to Stockholm to teach for PDA over the years. Courses with teachers that have both knowledge of theories and huge experience of practical applications are truly appreciated.

What would you say to somebody considering PDA membership? If you have an interest to stay updated in pharmaceutical and biotech industry and follow the development in regulatory areas and in scientific based practice only one answer is possible, *Join!*

Dinner with a Dash of Mycoplasma & a Day of Process Val at Lilly, continued from page 9

science as opposed to set standards.

The process validation guidance will have a monumental impact on how validation is done in the future. To learn more about the intricacies of the guidance, plan to attend the workshop that will be held after the Annual Meeting in San Antonio, Texas. Visit www.pda.org/annual2011 for more information.

I would like to thank both chapters for their hospitality.

PDA Who's Who

Jeff Boatman, Senior Subject Matter Expert, Medical Devices and Quality Systems, QPharma

Janet Bowen, Director, Quality Systems/ Compliance Services, Commission Agents

Allen Burgenson, Manager, Regulatory Affairs, Lonza and PDA Capital Area Chapter President

Kelly Davis, Associate Director, Regulatory Affairs, Baxter Healthcare

Steven Ensign, Assoc. Senior Consultant Engineer, Eli Lilly

Barry Friedman, PhD, Consultant and PDA Capital Area Chapter Treasurer

Scott Hartman, Manager of Engineering and Quality, Genesis Plastics Welding and PDA Midwest Chapter Member-at-large

Peter Noverini, Field Applications Scientist, Applications and PDA Midwest Chapter President

Susanne Resatz, Vetter Development Service, Vetter Pharma Fertigung

Christine Wright, PhD, Research Scientist, EMD Millipore

2009 Honor Awards Recipients

www.pda.org/2009honorawards

The PDA Honor Awards are bestowed on members who provide exceptional leadership and service to the Association, and have been awarded at the Annual Meeting since 1958. The 2009 award winners were announced at the 2010 meeting last March, and the *PDA Letter* has highlighted winners in each issue since.

Gordon Personeus Award

Presented in memory of the late Gordon Personeus, past PDA President and long-time volunteer, this award is intended to honor a PDA member for his or her long-term acts or contributions that are of noteworthy or special importance to PDA.

Sue Schniepp

Sue Schniepp is the Vice President of Quality at OSO BioPharmaceuticals. Sue joined PDA in 2000. She has presented at a number of PDA Meetings and participated on a number of Committees including co-charing the *2010 PDA/FDA Joint Regulatory Conference* Steering Committee, RAQC, Program Advisory Board, Technical Books Advisory Board, and The Membership Committee. In 2007, she was the recipient of PDA's Distinguished Author Award for the book, titled, *Understanding the United States Pharmacopeia and the National Formulary: Demystifying the Standards-Setting Process*. In 2008, Sue won PDA's Distinguished Service Award.

PDA President Award

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

Feng Chen

Feng Chen is the Senior Information Systems Manager for PDA. Feng joined PDA in July 2002 as an Information System Engineer and was promoted as Senior Information System Manager in June, 2008. He has always worked independently with much enthusiasm and initiatives to ensure all information systems and technology needs are being met in a timely, cost effective manner.

Antje Petzholdt

Antje Petzholdt is the Office Manager for the PDA Europe office. She has been with PDA since November 2006 at our office in Berlin. At the beginning she was involved in all activities running meetings, helping with members and chapters. Among her duties are: registration (a very complicated matter because of no on-line registration); contact with members and chapters; and handling of all initial contact to PDA Europe. Last year, she was very strongly involved in registration and spent a lot of weekends in the office. She even took care of registrations during her holidays. She always made sure that all request were answered ASAP.

Please Welcome the Following Industry

Kerstin Adolph, Synthes

Eda Akel, Sandoz

Yossi Aldar, SteadyMed

Stephen Allan, Unilife

Odete Almeida dos Santos, GlaxoSmithKline

Joe Ault, Merck

Steven Bane, Merck

Julie Barbieux, GlaxoSmithKline

Stefan Bartlewski, Bayer Schering Pharma

David Bastock, Sensitech

Corey Batsakis

Shirley Batt, GE Healthcare

Edgar Bauer, Bausch + Stroebel Maschinenfabrik

Mark Baxter, Watson Pharmaceutical

Willard Beckmann, Shire

Charlotte Bell, Newcastle University

Jeff Bennett, Sterigenics

Fabrice Berthaud, GlaxoSmithKline

Fabrice Berthelot, West Pharmaceutical Services

Riccardo Bini, Zambon Group

Jeri Ann Boose, Lancaster Laboratories

Arnol Borgers, Abbott Biologicals

Octaaf Bos, Progress PM&E

Marie Brassier, LEO Pharma

Patrick Bregy, CSL Behring

Mark Broadley, Biomet

Christian Brouillard, Sanofi-Aventis R&D

Elaine Brown, Lantheus Medical Imaging

Julie Browne, Allergan Pharmaceuticals

Martin Browne, GE Healthcare

Jason Buckingham, APP Pharmaceuticals

Katrin Buerkner, IDT Biologika

Jim Bufano, PCI

Coleen Burke, Merck

Bartosz Byczynski, Centre for Probe Development and Commercialization

Elaine Campbell, CompuPharma

Harry Carey, Biogen Idec

Laurie Case, QA Projects

Stuart Chambers, GE Healthcare

Audrey Chang, BioReliance

Nithin Choudhary, Biocon

Brendan Clancy, Genzyme

Kenneth Clarke, Allergan

Ivan Coemans, Helvoet Pharma

Frederika Coene, Pfizer

Sue Cooke, NIBRT Bioprocessing Research Inst.

Terry Corzine, Amgen

Davide Costella, Biogen Idec International

Kimberly Courtney, GE Healthcare

Joelle Crouch, Armed Forces Research Institute of Medical Sciences

Brian Cullinan, MSD

Sophia Czechowicz, Johnson and Johnson

Marc Dabckaussen, Simac Masic & TSS

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Shelly Diaz, Banner Pharmacaps

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Leaders to the PDA Community

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Michael Marino, Boston Scientific

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Carlo Martufi, Merck Serono

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Piovan Mauro, Fidia Farmaceutici

Paul McCabe, Pfizer

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Fran Meacle, Centocor

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Eugene Mehr, Biogen Idec

Ronald Meijer, Sanquin Plasma Products

Line Lykke Meilstrup, Novo Nordisk

Robert Menges, Merck

Stefan Merkle, Cilag

James Metzger, Emergent BioSolutions

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Andrea Mieskes, F.Hoffmann-La Roche

Maryse Migeon, Merck Sharp & Dohme

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Yves Moinard, Eli Lilly

Birgit Molander, Sanofi-Aventis

Angela Molaschi, Actavis

Serena Mori, Haupt Pharma

Masunmi Morimoto, CM Plus Corporation

Michael Moritz, W L Gore

Edward Moro, Dendreon Corporation

Please Welcome the Following Industry Leaders to the PDA Community

PTM Mossi-Brugmans, Sanquin Plasma Products

Mubarack Muthalif, BioMarin Pharmaceutical

Kellie Nadeau, Shire

Tobias Nemeth, Schott

Holger Neumann, Neumann + Hoffmann

Katarina Nilsson, Polypeptide Laboratories

Jennifer Nugent, AstraZeneca

Marcia O`Connor, West Pharmaceutical Services

Sinead O´Byrne, Pfizer

Kevin O´Hanlon, GlaxoSmithKline

Terry O´Rourke, Gelead Sciences

Miriam O´Sullivan, Pfizer

Hilary O´Sullivan, Genzyme

Andrew OBrien, Merrimack Pharmaceuticals

Niclas Ohlsson, TSS

Matthew Osburn, Commissioning Agents

Bernhard Ott, Fresenius Kabi

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Scott Overton, Merck

Israel Oyebade, Pfizer

Pamela Padgett, SurModics Pharmaceuticals

Kristin Paelinck, BD

Cristina Panizza, Zambon Group

Marco Panzino, Groninger

Jungmin Park, Celltrion

Deborah Pascoe, Genentech, Inc.

Valentina Pastanella, GlaxoSmithKline

Doli Patel, BioReliance

Fabio Paula, Merial Saude Animal

Anette Pauli-Bruns, Sanofi-Aventis

Miroslav Pavlov, Sopharma

Pierre Peignault, Septodont

Stefano Pelaia, Patheon

Emilie Pelletier, Laporte Consultants

Gary Perkins, Sigma-Aldrich

Frederic Perrier, GlaxoSmithKline

Nils Petzholdt, GlaxoSmithKline

Henning Pfeifer, Abbott

Vinh Pham, Teva

Fabienne Philippe, Sanofi Pasteur

Birgitte Philipsen, Leo Pharma

Constance Phillips, Boston University

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Alexander Plematl, Sandoz

Olivier Pourcel, BD

Bart Pouwels, Amsterdam Airport Schiphol Cargo

Sougata Pramanick, Emcure Pharmaceutical

Birgit Prause, CSL Behring

Linda Proctor, Blue Water Technical Services

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Nava Rabin, BiolineRX

Fabio Raguzzi, GlaxoSmithKline

Sinead Rainville, AstraZeneca

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Christophe Reynders, GlaxoSmithKline

Bryce Rich, Meridial Life Science

Mark Rienstra, West Pharmaceutical Services

Matthew Roberts, Pfizer

John Rocco, The Mundy Companies

Ralf Roepenack, NNE Pharmaplan

Marc Roveri, Cargolux Airlines International

Balaka Roy, Amgen

Colin Rush, Sanofi-Aventis

Erik Rydstrom, Sanofi Pasteur

Dan Sacunas, Particle Measuring Systems

Rishi Saini, Biotec Services International

Damien Saleur, Stelmi

Anna Laura Salvati, 1 St. Superiore Sanita

Alena Sandru, Genentech

Aline Santoro, BD

Michelle Satchell, Pfizer

Nancy Schaffner, MSD

Neta Scheinman, Enzymotec

Patricia Schimke, GTC

Arjen Schippers, Biogen Idec

Erik Schmidt, GE Energy – Sensing & Inspection

Christine Schneider, CSL Behring

Thomas Scholzen, F. Hoffmann - La Roche

Andreas Schwarz

Martin Sedlock, LSNE

Katherine Seifert, Seifert and Associates

Roger Seiler

Robert Sever, Praxair

Rob Severijnse, Progress PM&E BV

Tilman Seytter, Roche Diagnostics

Kamlesh Sheth, Amicus

Rajesh Shukla, Meridian Medical

John Silverthorn, Centocor

Andrea Simonetti, Bonfiglioli Engieering

Denise Simpson, Genzyme

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Fredrik Sjodin, Envirotainer

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Jan Slock, Pfizer

Mark Small, Retractable Technologies

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Bridget Smith, Steris

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Ruediger Sprengard, Schott

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Karen Storm, Sartorius Stedim

Timothy Stough, ProPharma Group

Helen Stuart, Sanquin Plasma Products

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Mariusz Suchodolski, Vetter Pharma-Fertigung

James Sudnik, Sanofi Pasteur

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Irina Svarinska, State Agency of Medicines

Shigehiro Tahara, CM Plus Corporation

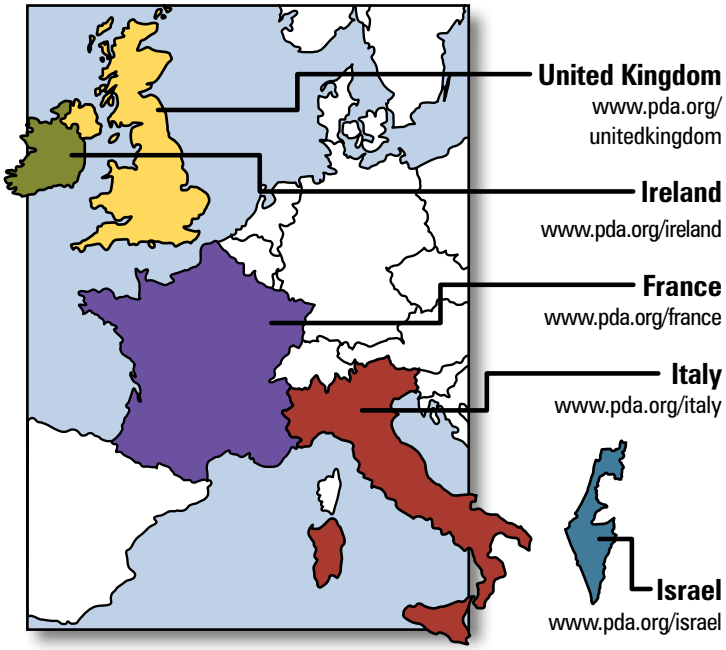
Attila Takacs, Taikisha

Andrea Tasior, Emergent BioSolutions

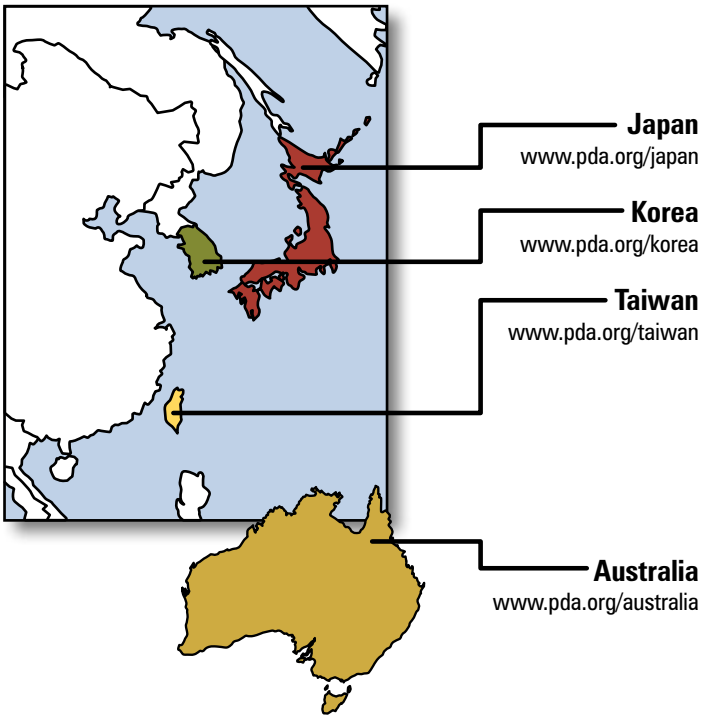
Chapter Contacts

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

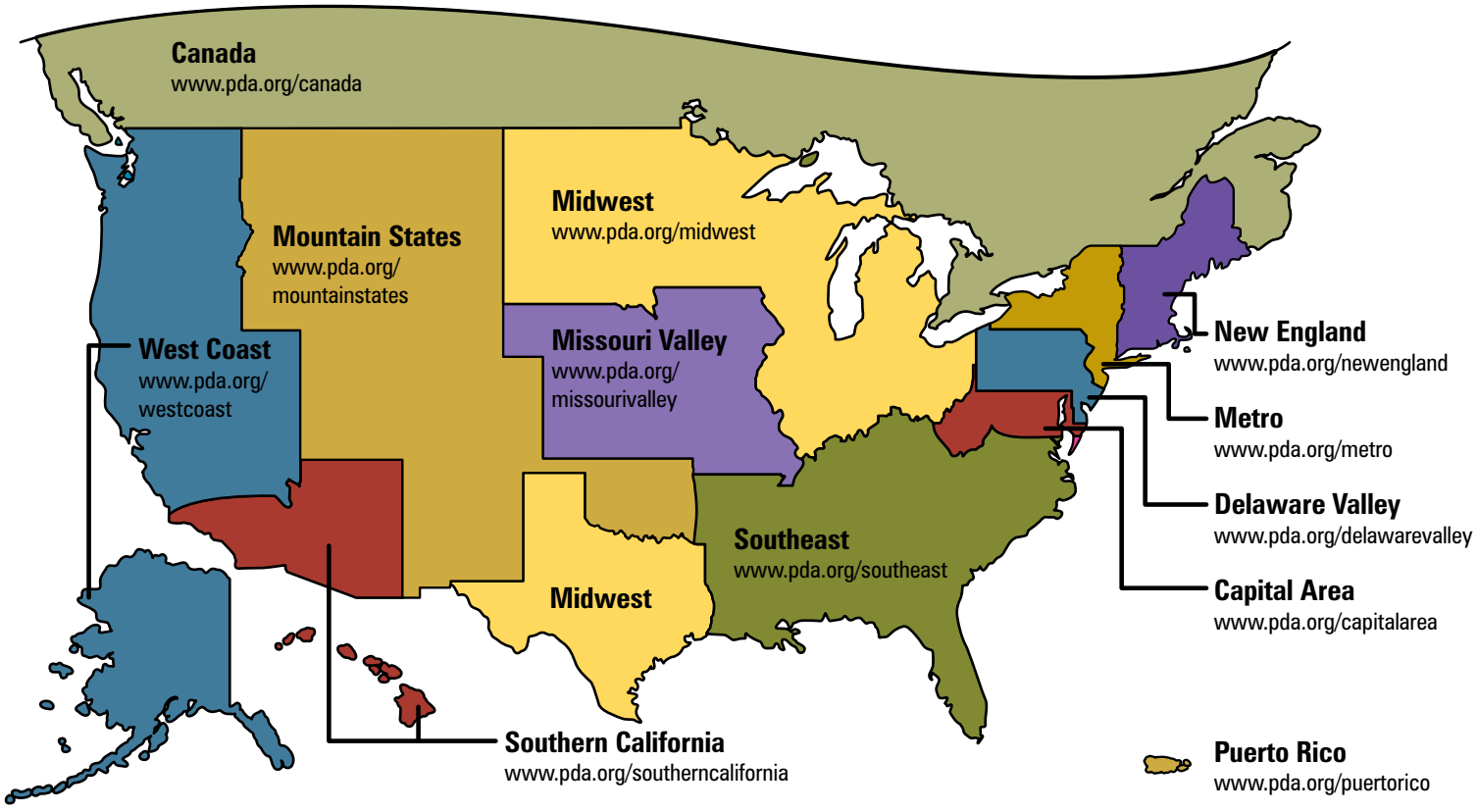
EUROPE



ASIA-PACIFIC



NORTH AMERICA



Faces and Places: Microbiology Conference 2010

Monday: Keynote Address

(l-r) Edward Balkovic, Genzyme; Lynne Ensor, U.S. FDA; C. Mark Ott, NASA

Tuesday: Keynote Address

(l-r) Edward Balkovic, Genzyme; Thomas Arista, U.S. FDA

Urban Myths

(l-r top) Edward Balkovic, Genzyme; Rich Levy, PDA

(l-r bottom) Barbara Potts, Biologics Consulting Group; Art Vellutato Jr., Veltek Associates

USP, EP, JP Global Compendial RMM Perspectives

(l-r) Radhakrishna Tirumalai, USP; James Akers, Akers, Kennedy & Associates; Hans van Doorne, University of Groningen; Tsuguo Sasaki, PMDA

Compendial Challenges with RMM

(l-r) Radhakrishna Tirumalai, USP; Scott Sutton, Microbiology Network; James Akers, Akers, Kennedy & Associates; Anthony Cundell, Merck

Ask The Experts Panel Discussion

(l-r) Scott Sutton, Microbiology Network; James Akers, Akers, Kennedy & Associates; Hans van Doorne, University of Groningen; Tsuguo Sasaki, PMDA ; Thomas Arista, U.S. FDA; Vivienne Christ, Therapeutic Goods Administration; Patricia Hughes, U.S. FDA; Dennis Guilfoyle, U.S. FDA

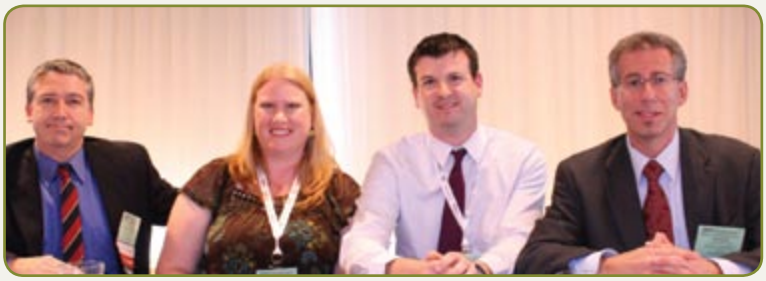
Summary of Compendial RMM Sessions – Lessons Learned

(l-r) Edward Balkovic, Genzyme; Lynne Ensor, U.S. FDA

Advancing the Practice of Moist Heat Sterilization

(l-r) William Fleming, MedImmune; Angela Coon, Baxter Healthcare; Kenneth Paddock, Baxter Healthcare; Eric Ward, Pfizer

New Technologies 2



(l-r) Edward Tidswell, Baxter Healthcare; Sara Polson, Accugenix; Kevin Luongo, Pfizer; Michael Miller, Microbiology Consultants

Objectionable Microorganisms in Non-Sterile Pharmaceutical Drug Products

(l-r) Vivienne Christ, Therapeutic Goods Administration; Renee Blosser, U.S. FDA; Anthony Cundell, Merck; David Hussong, U.S. FDA

New Technologies 1

(l-r) Amelia Tait-Kamradt, Pfizer; Michael Miller, Microbiology Consultants; Geert Verdonk, Merck Sharp & Dohme

Manufacturing and Product Attributes Impacting Sterility Assurance

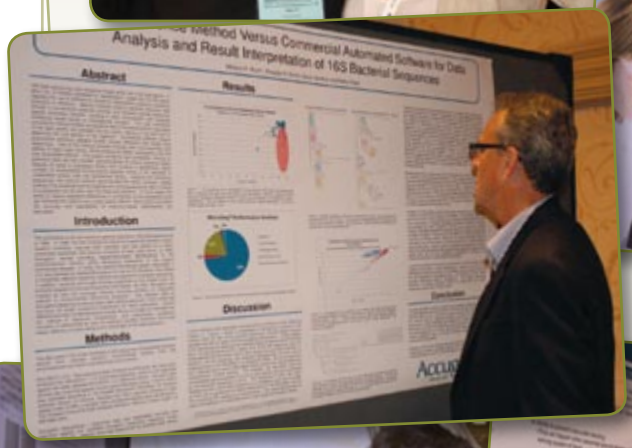
(l-r) Neal Sweeney, U.S. FDA; Dennis Guilfoyle, U.S. FDA; Lynne Ensor, U.S. FDA; Edward Tidswell, Baxter Healthcare

USP Compendial Luncheon

(l-r) Radhakrishna Tirumalai, USP; Anwar Huq, University of Maryland

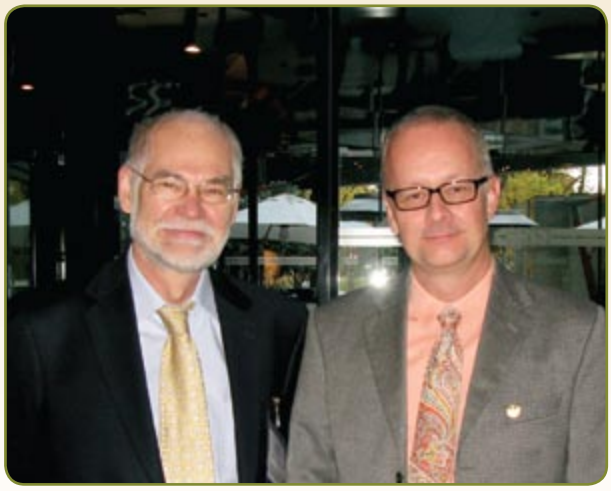
Faces and Places: Microbiology Conference 2010

Exhibitors Hall/ Poster Exhibit



Book Signing

Faces and Places: European Parenterals Meeting



(l-r) Georg Roessling, PDA; Tor Gråberg, Medical Products Agency

(l-r) Hal Baseman, ValSource; Michael Sadowski, Baxter Healthcare; Klaus Haberer, CASIM

(l-r) Mads Reedtz Espersen, Novo Nordisk; Bernd Renger, Vetter Pharma-Fertigung; Ingo Presser, Boehringer-Ingelheim; John Shabushnig, Pfizer

(l-r) Friedrich Haefele, Boehringer-Ingelheim; Volker Eck, PDA

(l-r) Volker Eck, PDA; Maik Jornitz, Sartorius Stedim

Georg Roessling talks to attendees during a session break

snapshot

Task Force *Corner*

Volunteers Needed for 9 Task Forces

*Contact **Iris Rice**, rice@pda.org for more information on these or other volunteer opportunities.*

Post Aseptic Fill Lethal Treatments

Led by **Kris Evans**, Director, Global Quality Compliance, Amgen, and **James Agalloco**, President, Agalloco & Associates, the mission of this task force is to develop a PDA position/technical bulletin on post-aseptic fill lethal treatments that will encourage its increased adoption. The completed document is expected to briefly address the advantages to patient safety and operating practices derived from lethal processes applied to aseptic filling and moist heat and radiation processes.

Investigational Medicinal Products (IMP) Manufacturing and Distribution (PCMO L01)

This task force, led by **Stephan Krause**, Principal Scientist, MedImmune, provides practical guidance on how ICH Q9 and ICH Q10 can be adapted to the IMP environment including the distribution of Clinical Trial Material (CTM).

Implementation of Quality by Design in Manufacturing (PCMO L02)

Interested in adopting the ICH Q8(R2) concept of Quality by Design in the manufacture of Clinical Trials material throughout the different development phases? This task force is for you. Led by **Ron Taticek**, Director, Genentech, special attention is given to the implementation of design space, control strategy etc. in the manufacturing process.

Knowledge Management (PCMO Q1)

This task force, led by **Christopher Smalley**, Associate Director, BioSterile Validation, Merck, is interested in how companies manage, use and retain knowledge. The Task Force will develop a solid foundation of and grasp of institutional historical knowledge that can be used to improve processes and products; an organization-wide understanding of key lessons learned which minimizes the repeat of costly mistakes; and improved compliance standards by enabling QbD and better product life cycle management.

Concept for Training of Employees (PCMO Q04)

Led by **Sue Schniepp**, Vice President, Quality, OSO BioPharmaceuticals, and **Karen Ginsbury**, CEO, PCI Pharmaceutical Consulting, this task force uses a modern, effective quality system approach to training and qualification of personnel at all levels within an organization. This task force uses a "drill down" approach based on the Deming/Juran model used in Japan in 1950's–60's.

Corrective and Preventive Actions (CAPA) (PCMO P05)

A practical model for the pharmaceutical manufacturing environment will be developed in this task force led by **Don Elinski**, Sr. Associate, Lachman Consultants, and **Shamik Pandit**, President, GMP Scientific. It covers a step-by-step identification of root causes and the concepts to be applied for preventive citations.

Risk-based Manufacturing (PCMO R01)

This task force provide guidance for application and implementation of Quality Risk Management principles for various types of manufacturing operations and define how to integrate Quality Risk Management into the Quality System and routine manufacturing operations. The leaders for this task force, **Emabelle Ramnarine**, Sr. Manager, Corporate Quality, Genentech, and **Véronique Davoust**, Manager, Global Quality Strategy, Global Quality Operations, Pfizer will use PDA's existing Technical Report No. 44 as the basis for this topic by using case studies for different techniques implemented in:

- Biotech manufactured APIs
- Sterile APIs
- Drug products (liquids and solids)
- Packaging and Labeling

Sterile Manufacturing (proposed task force)

This proposed task force, led by **Ed Tidswell**, Sr. Director, Sterility Assurance, Baxter Healthcare, has been asked to produce a gap analysis and identify salient EU and US guidance/regulations on terminal sterilization and aseptic manufacture, including PI 032 -1, *Technical Interpretations of Revised Annex 1 to PIC/S GMP Guide* and, *GMP Annex I, Interpretation of Most Important Changes for the Manufacture of Sterile Medicinal Products*. The task force will also produce an alternative gap analysis between PIC/S interpretation document PI 032 and Annex 1; and propose recommendations to reconcile differences found in the gap analyses.

Technical Report No. 32: Auditing Computer System Suppliers

Peter Miller, Senior Partner, Dynamic Compliance Solutions is leading this task force to participate in the update and revision of this essential industry standard. The Task Force will integrate updated theories and approaches based on the latest published documents from recognized industry groups; explore the viability of incorporating or separating the distribution of audit results and focus on the audit criteria and secondarily focus on the approach.

The Task Force is interested in working with Subject Matter Expert members, members who represent other industry groups with similar goals toward auditing, and other industry groups, where appropriate, to integrate the accepted approaches and published expectations.

Technology *Trend*

Green Chemistry: Paradigm or Profit

***Dave March**, Process Capital Productivity Specialist, Rockwell Automation, was a participant and speaker at this year's,* Third Annual Symposium on Green Processing in Pharmaceutical and Fine Chemical Industries.

Dave provides his thoughts, comments and review of this year's proceedings.

It is probably appropriate, though certainly not entertaining, to begin this article with a disclaimer. This article is a collection, probably disorganized, discordant and irreverent, of my thoughts regarding this year's *Third Annual International Symposium on Green Processing in the Pharmaceutical and Fine Chemical Industries* held between Sept. 30 and Oct. 1 at the University of Massachusetts in Boston. So for the disclaimer: "My memories, comments and opinions are entirely my own and do not represent those of my employer; Rockwell Automation."

The world is awash in Green and Sustainability hyperbola, with many of the most vocal pundits knowing very little about the science or more importantly, have any clue regarding practical solutions. We can't turn the clock back nor do we as a society possess the will and determination to reduce our standard of living to avoid ecological disaster. Remember the old saying "Better Living Through Chemistry?" Well, chemistry got us to today, and it's going to be chemistry that saves us and our planet tomorrow. Now if you want to meet the chemists that are going to save us, they attend this symposium. So it was my honor and privilege to attend and speak at this event.

The event is a convocation of Ph'D chemists primarily from the pharmaceutical industry. So as a somewhat lay person, I was concerned I would be very much out-of-place in such an august body. But the passion and camaraderie the participants share for their science and the planet is so infectious that it is virtually impossible not to be included in the family. It is that sense of community and the networking opportunities that it engenders, which in my opinion, is the most valuable aspect of the symposium. The presentations are appetizers that help identify people and research, but it's during the informal social gatherings that much of the science gets discussed and probably created. Presentations and research findings are not facts that punctuate an end, but ideas and momentum that foster inquiry and the question I heard countless times; "What about…?"

The symposium is highly technical with presentations from a wide range of interests, but taking a more abstract, or 30,000 foot view of the symposium, there were 4 main themes:

1. Catalysts
2. Reactors
3. Business
4. Paradigm and Profit

Catalysts were certainly the technology poster child of the event. Remarkable improvements in yield, efficiency, "greenness"

continued on page 24

Journal *Preview*

U.S. FDA Reps Author Two Articles in Jan/Feb Issue

PDA always welcomes opinions of industry professional of all stripes, including our colleagues in the regulatory bodies. In the January/February edition, the Journal's Associate Editor and U.S. FDA CBER official **Kurt Brorson** discusses the role of public standards for biotech products in the issue's editorial. Also contributing from the U.S. FDA are **Anastasia Lolas** and **John Metcalfe** in their "Technology/Application" manuscript that links QbD to microbial growth potential of drug products.

The issue also offers a number of industry voices with six research manuscripts on various areas relevant to manufacturers, including the use of headspace moisture analysis for studying water dynamics in a sealed vial and the assessment of similarity in bioanalytical methods. Tying in nicely with the Editorial is a "Technology/Application" article on ASTM/ASTME-BPE standards. A third technology article looks at methods for assessing in vivo precipitation of injectable drugs.

Editorial

Kurt Brorson, "Future of Consensus Standards in Biotechnology"

Research

Isobel Ann Cook and Kevin Richard Ward "Applications of headspace moisture analysis for investigating the water dynamics within a sealed vial containing freeze dried material"

Amelia M. Avachat, et al., "Formulation and Characterization of Expandable Gastroretentive System of Carvedilol Phosphate by 32 Factorial Design"

Mahesh Dabhi, et al., "Formulation Development of Ambroxol Hydrochloride Soft Gel with Application of Statistical Experimental Design and Response Surface Methodology"

Anil K. Philip and Betty Philip, "In-Situ Phase Transited Asymmetric Membrane Capsule: A Means for Achieving Delayed and Osmotic Release for pH Solubility Dependant Drugs"

By Jennifer C. Gray, et al., "Identification of micro-organisms after Milliflex Rapid detection – a possibility to identify non sterile findings in the Milliflex Rapid sterility test"

Jason J.Z. Liao, et al., "Assessing Similarity in Bioanalytical Methods"

Technology/Application

Agam Sheth, "In vitro screening methods to assess the potential of in vivo precipitation of injectable formulations upon intravenous administration"

Anastasia G. Lolas and John W. Metcalfe, "Evaluation of the microbial growth potential of pharmaceutical drug products and Quality by Design"

William M. (Bill) Huitt, "ASTM and ASME-BPE Standards – Complying with the Needs of the Pharmaceutical Industry"

To access the Journal, go to http://journal.pda.org

Green Chemistry: Paradigm or Profit, continued from page 23

and e-factors were all attributed to these amphetamines of synthesis. New catalysts ranged from complex molecular biocatalysts to conceptually simple but rare atomic metals. While I found all of the catalyst discussions fascinating, my favorite was "Custom Evolved Biocatalysts" by **Gjalt Huisman**, PhD, Vice President, Project Development and Management, Codexis. The concept of evolving enzymes to facilitate unique chemistries could have revolutionary implications. Today, I find the chemistry world divided into two camps: the organic synthesis crowd and the biomolecular fraternity; each having their own codex of creation. Custom evolved catalysts may become the bridge between the two domains, creating a new hybrid synthesis model where the combined tool sets allow us to economically build new compounds which prior we could only conceive. It is at events such as this, that these new horizons are envisaged.

Reactors, at least traditional batch reactors, are dinosaurs that should be gently, or not, guided towards the dustbin of extinction. A number of papers discussed the virtues of micro-reactor technology. These talks ranged from real time Process Analytical Technology applying in-process microscopy and ATR-FTIR, presented by Mettler Toledo to a very detailed evaluation of the applications and market potential of micro-reactors by Newry Corporation, a management consulting firm. My personal favorite was "Greening Up the Grignard Reaction" by **Michael Kopach**, PhD, Principal Research Scientist, Eli Lilly. All of us in the pharmaceutical industry share a love-hate relationship with the Grignard Reaction, and Kopach took this synthesis mainstay to an entirely new level with a continuous stirred reactor process. The economics of micro and continuous reactors in pharmaceutical manufacturing, combined with their improved flexibility and capital investment make this an area of considerable interest. I believe that adoption of these technologies will have a profound effect on pharmaceutical manufacturing efficiency in the future.

Business is at the heart of all Green Chemistry. Every participant is easily capable of reciting the 12 Principals of Green Chemistry. However, missing from this doctrine is the all too present; "it must make economic sense." This is a very practical law indeed. It certainly does not help the sustainability of our industry or our planet, if green measures are not adopted because they are not "economically superior" to their less green brethren. **John Warner**, PhD, President and Chief Technology Officer, Warner Babcock Institute for Green Chemistry, Keynote Speaker and one of the founding fathers of Green Chemistry and developer of the 12 Principals, continuously reinforced the economic necessity during his outstanding and inspiring address. While almost all presentations noted their economic benefit, some presentations were less abashedly economic and business oriented. These ranged from my own; "Optimizing Sustainability Through Model Predictive Control" to a number of talks on reducing solvent consumption through improved solvents, chromatography technology and selective separation with fluorous compounds from **Wei Zang**, PhD, Associate Professor, Department of Chemistry, UMASS. By this time, I had comfortably settled in and was feeling rather altruistic that we knew how to save the planet, my euphoric haze if not naivety was shattered by a controversial talk given by **Jeff Mitten**, Sales Manager, Synthetic Molecules, Novasep, entitled, "Hazardous Chemistry at Production Scale: The Green Chemistry Paradox," which shook the very foundation of what I knew about Green Chemistry, under-

The Twelve Principles Of Green Chemistry

1. It is better to prevent waste than to treat or clean up waste after it is formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary whenever possible and, innocuous when used.
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material feedstock should be renewable rather than depleting whenever technically and economically practical.
8. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11. Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.
12. Substances and the form of a substance used in a chemical process should chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Green is a relative or comparative view rather than an absolute.

scoring that there is much work still to be done and giving rise to the last of my four themes.

Mitten's presentation questions a number of assumptions regarding the subject of Green Chemistry. First, are the twelve principals of Green Chemistry, reprinted on the previous page. Should they be considered a guidebook or a rule book? At the heart of the dilemma is "What is Green?" Mitten provided a number of examples and case studies where a synthesis route that violated one or more of the principals results in less waste, less solvent usage, less negative environmental impact, lower energy consumption and improved economics. The question before the audience is: if these are not green by definition, are they not more sustainable? If the market is the final arbiter of what survives, and thereby defines what is sustainable, isn't there an inherent conflict between the Green Chemistry Principals and sustainability? Warner had repeatedly mentioned during his address that Green Chemistry must be economically superior to be successful. Unfortunately, the skeptic in me is not willing to accept a priori, that there will always be a superior economic solution that abides by all the principals, even if we had infinite rules. Green is a relative or comparative view rather than an absolute. I don't believe there will ever be an absolute anything if the final arbiter is the free market, but I do knows as did all those in attendance, that we can certainly do better.

The symposium is science at its best. Science by definition is conflict; a melting pot of ideas, data and differences of opinion. Green Chemistry is like any other scientific discipline; evolving, growing and solidifying. The 12 Principals of Green Chemistry may not be absolute rules that can be applied rote and blindly, but rather a wake-up call for all of us to more deeply consider what we do, how we do it and the implications of our actions. I look forward to next year and the *4th International Symposium on Green Processing in the Pharmaceutical and Fine Chemical Industries.* I believe that the subject is too important to be left to the chemists and strongly recommend that an additional track for business leaders and policy makers be added. Green Chemistry may well be the key to saving the planet. It is both paradigm and profit.

About the Author

David March has over 30 years experience in engineering, operations and sales in high-technology process markets. He currently focuses his efforts helping pharmaceutical and biotech companies improve operational efficiency as a Pharmaceutical Capital Productivity Specialist for Rockwell Automation.

Commentary: Can AQL be Zero?

Lynn Torbeck, Torbeck and Assoc. and Suzanne Seeley, Merck

Some companies have written SOP's for sampling that set the Acceptable Quality Limit (AQL) for a critical nonconformity as 0.0%. Can an AQL be zero?

In a word: No. It is not possible for an AQL value to be zero.

To understand why, let's start with the definition of AQL. The most often used reference is ANSI/ASQ Z1.4, *Sampling Procedures and Tables for Inspection by Attributes*. On page 2, we find the definition of the Acceptable Quality Limit: "The AQL is the quality level that is the worst tolerable process average when a continuing series of lots is submitted for acceptance sampling."

Note then the average would have to be zero. If the average is zero, then all of the results would have to be zero as well, because there are no negative nonconformities. If we believe that all the nonconformities are actually zero, we would have no need for a sampling plan.

But an AQL level or limit is a requirement of CGMPs, specifically CFR 210.3(20): "*Acceptance criteria* mean the product specifications and acceptance/rejection criteria such as acceptable quality level and unacceptable quality level, with an associated sampling plan that are necessary for making a decision to accept or reject a lot or batch."

Also in 21 CFR 211.165(d), we find: "The statistical quality control criteria shall include appropriate acceptance levels and/or appropriate rejection levels."

But most important, an AQL equal to 0.0% is not statistically possible. The AQL value is determined as soon as the sample size and the acceptance number are selected. This includes "accept on zero nonconformities." The values are available from the graphs and tables in Z1.4. **Table 1** shows the true AQL values for different sample sizes and the criteria of "accept on zero" and "reject on one nonconformity."

Typically, AQL is expressed as the percent of nonconformance's (e.g., 0.0163% is 0.000163 or 163 out of one million units) for which lot acceptance has a high probability, usually 95%.

It is important to separate the business philosophy and goal of zero nonconformities from a requirement of an AQL equal to 0.0%. To that end, classifications of Critical, Major and Minor nonconformities allow a distinction based on their potential risk and impact on patient safety. Setting an AQL specification for nonconformities requires a balance between the pharmaceutical company's goal of perfection for its outgoing products and the current production capability of manufacturing technology.

The above discussion for AQL values is for processes where nonconformance levels can be sampled and estimated statistically. However, it is not recommended to assign AQL equal to 0.0% to nonconformities not allowed under any circumstances for any sample size. A classification of "None Allowed" has been recommended by author **Suzanne Seeley**.

The classification "None Allowed" is for a nonconformance, error or mistake that is unacceptable at any level. These include, for example, incorrect components such as the wrong size, color, or type of materials. While these errors may or may not affect the whole lot, they do represent a significance deviation from the intended product. If these nonconformities are found at anytime, anywhere, the entire batch is immediately rejected without further sampling or inspection. It is recommended that the term "None Allowed" be defined and used in place of AQL equal to 0.0% for this application.

To summarize, AQLs cannot be zero but the concept of "None Allowed" will meet the objective of zero nonconformities for given categories of defects.

Reference

This is an edited version of section 3.2.3 Acceptable Quality Limits from PDA.

About the Author

Lynn Torbeck is a president of Torbeck and Associates, specializing in applied statistics and designed experiments for quality assurance, quality control, validation and manufacturing under the CGMP's. Lynn was elected to the USP Expert Committee for Statistics in 2001 and 2005 and is a coauthor of USP<1010>. Lynn welcomes comments on this article. Contact him at: Lynn@Torbeck.org.

Suzanne Seeley is a Process Engineer at Merck.

Table 1 Example AQLs by Sample Size

Letter Code	Sample Size	True AQL: Single Plan
J	80	0.0641
K	125	0.0410
L	200	0.0256
M	315	0.0163
N	500	0.0103
P	800	0.00641
Q	1250	0.0041

Have Your Say

Does your company's sampling plan include AQLs for a critical noncomformity at zero?

Does "None Allow" make sense to you?

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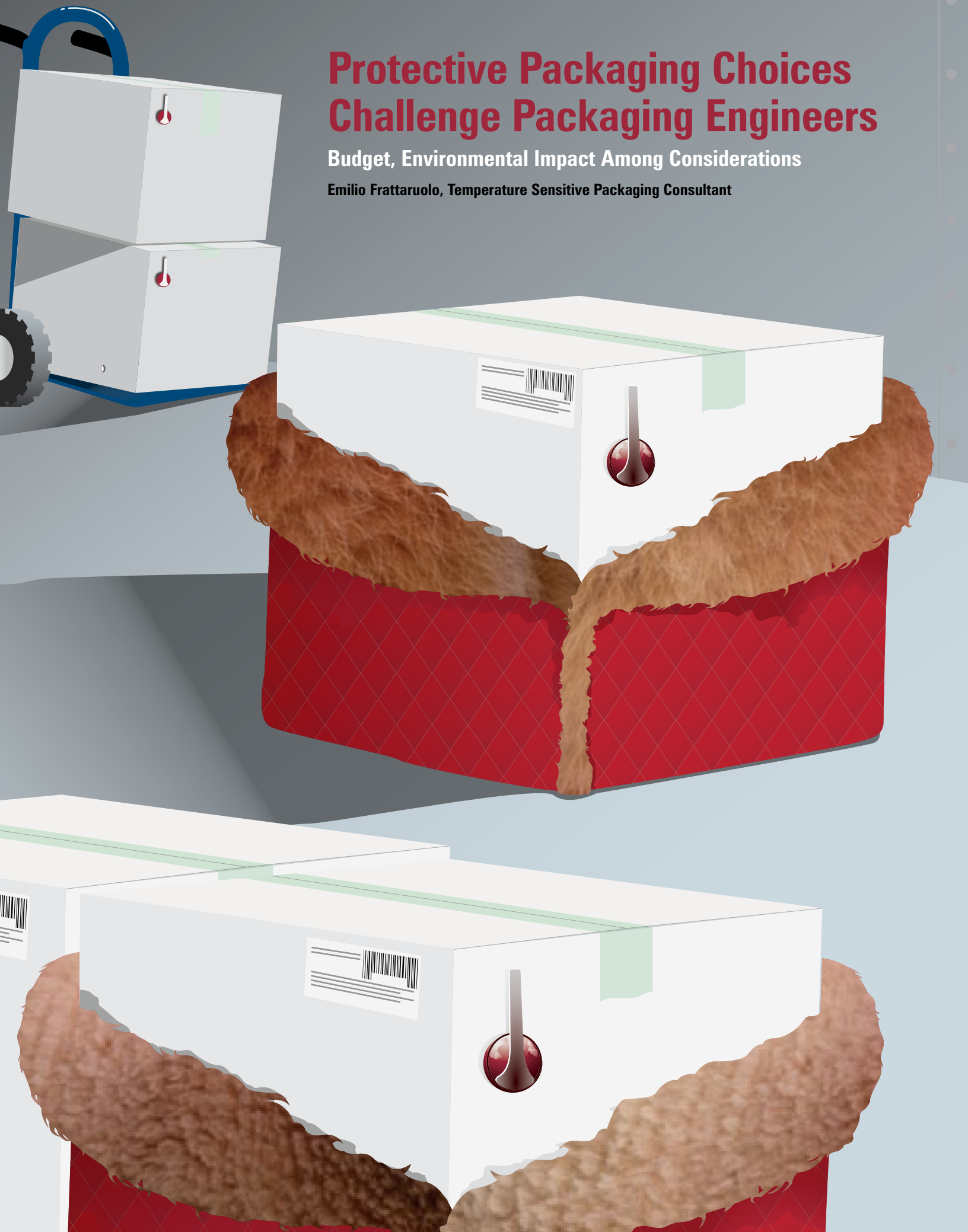
Protective Packaging Choices Challenge Packaging Engineers

Budget, Environmental Impact Among Considerations

Emilio Frattaruolo, Temperature Sensitive Packaging Consultant



As more and more companies release drug products requiring temperature management during distribution, the role of the distribution packaging engineer has become quite challenging. From controlled room temperature products to those requiring subzero conditions, there can be an intimidating amount of protective packaging solutions available. While the staggering amount of packaging solutions can be a blessing, it can also result in excessive amounts of waste, labor and costs. The challenge is compounded for those companies just now offering biological products or those who are now being scrutinized by regulatory bodies for controlled room temperature drug products that, in the past, were never shipped with thermally protective overpackaging.

From a developmental viewpoint, the key areas of concern with cold chain packaging are the temperature requirements of the drug product, temperature profiles, overall environmental impact and costs.

Temperature requirements are something that must be clearly defined prior to beginning the development of a cold chain shipping system. The engineer must understand the high and low temperature ranges and the allowable excursions. These allowable excursions are an important consideration, as some companies may choose to ship outside of label claim if there is enough stability data to support short duration excursions.

Another consideration is the temperature range of all products, including potential future temperature-sensitive drug products that may eventually ship to the same locations. The cold chain packaging engineer should take into account the full range of potential products, because it is advantageous to design a package that can be used for multiple products with similar temperature requirements and secondary carton sizes.

For example, if an engineer was presented with a liquid drug product with a temperature range of 2°C to 8°C and a lyophilized drug product with a range of -5°C to 10°C, the logical next steps would be to design the package around the drug product with the tighter temperature requirements. By doing this, the engineer would allow themselves to qualify one package for two products. Additionally the engineer could calculate minimum and maximum payloads using comingled payloads, which would allow not only for both products to ship utilizing the same cold chain shipper, but that shipper could also potentially handle comingled loads. From a packaging and logistical standpoint, this would be highly beneficial.

The next area of concern for the cold chain packaging engineer is the temperature profile utilized for the qualification of the package. When considering temperature-sensitive drug products, one must consider not only the final commercial packaged product, but also the Active Pharmaceutical Ingredient (API), bulk product presentations, and product bound for final package by either internal sites or external contract packaging sites. During each stage of the product lifecycle (i.e., formulation to final commercial packaging and distribution), the drug product may be exposed to a varying set of temperatures. It is vital that the engineer understand these exposures and utilize an accurate temperature profile when qualifying.

There are many options for a packaging engineer when it comes to temperature profiles. Depending on the groundwork already in place at the company and the urgency of the need, an engineer may choose to create a custom temperature profile based upon historical shipment data, use a profile supplied by their cold chain packaging vendor or reference the profile presented in section 7E of the ISTA handbook.

Balance Impact on Budget, Environment

Environmental impact and overall system costs are other challenging areas the cold chain packaging engineer must address. As the cost of fuel continues to rise, it is inevitable that the pharmaceutical industry will begin to move away from overnight air shipments of small parcels and pallet sized shipments whenever possible. This is where the more exotic methods of cold chain transportation come into play. While an Expanded Polystyrene (EPS) cold chain shipper with water-based gels is usually sufficient for overnight shipments, they are usually not suitable for deferred air or 2-3 day ground shipments, without getting excessively large and or heavy.

For these extended duration small parcel shipments, engineers must balance both the costs of transportation and the container itself. While a reusable Vacuum Insulated Panel (VIP) shipping container with custom phase-change materials may seem like the perfect solution for inter-company, closed loop shipments of API, small quantities and samples, an engineer would need to perform extensive business case and costs analysis before considering implementing a high cost container when shipping direct to customer, as the likelihood of a high return rate would be low.

Article in a Packing Peanut Shell

- Design a packaging solution that is flexible enough to work with all current and potential future products
- Balance packaging solution's benefits against costs
- Consolidate and reduce packaging components whenever possible

Forward planning and a solid understanding of the practices within the logistics, distribution and packaging groups can result in a mutual win for all groups

There are also times when an engineer may be asked to determine the best cold chain management system for larger quantities, such as pallet loads of products sent to third party distributors or even replenishment or launch quantity shipments to company distribution centers in other countries.

The types of solutions for these large shipments can vary from the very simple and ubiquitous passive EPS or Polyurethane (PUR) Pallet Shippers to very expensive leased active systems, which can be as small as a single pallet RKN* sized unit meant for air freight or as large as actively controlled sea containers. While the idea of an actively cooled and heated pallet shipping system may seem perfect for every situation, it would be foolish to ignore the fact that passive systems can be just as effective, if the engineer is able to confidently test and qualify the system against a temperature profile that accurately represents the temperatures and durations experienced by the product.

With the green movement gaining serious momentum, the packaging engineer is presented with both a challenge and an opportunity. The challenge is to create a low-cost, user-friendly, low environmental impact container; the opportunity is to streamline the cold chain packaging process, reduce system costs, and reduce end-user waste burdens. By carefully selecting an appropriate mode of transport, realistic temperature profile, and consolidating and reducing the number of components used, the engineer can meet some, if not all, of these goals.

Change Pack-Out Configurations to Extend Package Life

Going back to the example of having multiple packages for similar products, it is possible for an engineer not only to comingle products but to use the same container for shipments to multiple destinations and over multiple durations by changing the pack-out configurations. For example, an engineer may design a small, medium, large and extra large container meant to contain all of a company's cold chain products. By varying the gel pack configurations and preconditioning temperatures, as well as other aspects such as the payload box or placement of dividers and buffer pads, the engineer could utilize four containers for all products shipped during all seasons. The potential benefits of a system like this are a decrease in:

- The number of individual packaging components needed
- Individual system costs due to the ability to purchase more of the same containers
- Overall labor and training costs as the technicians packaging the products will not have to learn to pack as many containers

**RKN is the IATA code for an LD3 sized air cargo unit load device (ULD) that has refrigeration capabilities. More information can be found at www.boeing.com/commercial/startup/pdf/CargoPalletsContainers.pdf*

Forward planning and a solid understanding of the practices within the logistics, distribution and packaging groups can result in a mutual win for all groups.

While this process is never as cut and dry as this article may paint it to be, it is possible and has become much less stressful due to the ever growing number of specialty cold chain packaging suppliers and the ever growing awareness and guidance available from regulatory bodies and industry groups.

About the Author

Emilio Frattaruolo, CPP, is a Cold Chain packaging consultant based out of New York. As a Cold Chain subject matter expert he is continually identifying and exploring new and innovative cold chain solutions. Frattaruolo is an IoPP Certified Packaging Professional and is currently providing consulting services within the Pharmaceutical industry. If you have any questions for Emilio you may reach him at Emilio.Frattaruolo@gmail.com

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A Look into the Future of Parenteral Manufacturing: Part 1

Volker Eck, PhD, PDA

PDA held the *Parenterals 2010 Conference* in Berlin on Oct. 26–28, 2010. Approximately 250 delegates from 20 countries representing over 95 companies and 9 regulatory bodies attended The conference centered around the following topics:

- Future of parenterals
- Component quality
- Manufacturing flexibility
- Innovative plants
- Manufacturing control
- Application systems
- Regulatory trends

The program gave an overview on existing issues and potential solutions as well as future trends. As the participants expressed vivid interest in the topic, PDA has offered to organize a second edition in two years time.

While it is impossible to give a details of everything that was presented, the following review offers some highlights that might convey the spirit and value of the event.

[Editor's Note: Volker's report of the Parenterals 2010 Conference has been divided into two parts. This is the first part, and the remainder will be published in the February 2011 *PDA Letter*.**]**

Regulatory Trends

Daniel Müller, Regierungspräsidium Tübingen, Germany, and **Roland Guinet**, Sr. GMP Inspector, the French Agency for Security of Health Products, AFSSAPS, France, discussed regulatory trends for parenteral manufacturing and biologics.

Müller elaborated on the impact of Annex 1 of the EU GMP Guide and gave some hints for interpretation. He underlined the differentiation between classification and monitoring requirements, and addressed the closing/capping issue. Regarding the latter, there are two possibilities: capping in the aseptic area as an aseptic process or in a clean area outside the Grade A environment. There will be a survey published on industry practice, but, based on his personal experience, Müller believes there is a 40/60 divide between aseptic and clean processes employed.

He also discussed the use of ready-to-fill or ready-to-use components. He stressed that these comprise manufacturing operations like sterilization of components and, hence, are subject to GMP oversight. It is expected that the marketing authorization holder is aware of deviations and other changes at the component manufacturer's side, has regularly performed audits and has evaluated the validation procedures, practices and execution. On audits, he said, "Third party audits are acceptable only if equivalent and conducted with the same perspective of audit." He emphasized that risk-based approaches are an important tool and should be implemented with competence, adding that quality should be the "basis for decision processes and measures."

During inspections, Müller often encounters scarce attention to quality aspects like specifications, crucial testing criteria, and audits not appropriately addressing critical quality characteristics.

Guinet referred to the opening lecture by **Friedrich Haefele**, PhD, Vice President, Biopharma Operations, Boehringer-Ingelheim, reiterating the fact that biologics are a challenge for analytical characterization. He reminded the audience that vaccines and blood products are not in the scope of ICH Q7A, however, they are included in the EU GMP Guide Part II. He gave a short update on the draft version of Annex 2 to the EU GMP Guide, which will provide general guidance similar to the current version in Part A, but will go into much more detail in Part B for specific biological products.

In this context, he discussed the requirements of Annex 1 on failed media fill exercises. In his opinion, it should be made clearer that any positive unit found should trigger an investigation. If a root cause is identified, it is justifiable to repeat only this particular media fill run after implementing corrective actions. If there no root cause is found, he very much insisted that a revalidation should take place, including three additional medial fill runs, as there are very likely several corrective actions taken to mitigate identified potential causes. He also emphasized the need to have a successful growth-promotion test for the media to justify the media fill results obtained thereafter.

Guinet was clear about the expected actions following failed media fill exercises. "Quarantine batches that had been produces after this failure, investigate all batches produced since the last successful media fill exercise, and quarantine all not released batches. Put an emergency plan in action, as the investigation might force the manufacturer to recall a volume equivalent of 6 months of production. Document all results and the root cause identification very well, so it can be easily followed and understood." His final recommendation was to "perform a media fill run before a prolonged stop with shut down, opening of the aseptic area and/or maintenance operations to be sure everything worked well until this point in time."

He encouraged everybody to study *PDA's Technical Report No. 44: Quality Risk Management for Aseptic Processes* and *Technical Report No. 22: Process Simulation Testing for Aseptically Filled Products* **[Editor's Note:** TR-22 is currently being revised, and the new version will be released soon**]**, and, in particular, the risk assessment and risk management examples they give. When inspecting biotechnological ➤

Report From **Parenterals 2010 Conference**

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manufacturing sites and aseptic production areas, he often encounters poorly performed risk studies that have resulted in deficient practices and warranted regulatory observations of major criticality.

To conclude his talk, Guinet challenged PDA's membership to publish an updated technical report on Isolator/RABS validation practices to help the community improve their practices to state-of-the-art procedures.

Component Quality

Packaging components and their impact on process and product quality was a major topic during the conference. **Ingo Presser**, PhD, Associate Director, Boehringer-Ingelheim, highlighted the efforts and programs implemented to reduce product-bearing defects. He pointed out that non-randomly distributed defects are not easy to detect by incoming quality checks. He showed that although only 11% of components sorted out because of defects, such defects still caused 20% of all deviations in manufacturing. In order to reduce this significantly, a 100% inspection at the supplier was introduced. The visual inspection reduced the rejection rate when delivered from 11% to less than 8%, but introducing an automated camera system pushed it down to less than 0.3%. The same experience was made for glass components, where the introduction of first visual and then automated inspection reduced the rejection rate at delivery to a fourth for particles glassed in, by more than a factor of 8 for cracks and 20 fold for chips found in the components. In all cases, "this requires open communication and commitment of customer and supplier to enable continuous improvement in the component manufacturing process, not to forget the impact on cost and implementation times," he added.

Bernd Renger, VP, Quality, Control, QC, Vetter Pharma Fertigung, cautioned that, because manufacturing of components involves technical processes, there will inevitably remain a certain defect rate. The clue will be to reduce this to a reasonable minimum, bearing in mind that pharmaceutical manufacturing often is not better than a 3 sigma process.

Mads Espersen, Principal Scientist, Novo Nordisk, highlighted that all weakening of glass is irreversible and that the probability of breakage at any given point in any given population of glass depends on the property of the load applied at that point as well as the Weibull Modulus of the population. The Weibull Modulus for a glass population will depend on upstream glass-to-glass contact as well as upstream impacts and loads according to the Griffiths Equation. Glass containers are vulnerable to impact due to relatively undamped natural oscillations. More chips and cracks can be expected to occur in a population with more flaws. He advised that containers be designed in such a manner that stress maxima in mode shapes are minimized (i.e. natural oscillations are well damped) and to ensure that stress maxima does not coincide with weak areas. Weak areas are areas that are subjected to glass-to-glass contact in normal handling and processing and areas where the container design causes stress concentration, like sharp edges. Dynamic FEM analysis may be applied for this purpose to identify such problems.

During inspections, Müller often encounters scarce attention to quality aspects like specifications, crucial testing criteria, and audits not appropriately addressing critical quality characteristics

He suggested avoiding glass-to-glass contact wherever possible and to reduce glass-to-glass handling to an absolute minimum. To do so it is advisable to avoid dead zones in junctions between conveyors, scrolls and wheels. Also it is important to reduce all loads, static as well as dynamic, on glass, avoid squeezing in the manufacturing process due to misaligned or unsynchronized scrolls and other conveying parts and remove glass debris from the manufacturing processes. In conclusion, he said:

- Avoid impact loads
- Validate transportation of glass from supplier, dispatch to warehouse receipt
- Use care when depalletizing
  Ensure that all washing and siliconization needles, and the like, are optimally aligned on washing and filling lines
- Avoid any increasing shift of level between conveyors and dead plates and the like,
- And finally, "Use your ears to find glass impact loads!"

The suppliers of components like **Reinhold Zimmermann**, VP, Global QA, West Pharma and **Joachim Pfeifer**, PhD, Dir. Product Managment, Schott-Rohrglas emphasized the value of cooperation with the customer and told their success stories of achievements in improving quality. The measures taken include clean room conditions in some production areas, use of purified water for rinsing, and automated camera inspection of the finished stoppers, Zimmermann reported. Improvements in stopper manufacturing reduced the defect rate by two-thirds, but automated camera inspection drove it down another 80%. Also more focus will be put on extractables and leachables, so a "Certificate of Analysis will provide key extractables, results of analysis with quantity of extractables, specifications for extractables, fingerprint profile chromatogram," Zimmermann stated.

Pfeifer elaborated on the difficulties of compling with worldwide standards, including the Japanese Pharmacopoeia for amber glass. Another quality issue is the alkalinity of the surface, even though it will conform with the requirements for Type 1 glass. "But the container alkalinity is dependent on the container manufacturing process. Small volume vials are most critical! The trend found indicates low alkalinity leads to low leachables, which is important for biotech drug stability," he added.

Gesche Ahrens, Assoc. Dir. Operational Excellence, Nycomed, reported her experience using an automated leak ➤

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testing system to screen all manufactured products for integrity after having analyzed 270 million vials. The case study builds on the need to change stopper from a fluoropolymer coated stopper, that caused several problems, to a bromobutyl uncoated stopper. Although this change improved the rejection rate to a large extent, after some time an increased rejection rate was detected. Investigation revealed that this was due to one component supplier that had occasionally non-conforming inner vial diameters. This could be mitigated by adding a 100% in-line testing of the vial diameter at the supplier. When a similar rejection rate reappeared some time later, another vial supplier was identified to produce occasionally non-conforming vials. This time, software problems with the camera settings for inspection were identified to be the root cause. Her conclusion was, that after 3300 batches and more than 270 million vials produced, it was safe to state that the vials filled under vacuum and in an appropriate container-closure system can hold vacuum over some time and hence could be considered hermetic. "There was no significant impact of manufacturing sites and suppliers, no impact on freeze dryers, and no impact of elapsed time between stopper seating and crimping. But there was a significant impact of glass vial geometry especially in case of non conformities of their inner diameter, and an impact of stopper primary sealing properties. Our conclusion is vials with appropriate container closure system are vacuum-proof."

Roland Guinet, Sr. GMP Inspector, the French Agency for Security of Health Products, AFSSAPS, next opened a discussion on the integrity of bagged components about ready to use and ready to fill systems in an aseptic sterile process. His challenging question was, if there wouldn't be a need to verify integrity of the bags the sterile components are packed in, as during transport, storage and before entering an aseptic area, they could have been compromised. The argument disputed that this would also be true for medical devices, however, in this case, the validation performed was accepted as evidence to refrain from such a requirement. Also, as the components are delivered bagged in several protective layers and as there are several decontamination steps during the passage into an aseptic processing area, a risk assessment study could show if there was indeed a not acceptable risk remaining.

Speakers at Biennial Training Conference Rate a 4 out of 5

Joyce Winters, J Winters Consulting

GMP and regulatory compliance trainers from locations around the world came together this October in Baltimore, Md., for the *2010 PDA Biennial Training Conference*. The theme of the conference was *Compliance Training and Performance in a Changing Environment.* The speakers and topics focused on how to maintain training excellence in the face of changing conditions. The evaluations from the conference proved that the participants gained valuable "take aways" to enhance their training.

One of the general sessions included U.S. FDA speaker, **Rebeca Rodriguez**, National Expert Investigator, who provided the agency perspective on current training issues. The comments on her presentation found her message particularly of value for management, and, specifically, one attendee stated, "it was a useful approach that we can go over with our management team and staff."

The keynote speaker was **Allison Rossett**, PhD, Professor, Educational Technology, San Diego State University, well known in the field of training and education, who spoke about job aid and performance support. The feedback from her session indicated that it gave attendees a better understanding of job aids. Her session also focused on the fact that no matter how good the initial knowledge transfer is, if the information is not in real time when the trainee needs it, it's minimally effective.

The concurrent sessions featured a wide variety of speakers from the industry. The interactivity and audience participation was a hit with all speakers average ranking being above 4 on a scale of 1-5. Additionally, the new mini-track featuring facilitated attendee brainstorming and questions and answers around timely training topics was enthusiastically received.

The conference vendor exposition provided additional opportunities for attendees to be exposed to the latest and greatest in commercially available training programs and services.

Trainers left the conference with real examples to apply in their own workplace and invigorated with new resources. The participation and interest of the participants made the conference a success.

On behalf of the 2010 Conference Committee, I would like to thank all attendees, speakers and vendors for their continued support. Together we can help employees perform competently and ultimately provide quality products.

About the Author

Joyce Winters is the owner and principal consultant at J. Winters Consulting. She has had over 15 years experience designing and delivering global GMP training and management development courses.

PDA's 5th Annual Microbiology Conference Hits Blogosphere

***Michael Miller**, PhD, President, Microbiology Consultants, manages a website on one of his areas of expertise—**rapidmicromethods.com**. As part of the site, Dr. Miller blogs about various topics of interest. This year, he covered* PDA's 5th Annual Pharmaceutical Microbiology Conference*, and has graciously allowed us to share some of his posts in the* PDA Letter.

Opening Session at PDA Global Microbiology Conference

Opening the conference, **Mark Ott**, PhD, Chief Microbiologist, NASA, spoke on the topic of minimizing infectious disease risk while decreasing the necessary resources required during a spaceflight mission. Floating basketball-sized condensate harboring bacteria and fungi have been found on recent missions, making microbial monitoring extremely challenging!

FDA's Hussong Discusses Objectionable Organisms and RMMs

David Hussong, PhD, Associate Director, New Drug Microbiology, Office of Pharmaceutical Science, U.S. FDA, reviewed the impact that B. cepacia can have on pharmaceutical product and the reasons why this organism may be considered objectionable for certain dosage forms. He stated that current test methods, including finished product testing, may not be sufficient in detecting objectionable organisms and that it is more critical to look for these types of organisms during in-process screening using rapid methods.

Pharmacopoiea Perspectives on RMMs Provided by USP, Ph. Eur. and JP Expert Committees

The Chairs of the USP, Ph. Eur. and JP provided their perspectives on the current and future state of rapid methods and plans for revisions to existing monographs and information chapters.

James Akers, PhD, President, Akers, Kennedy & Associates, and Chairman of the USP Expert Committee, explained that any new United States Pharmacopoeia referee method must be very broad in application and suitable for use with the vast majority of monograph product. Furthermore, new candidate methods must not be from a patented, single-source technology. It is also critical to be clear on the distinction between QC quality control release testing versus in-process testing and monograph requirements. Therefore, companies that desire to submit a RMM for inclusion in the USP as a referee test must take these points into consideration. USP 1223 was developed to provide guidance on the implementation/validation of alternative methods, and this chapter should be used to support the use of a RMM as an alternative to a compendial test. To clarify, RMMs and alternative methods are already allowed under USP 62, as long as they are appropriately validated. Finally, the USP is looking to the industry to comment on the existing chapter 1223 in order to support future revision processes in this area.

Han van Doorne, PhD, Assistant Professor, University of Groningen, and Chair of EDQM, stated that the General Notices section of the European Pharmacopoeia and Chapters 2.6.12 and 2.6.13 state that alternative methods may be used as long as they have been shown to be equivalent to the existing compendial methods. Chapter 2.6.27 states that automated systems may be used for the control of cellular products (e.g., for the daily observation of sterility). A separate chapter on the use of nucleic acid technologies for the detection of Mycoplasma (2.6.7) is also available, and Ph. Eur. 5.1.6 was developed to provide guidance on the validation of alternative microbiological methods. Dr. van Doorne then discussed the committee's plans to revise Chapter 5.1.6. They would like to add more information on Process Analytical Technology (PAT), a better distinction for methods for isolation and detection and for microbial identification. The examples at the end of the current chapter should be improved and expanded to include the validation of ID methods. However, these examples will not appear in a future revision of the chapter, but rather, it will be published as a separate white paper in PharmEuropa. The future revision of this chapter will also include updates to technologies and applications and a greater explanation of DNA-based methods. Finally, he discussed a survey that was sent to the industry asking what companies would like to see in a revision of Chapter 5.1.6. Questions included the following: what applications have been approved for use with RMMs; do you use RMMs for testing other than batch release; would you favor more validation examples; what are the strengths and weaknesses of the existing chapter; did the chapter facilitate applications to regulatory bodies; do you consider the chapter example (Annex) useful; and what compendial methods have been replaced by a RMM.

Tsuguo Sasaki, PhD, GMP Expert Office of Compliance and Standards, PMDA, described two new RMM chapters that are now part of the Japanese Pharmacopoeia. These include Chapter 22 (Rapid identification of microorganisms based on molecular biological methods) and Chapter 33 (Rapid enumeration of bacteria based on a fluorescence staining method). He then provided some examples of where RMM validations were not at a level that was accepted by the Pharmacopoeia. For example, an ophthalmic manufacturer submitted a validation package for a RMM with a shortened sterility test (2 weeks for the compendial method to a 1 week incubation followed by ATP bioluminescence technology). The company validated the system using soybean casein digest medium instead of a medium that would recover more stressful or injured microbes. For this reason, the submission was not approved. Dr. Sasaki ➤

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then presented data demonstrating that micro-colonies of a particular organism developed on R2A medium but not on TSA (this is one reason why the original submission was rejected). Therefore, the company would be required to go back and investigate the most appropriate media for this purpose.

USP Discussion on RMMs and Recommendations for USP Chapter 1223

The final session of this year's Global Conference on Pharmaceutical Microbiology is focused on the direction that the USP will take with the existing informational chapter 1223, Validation of Alternative Microbiological Methods. Questions were provided to the meeting attendees and here is an excerpt of some of the comments and responses:

Question: Has USP 1223 Validation of Alternative Microbiological Methods been useful or an impediment for the selection, validation and implementation of RMMs?

Response 1: Yes, the chapter has been useful as providing guidance for RMM validation.

Response 2: Yes, but we would like to have more guidance on sensitivity and limit of detection strategies. For example, methods for developing very low inoculum levels, such as 1 cell.

Response 3: The use of statistics for each validation criteria should be more clearly defined and relevant.

Response 4: Much work has been done on limit of detection for sterility testing and these methods are appropriate for use and should be incorporated into the USP guidance.

Response 5: There needs to be a good balance between specific guidance, such as acceptance criteria, and background information into the reasons why the guidance is provided. The chapter should not be a white paper.

Response 6: We need a simple benchmark on how to validate RMMs. The food industry and AOAC have addressed this 20 years ago!

Question: Do you like to see examples?

Response 1: In the EU, regulators took the example in Ph. Eur. 5.1.6 as gospel and that caused many problems for companies validating RMMs. As a result, the next revision of 5.1.6 will not contain an example but will be published in PharmEuropa.

Response 2: I want to see real, practical and successful case studies of how RMMs have been validated, not theoretical examples.

Response 3: Recommendation is not to have an example but to put this information in Pharmacopeial Forum and/or reference other guidance documents that will provide examples, such as PDA Technical Report #33.

USP intends to provide better guidance on the use of alternative methods with input from stakeholders

Response 4: I want to see guidance on controls based on technology platforms and applications (e.g., negative and positive controls). But don't provide specific examples, but more suggestions on good controls that should be run.

Question: Should compendial guidance documents (JP, USP, and EP) on the validation of RMMs be harmonized?

Response 5: By a show of hands, many in the audience said yes.

Final summary statements from the USP based on these discussions:

We may be making this much harder than it should be. We need to go back and take a closer look at our recommendations in this chapter and provide a more "user-friendly" set of recommendations. Because there are many different processes and products that would utilize RMMs, it is really up to you, the users of RMMs, to define how to best validate these new systems. USP intends to provide better guidance on the use of alternative methods with input from stakeholders.

USP 1223 needs to be revised. There needs to be a clarification of sensitivity, limit of detection and limit of quantification, with specific validation criteria and not sole reliance on parallel testing. The use of CFUs is difficult because there is no good quantitative definition of what a CFU is. Statistical models used with validation criteria needs to be revisited. Microorganisms chosen during validation should be appropriate for the intended applications, process and product. We need to consider how to handle slow growing microorganisms, and address the use of appropriate controls.

Next, it appears that specific examples should not be included to avoid regulatory expectations that may not be appropriate. Instead, maybe we should reference PDA TR–33 and/or submit a Stimuli Article. Any reference to specific RMM technologies should not be included.

We should address the relevance of referee tests for short shelf-life products such as biologics.

We should work toward harmonizing all RMM guidance documents; however, this may be easier said than done. This ➤

James Akers addressed USP methods during the session covering USP, EP & JP compendial perspectives

Regulatory Briefs

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

North America

PhRMA Comments at Public Hearing on BPCIA

PhRMA spoke at the U.S. FDA's public hearing on the implementation of the Biologics Price Competition and Innovation Act (BPCIA).

At the hearing, PhRMA requested the Agency to require:

- High quality, well-designed comparative studies beginning with molecular evaluation and ending in safety and efficacy trials in patients
- Post-marketing commitments to biosimilars using the same scientific rigor and criteria as for any new product
- Any difference in structure of the product accompanied by data demonstrating differences in safety, purity or potency from a previous product to warrant a product receiving its own 12-year exclusivity period.

The Act authorizes the approval of biosimilars and interchangeable biologics in the United States.

Postmarketing Requirements and Commitments Published

The summary of Postmarketing Requirements and Commitments has been published by the Agency. Fulfilling a requirement of the Food and Drug Administration Modernization Act requiring FDA to report annually on the status of these postmarketing commitments, information in this report covers any postmarketing requirements (PMR)/postmarketing commitments (PMC) that were made, in writing, at the time of approval or after approval of an application or a supplement to an application, including postmarketing requirements required under FDAAA.

Agency Extends Comment Period on PDUFA until Oct. 2011

FDA has extended the comment period for stakeholders to comment on the reauthorization of the Prescription Drug User Fee Act. To ensure that all interested person have sufficient opportunity to share their views, FDA is re-opening the comment period until October 31.

Europe

Danish Medicines Agency to Extend Labeling and Packaging Updates

The deadline for implementation of updates to labeling and packaging should be extended to 12 months or take place in connection with the next production, instead of six months, according to the Danish Medicines Agency. This implementation of the Danish Government's "Easy Administration" program, which was enacted to reduce the bureaucracy in business, stresses that the labeling and package leaflet must be updated at the same time.

Measures required by the Danish Medicines Agency to initiate the extended deadline will be carried out during spring 2011.

Any comments to the proposal must reach the Danish Medicines Agency by November 29. Please send your comments to sgh@dkma.dk with a reference to file number 2999-36.

Key Regulatory Dates

Comments Due:

October 31 — PDUFA reauthorization

Asia-Pacific

Australia's TGA Increases Transparency of Prescription Medicine Regulatory Process

Australia's Therapeutic Goods Administration (TGA) has increased the transparency of its prescription medicine regulatory process with a public assessment report (AusPAR).

Before a prescription medicine can be made available in Australia, the company legally responsible for supplying the product must lodge a submission with the TGA. The TGA will then evaluate the safety, quality and effectiveness of the product to determine if the benefits to people taking the medicine outweigh the risks. AusPAR provides information to companies about the evaluation of the prescription medicine and the considerations that led the TGA to approve or not approve an application.

Correction

The October issue of the *PDA Letter* misidentified senate bill number S3690 as S3409.

is not a simple matter and could be time consuming. However, we will discuss how we can interact with other organizations to determine if our revisions can take into account other guidance documents.

Finally, we need to have more discussions with the stakeholders of RMMs more frequently than we have in the past, and we will discuss how we can seek out mechanisms to make this happen.

About the Author

Michael Miller has more than 22 years experience in the pharmaceutical and medical device industries. He is currently the president at Microbiology Consultants, LLC. Prior to this, he worked at Eli Lilly for five years.

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PDA and the European Medicine Agency welcome you to the 2011 PDA-EMA Conference in London. Planning for this year's conference, the fourth in this series, started in May of 2009 with the recruitment of our superb scientific planning committee. The committee has worked over the summer and fall to bring you a very special program. The 2011 Conference will be a milestone as there has been a decision to broaden the content beyond Good Manufacturing Practice (GMP) to include the full palette of quality issues around pharmaceutical development, production and quality management. The committee has input from EMA's Quality Working Party (QWP) and Biologics Working Party (BWP), with the result being substantial CMC-related content in the agenda. The program has been extended from 1¾ days to a full 2½ days, and the number of concurrent tracks increased from 3 to 5, to make room for the expanded content. The number of EMA speakers, and speakers from the national health authorities is very impressive, due in part to the decision to locate the meeting near London's Heathrow Airport.

The Parenteral Drug Association presents...

2011 PDA/FDA Atypical Actives Workshop

March 9-10, 2011

Hyatt Regency Bethesda
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Atypical Actives are chemicals that do not have an obvious medical function and yet have been designated as the API in the marketing authorization. More often than not, these Atypical Actives are not manufactured according to ICH Q7 because they are intended for use in other industrial sectors. **Continued use of APIs not manufactured according to ICH Q7 brings the drug product holder in conflict with legislative requirements.**

Plenary sessions with over 15 presentations given by **FDA, EMA and industry experts** will discuss:

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- Regulatory and EMA Perspectives
- User and Maker Legal Perspectives (US and EU)
- How do you Obtain Atypical Actives Meeting Appropriate Regulatory Requirements?
- What Happens when your Excipient is used as an Atypical Active?
- *And more!*

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

www.pda.org/atypicalactives2011

Managing Integrated Supply Chain Theme of Cold Chain '11

Bethesda, Md. • March 1-2 • www.pda.org/coldchain2011

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

Temperature-controlled pharmaceuticals, bio-pharmaceuticals and vaccines are increasing in number to address many of the unmet needs to help the patient. The handling, storing and distribution of these products on a worldwide basis require reaching for global scientific consensus for patient safety. The industry, their partners and service providers must cooperate to ensure that the quality, integrity, potency and efficacy of pharmaceuticals are not compromised during the various handlings until it reach the patient.

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

We have designed a session on stability budget as a means of protecting drug quality in the distribution environment. The presenters will describe and justify the studies using scientific data and rationale necessary to determine an appropriate stability budget for a drug substance or drug product. This will also include a status update regarding the publication of the PDA's PCCIG Task Team Guidance.

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

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

The two-day conference will conclude by invited guests from the FDA presenting on Good Distribution Practices, Good importation Practices and labeling requirements.

On behalf of the Program Planning Committee, I am extending a personal invitation to you and your colleagues to join us on March 1–2 in Bethesda, Md., for what is promising to be an informative, stimulating and engaging conference.

Extend your stay in Bethesda for the PDA Training and Research Institute (TRI) course, "Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems," March 3-4, 2011 at the PDA Training and Research Institute in Bethesda, Md.

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

Workshop to Discuss Intent of Process Validation Guidance

San Antonio, Texas • April 13-14 • www.pda.org/processvalidation2011

Hal Baseman, ValSource and Scott Bozzone, PhD, Pfizer

We want to inform you of an important industry meeting and workshop, the *PDA Process Validation Guidance Workshop: Meeting Compliance Expectations and Practical Implementation Strategies*. In order to make it as convenient as possible for you to attend, we have planned it to coincide with the conclusion of the 2011 PDA Annual Meeting on April 13 and 14, 2011 at the JW Marriott in San Antonio, Texas.

The industry has known of this significant guidance for some time, having had the opportunity to review and comment on the November 2008 draft version. Throughout 2009 PDA conducted a series of workshops to educate the industry on the content of the Process Validation guidance and convey additional comments and reaction. The U.S. FDA has received industry and other input and has worked for the past few years to prepare this final document. As promised, much is left to the industry to develop programs to meet the stated expectations presented in the guidance. As a result, some of the critical questions we must consider include:

- How does what you do to validate the process prove that the process is under control?
- What scientific evidence do you have to assure that the process is capable of consistently delivering quality product?
- How can you obtain useful and needed information from process development? ➤

- What must you complete before you have the confidence to go into commercial manufacture?
- How much testing will you do and for how long?
- What will the regulators ask for?
- How do we implement the new FDA guidance into our existing validation program?

The objective of this meeting and workshop is to inform and further educate the industry on the content and intent of the anticipated *FDA Guidance on Process Validation: General Principles and Practices*. It also will provide a forum for the industry and regulators to directly present and discuss challenges faced with interpretation and implementation of the guidance, and identify workable solutions and approaches to meet and address those challenges. To that end, PDA and the planning committee have designed a program, including interactive workshops, with regulators and industry leaders in process validation as presenters, facilitators and participants.

Speakers will include FDA guidance authors and decision makers, PDA and PCMO task force science leaders and industry process validation experts. The agenda presents a sampling of planned topics, sessions and presentations to be addressed at the meeting. As this meeting there will be an interactive, networking workshop where other input and discussions are likely to emerge.

We must not miss this is opportunity to influence and begin to set the standard for validation of drug product manufacturing processes. In the end, the objective we hope to achieve will help the industry develop an effective program for drug product manufacturing process control and validation; thus, further assuring continued quality of products and patient safety in an ever changing and more complex business environment.

Learn more about the workshop, visit www.pda.org/processvalidation2011.

PDA to Hold a Workshop on Atypical Actives

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

Sue Schniepp, OSO BioPharmaceuticals

The Parenteral Drug Association, in conjunction with the U.S. Food and Drug Administration and the pharmaceutical industry, is conducting a workshop March 9-10 in Bethesda, Md., for the purpose of discussing and recommending approaches regarding the use of atypical actives used in some of today's pharmaceutical products.

Medicinal products must contain at least one active pharmaceutical ingredient (API). An atypical active is a chemical which does not have an obvious medical function but is considered the API in approved regulatory filings. These special atypical APIs are most predominately used in other industries (e.g., food, cosmetics) and are not manufactured according to ICH Q7. This creates an issue for the manufacturers of these products because they are not prepared to be audited against the ICH standards for APIs. Continued use of these APIs in dosage forms has the potential to bring the drug product manufacturer into conflict with current regulatory requirements. Some examples of atypical actives include:

- Mannitol used in injections given to patients in the last stages of kidney failure
- Glycerin used in suppositories
- Isopropyl Alcohol used for cleaning cuts and wounds
- Charcoal used as an emetic

The impact of the use of atypical actives as APIs in pharmaceutical dosage forms has not been openly discussed and debated by industry and regulators. This workshop is designed to bring the topic into the open and enable participants to brainstorm, discuss and debate the issues and challenges to arrive at realistic expectations based on science and risk. This workshop will bring together industry and regulators and will focus on the current situation, global regulations and requirements for atypical actives. The workshop will also provide opportunities for participants to help develop and create realistic, practical solutions to meet the needs of patients, industry and regulators.

The workshop is divided into two days. Day one begins with an overview of the situation presenting industry, regulatory and legal perspectives. In addition, the issue of how to distinguish requirements between these items when used as an atypical active or an excipient will be discussed.

Day two starts off with case studies which will be the basis for discussion in the two breakout sessions. Breakout Session A will focus on technical considerations, and Breakout Session B will focus on regulatory considerations. These breakout sessions will repeat in the afternoon so participants will have an opportunity to express their opinions on both aspects.

The conference organizers will end the workshop with a comprehensive report regarding the discussions from the breakout sessions and a list of action items and steps to continue the progress forward in resolving the current dilemma. The ultimate goal of the workshop is to establish a reasonable set of requirements for the industry when they need to use atypical actives in their products.

If the issue of atypical actives is of concern to you and your company, please plan on attending the *2011 PDA Atypical Actives Workshop*, March 9-10 in Bethesda, Md., to come together with regulators and industry to develop solutions.

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The conference will center around: Fast Track in Formulation Development • Fast Track in Sterile Clinical Trial Material Manufacturing • Safety Issues in Manufacturing Biopharmaceutical Clinical Supplies • Clinical Trial Material Packaging and Distribution Challenges • Batch Size Challenges • Regulatory Issues and Developments

Myriad of Micro Topics on Agenda of Two-Day Conference

Berlin, Germany • March, 15–16 • www.pda.org/europe

Sebastien Ribault, Millipore and Jeanne Moldenhauer, Excellent Pharma Consulting

It is a great pleasure for the organizing committee to invite you to attend the *Pharmaceutical Microbiology/Mycoplasma—Enhancing Quality in Process and Product Conference*, which will be held on March15-16 in Berlin, Germany. The first meeting last year in Europe was a great success; therefore, a sign that we should continue in this direction for 2011. We received so many abstracts that we had to organize the program to offer plenary as well as parallel sessions.

The mycoplasma and virus detection session will include an overview of traditional methods, as well as new tools, including molecular testing and validation using PCR. Speakers will share their experience on how to implement these methods successfully in-house.

New methods available for identification including MALDI-TOF and Mass spectrometry and their application to virus, mycoplasma and bacteria will be discussed.

Microbiological quality will cover issues concerning objectionable microorganisms, recovery of isolates in environmental monitoring, contamination control and sterility assurance as well as failure investigations in case of microbiological deviations.

Statistics applied to biology is a difficult subject especially when the comparison of rapid and compendial methods must be addressed. The invited speakers will discuss sampling plans, statistic tools that could be used as well as how the interpretations and conclusions could be drawn.

The program will also include presentations given by representatives from regulatory authorities coming from Europe as well as the United States. We are convinced the participants will benefit from examples shared by the different speakers.

The workshop sessions will allow you to discuss more specific issues with experienced users. They will address mycoplasma and virus testing, failure investigations for microbiology data deviations and statistical analysis.

We're looking forward to welcoming you in Berlin and sharing your own experience, expertise or questions with the audience and experts.

2011 PDA Europe Conferences & Events

February 15-16	Clinical Trial Material	Conference, Exhibition	Berlin, Germany
March 1-3	Technical Report – Update	Workshop, Exhibition, Training Course	TBD
March 15-17	Pharmaceutical Microbiology/ Mycoplasma	Conference, Exhibition, Training Courses	Berlin, Germany
March 22-24	Parenteral Packaging	Conference, Exhibition, Training Courses	Berlin, Germany
March 24	IG Pre-filled Syringes	Interest Group Meeting	Berlin, Germany
April 5	IG Freeze Drying	Technology Interest Group Meeting	TBD
April 6- 7	Stoppers + Elastomers	Workshop, Exhibition	Rennes, France
May 3-6	PDA/EMA	Joint Conference Conference, Exhibition Training Courses	London, UK
May 26	IG Visual Inspection	Interest Group Meeting	TBD
June 7-8	Advanced Therapy Medicinal Products (ATMPs)	Workshop, Exhibition	Helsinki, Finland
June 7-8	4th Monoclonal Antibodies Workshop	Workshop, Exhibition	Basel, Switzerland
June 28-30	Virus / TSE Safety Forum	Conference, Exhibition	Barcelona, Spain
September 27-30	Pharmaceutical Cold Chain Management & Good Distribution Practice	Conference, Exhibition, Training Courses	Berlin, Germany
October 25-28	Freeze Drying Technology	Conference, Exhibition, Training Courses	Barcelona, Spain
November 7-11	The Universe of Pre-filled Syringes & Injection Devices	Pre-Conference Workshop Conference, Exhibition Training Courses	Basel, Switzerland
November 15-16	Green Pharmaceutical Production	Conference, Exhibition	Copenhagen, Denmark

PDA Interviews TRI Instructor J. Kirby Farrington

Microbiologist **J. Kirby Farrington** calls himself a "plank owner" of TRI, having been invited by then PDA President **Michael Korczynski** to teach at the new facility in 1997. Kirby taught courses for PDA even before the Institute was founded. Over the course of his 35 year career in the industry, Farrington has worked with a variety of consumer and prescription products, including foot creams, contact lens/solutions and cosmetics. For TRI, he shares his expertise in microbiology water systems, antimicrobial preservative systems and HACCP/Annex 20 risk approaches.

He now works for Auburn University. In this interview, Farrington shares his opinion of the role of microbiologists in pharmaceutical companies.

PDA Letter: What about the topics you teach excites you?

Kirby: Well, one, it was a part of my normal job functions within the pharmaceutical industry. And the HAACP—I started out in foods. I was a microbiologist for the wet process division at Kelloggs, and we were definitely into HAACP over there. So when I went over to the pharmaceutical industry, it struck me as natural, 'Hey, why aren't we doing this here?' The pharmaceutical industry in a lot of ways is very conservative and reluctant to bring in ideas and approaches from other disciplines or other industries, which is really kind of conceited to tell you the truth. When you get into, particularly, microbiology contamination control, that type of thing, that all originated in foods to begin with.

PDA Letter: So you come in to the industry from foods, what was one of your first challenges? Were you asked to implement these systems from foods, and were you also required to teach what you knew? Was that part of your job?

Kirby: Well, yeah. Education is big part of it. I came into Schering Plough (Plough division) right after the merger of Schering and Plough. Abe Plough that founded Plough was still alive. In fact, I knew him. But at that time, they owned Coppertone, Tropical Blend, Maybelline and DAP automotive products, as well as a large number of OTC drug products. So I got in there and they said, 'Hey, you are starting a microbiology department.' I said 'okay.' That's what I was hired for. A lot of people look at my resume and say, 'Where in the world did you work on all this stuff?' I say, 'Well let me tell you.' [Laughter]. You know, it was a conglomerate with different facilities, different places.

PDA Letter: Why do you get excited about microbiology?

Kirby: Well, it's what I have done all my life. I have been in a lot of standard setting groups, and I try to debunk a lot of what people think about microbiology. One of the big problems we have particularly in the pharmaceutical industry is microbiologists are treated as second class citizens. I have said as much at meetings.

The first thing is chemists are the ones who are normally running the quality control groups, and micro is looked more like voodoo to a lot of people. In some companies, it is your chemists and engineers in quality control, and they are looking at absolute values. If you test something today and you get a value, you send it half way around the world and get somebody to test the same thing using a validated method, they should come up with something near the same answer. That doesn't happen in micro. You are dealing with living systems and it doesn't make sense to them (chemists/engineers), yet they are put in a position where they are responsible for the micro department.

One of the big issues is that you have very few microbiologists actually running the quality control departments, because they are not considered trained well-enough even though a microbiologist has extensive chemistry training.

PDA Letter: So when you are teaching do you see a lot of chemists? Are they quality people who are trying to figure out what's important in these areas?

Teaching for PDA before TRI was even founded, Kirby Farrington has shared his expertise with many of PDA's TRI's students

Kirby: We do have a lot of people who are not microbiologists signing up for these courses, because a lot of them running the departments that are responsible for the investigation and adequacy of the investigation. They don't understand the discipline, and they don't want someone talking about or saying something they don't at least have a minimum understanding of. I think that is the value of a lot of these courses. That is why I like the one-day format. I mean you don't get down in the weeds, but yet you cover the basics. You make someone conversationally aware of it or at least let them know what they don't know.

A lot of times I actually have the microbiologist in the class, and they say, 'Yeah, what you are saying is perfectly true, but we just don't have the nerve to say it in our own shop.'

PDA Letter: What do you advise people who say that? It doesn't sound like to us that you lack the nerve to tell people how things should be. What do you tell them to do?

Kirby: Well, again, that is what I teach. I simply explain that everybody has the same situation a lot of times. They are talking to people who really don't understand what they are talking about. So you have

a couple of options there. You can try and educate them. You can suggest that they get a consultant in. But the U.S. FDA and the regulatory agencies are helping us—us being the microbiologists—pretty well now, because they are saying anything dealing with micro needs to be handled by a microbiologist. Not someone who calls himself one, but someone with the credentials. And they are enforcing that.

I don't hesitate to point that out in these courses. 'Hey, microbiologists, the regulatory agencies are requiring you to be involved with this.' You don't want to be obnoxious about it.

PDA Letter: So it sounds like what you teach is pretty tied directly to everything you've done in your career. Has it changed over time? Are there things you taught 12 or 15 years ago that you just don't teach now because things have changed?

Kirby: I try to keep things updated. Things have definitely changed within the science. You know, we have different capabilities. They said the '70s was the era of the microbiologist within the pharmaceutical industry, and then it kind of tapered off again. The '90s was another era of the microbiologist. It goes in waves. A lot of it's tied to the technology.

PDA Letter: Do you get a lot of students from small companies? Do you feel they really need the help?

Kirby: Well, all the companies need the help, the smaller companies in particular. They'll hire someone with very limited experience, plop them down and say, 'You are responsible for all this.' A lot of those people don't know where to go next. They've told me that many times.

PDA Letter: It seems like everything has gone full circle for you. You received your PhD in microbiology-pharmaceutical/veterinary medicine from Auburn University, and now you are back there as a faculty member. Will you have time for TRI?

Kirby: I am running the labs and teaching. I have 600 students. I absolutely will still have time for TRI; the University supports that.

PDA Letter: Anything else you would like to say?

Kirby: Just that I've seen the numbers going down a little, and I know that has to do with the ability of companies to send people out for training.

PDA Letter: That is a very interesting point to make, and I'm glad we closed with it. We know the economy is bad, but we don't know if you can replace the experience gained going to a place like TRI, or wherever else you may chose to go, for training. We feel that, when you chose to stay within your company for training, you are limiting what you learn.

Kirby: That's right, your people don't feel free to discuss things. When you are in-house, they are constrained. I mean, people are constrained elsewhere because they are afraid if they say something and someone is there from their company, it will get back. But the best courses I've seen are where you have a single person from one company and you have multiple companies there, and pretty soon everybody starts talking to each other and you end up being a facilitator.

PDA Letter: So it becomes a community of microbiologists or chemists dealing with a problem versus a group of employees from the same company.

Kirby: Correct. You are not saying to yourself, "If this gets back to my boss, I'm had."

PDA Letter: Well, we hope people continue to get resources for this training, and we hope they find time to attend one of your TRI courses. Thank you so much, Kirby.

About the Instructor

Kirby Farrington is a Coordinator for the Microbiology Teaching Labs at Auburn University. He has been a research scientist with Eli Lilly in Indianapolis, Indiana, responsible for technical training and specialty issues for the Manufacturing Sciences and Technology (MS&T) organization. Previously, Kirby was the Director of QA/RA for the Pharmaceutical Development Center (PDC), Research Director for Microbiology for Schering-Plough and VP Operations for Plough Laboratories. He also holds certifications as a registered microbiologist in food, dairy, sanitation and pathogenic microbiology, a Specialist certification in public health and medical laboratory microbiology and as a Specialist Microbiologist for the American Society for Clinical Pathology. He is also a member of the 2005-2010 USP Microbiology and Sterility Committee of Experts.

Below are a sampling of courses he has taught for TRI:

"Introduction to HACCP and Other Risk-Based Systems as Applied to Aseptic Pharma Manufacturing"

"Microbiological Issues in Non-Sterile Manufacturing"

"Use of HACCP for Microbiological Control in Pharmaceutical Manufacturing"

"Environmental Monitoring in Pharmaceutical Manufacturing"

"Investigating Microbiological Failures"

A Look Back at 2010 and a Look Ahead to 2011

Bob Dana, PDA

In Roman mythology, **Janus** (or **Ianus**) is the god of gates, doors, doorways, beginnings, endings and time. His most prominent remnant in modern culture is his namesake, the month of January, which begins the new year. Most often he is depicted as having two heads, facing opposite directions; one head looks back at the last year while the other looks forward to the new, simultaneously into the future and the past.

So in this first issue of the *PDA Letter* for 2011, I thought it might be appropriate to steal a page from Roman mythology and take a look back at the PDA Training and Research Institute's year in 2010 while looking ahead to the coming year.

2010 was an interesting year for TRI, featuring both successes and a few disappointments. We started our year in San Diego, with a course series focusing on biotechnology-related topics. We believed that, due to the demographics in the area, biotech-related courses would draw well there and some did, with a couple exceeding our attendee forecast. Our course "Biotechnology: Overview of Principles, Tools, Processes and Products," taught by **Tony Moreira** was especially well attended.

PDA's Annual Meeting was held in Orlando, where we had the opportunity to honor faculty member **Barry Friedman** as the recipient of the 2009 James P. Agallaco Award for excellence in teaching. A number of our courses held at the Annual Meeting exceeded our expectations, including "The Role of the Quality Professional in the 21st Century" taught by **Bob Kieffer**, Cleanroom Design" led by instructor **Bob Ferer** and "Bioprocess Validation" taught by instructor **Trevor Deeks**, who traveled all the way from England for the event.

As seems to often be the case, our "Global Regulations and Standards: Influences on Cold Chain Distribution Practices: Development and Testing of Cold Chain Packaging and Transport Systems" course, held in conjunction with PDA's Pharmaceutical Cold Chain Management Conference in Bethesda, Md., was sold out again in 2010. Our classrooms here at the TRI facility were bulging at the seams to accommodate more than 30 students who attended the course taught by faculty members **Rafik Bishara** and **Tom Pringle**. Jumping ahead a bit, we'll be running this course again in March 2011 in conjunction with this year's Pharmaceutical Cold Chain Management Conference, so be sure to register early to ensure that you secure a seat!

PDA co-sponsored the PDA/FDA Vaccines Conference this year, and a last minute addition to the Conference was the scheduling of three vaccine-related courses. The courses "Vaccines 101"; "Uses of Bioassay for Vaccine Development and Product Control" and "Principles of Microbiological Containment" were all quite successful.

In October, we had the opportunity to partner with the Mountain States Chapter to sponsor three courses in Denver. This arrangement turned out to be mutually beneficial, and we would love the opportunity to partner with some of our other Chapters in 2011. Let your Chapter leadership know what topics you'd like to see TRI offer close to your home. Of course, I'm not sure I'll order rattlesnake for dinner again as I did in Denver!

Also in October, we were in Las Vegas for the *Universe of Prefilled Syringes and Injection Devices* Conference and Course Series. Our two courses,"Syringes and Elastomers: Understanding the Effects on Quality and Demonstrating the Production Process, Influences and Needs" and "Technical Development of Prefilled Syringes, Autoinjectors and Injection Pens," taught by **Michael Gills**, **Patty Kiang** and **Wenzel Novak** were wildly successful; so much so that we will be running a Prefilled Syringe Week at our Bethesda training facility in 2011. We will repeat these two courses with a regulatory component added and will also be including our laboratory course "Development of Prefilled Syringes." If you are involved with prefilled syringes, you need to take the opportunity to participate in one, two or all three of these courses during TRI's 2011 Prefilled Syringe Week. Visit our web site, www.pdatraining.org/prefilledweek, for details of this innovative training opportunity.

We closed out the year on the road in San Diego, back where we started, with a course in conjunction with the PDA Pharmaceutical Freeze Drying Workshop.

In addition to all these lecture courses, we were busy at our facility in Bethesda. PDA's flagship course, the *Aseptic Processing Training Program*, led by **Dave Matsuhiro** and **Hal Baseman**, experienced five sold out sessions again this year. This program, which is an absolute must if you are involved in aseptic processing operations, will be held five times again in 2011. Visit our website, www.pdatraining.org/aseptic for more details and to register for this course.

In April, we had an interesting and unique opportunity to provide hands-on and lecture-based training to almost 50 FDA staff members in Bethesda. Several volunteer faculty members collaborated to provide a hands-on experience with lab-based inspection principles and equipment operation. This was a well-received opportunity that we hope to repeat in the future.

We also responded to our member needs by planning and conducting several customized training programs which were delivered on-site at client facilities in the U.S. and Canada.

So what about the future? What does our Roman mythologist see happening in 2011? In the November/December 2010 issue of the *PDA Letter*, **James Wamsley** of our staff wrote about some of the changes TRI will be making in 2011. Our strategy is two-pronged and will feature a modified course schedule ➤

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Week1: January 10-14, 2011
Week 2: February 7-11, 2011
Bethesda, Maryland | www.pdatraining.org/aseptic

March 2011

Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems
March 3-4, 2011
Bethesda, Maryland | www.pdatraining.org/GlobalRegulations

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

Prefilled Syringe Week
March 21-25, 2011
Bethesda, Maryland

- Solving Strategic Quality, Regulatory and Technical Issues During the Development of Prefilled Syringes, AutoInjectors and Injection Pens
- Development of Prefilled Syringes
- Syringes and Elastomers: Understanding the Effects on Quality and Demonstrating the Production Process, Influence and Needs

Laboratory Courses

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

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

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

to bring more resources to bear on the courses we will be running, as well as developing new course content which will provide us greater flexibility in planning and scheduling courses. As James indicated, this approach will allow us to opportunistically schedule courses based on current hot topics, similar to what we did in Las Vegas with the prefilled syringe courses and the vaccines courses in Bethesda.

Our modified course catalog will still include many of the courses that have successfully met the needs of our students over the years, including courses in the areas of aseptic processing, biotechnology, environmental monitoring, microbiology, validation and visual inspection.

subject matter area and will also be available on the PDA TRI website.

We will also actively work with our members to ensure they and their companies view TRI as a resource to help meet their training needs. Our facility includes a completely operational clean room with supporting laboratories and equipment for courses in microbiology, environmental monitoring, visual inspection, cleaning validation, moist heat sterilization technology and biotechnology. Our cadre of instructors includes over 100 subject matter experts who teach in the areas where they work, ensuring our students receive a practical, up-to-date educational experience. We would love to work with you and your company as a partner in helping to meet your training and education needs. For more information on TRI, our facility and capabilities see **Emily Hough's** article "Need Training? Give TRI a Try" in the October 2010 *PDA Letter*.

PDA's flagship course, the Aseptic Processing Training Program, led by Dave Matsuhiro and Hal Baseman, experienced five sold out sessions again this year

In a similar manner to our Prefilled Syringe Week, we will also be offering Filtration Week (October 24–28) and Lyophilization Week (June 20–24) here at the Bethesda facility. Focusing our offerings in these specific topic areas allows our prospective students and us to take advantage of more efficient and cost-effective scheduling, a win for both our members and PDA.

Another difference in 2011 will be the absence of our remote, stand-alone course series. The logistics and costs associated with planning and scheduling these series were just not commensurate with the returns to PDA and were clearly not meeting the needs of the students and industry we serve. We will continue to hold courses in conjunction with the major PDA U.S Conferences, as well as at our facility in Bethesda. You will be able to see a listing of all our planned courses in the 2011 Catalog and on the TRI website (www.pdatraining.org).

Speaking of our catalog, 2011 will mark the second year of our all-electronic catalog. This catalog will provide a complete up-to-date listing of all our courses by

None of our 2010 successes and 2011 plans could have been realized without the dedication, hard work and commitment of all of our instructors. I am deeply grateful to all of them. I also want to thank all of the nearly 1000 students we trained this year. As I noted in my year end summary in December 2009, without them, there would be no TRI. Finally, I must say a heartfelt thanks to my capable, dedicated and hard-working staff. Without James Wamsley and **Stephanie Ko**, our Senior Managers for Laboratory and Lecture education, none of this would have been possible. Thank you James and Stephanie!

So, as we embark on another year, I would like to wish all of our readers a safe, happy, healthy and prosperous 2011. I hope to see many of you at one of our TRI courses this year.

PDA's Who's Who

Hal Baseman, COO, ValSource

Rafik Bishara, Leader, PDA's Pharmaceutical Cold Chain Interest Group

Trevor Deeks, Senior Consultant, CMC and Manufacturing Development, Emergent Biosolutions

Bob Ferer, President, The Ferer Group

Barry Friedman, PhD, Consultant

Michael Gills, Technical Customer Support Process Engineer, West Pharmaceuticals

Emily Hough, Writer/Editor, PDA

Patty Kiang, PhD, Kiang Consulting Services

Bob Kieffer, President, RGK Consulting

Stephanie Ko, Sr. Manager, Lecture Education, PDA

Dave Matsuhiro, President, Cleanroom Compliance

Tony Moreira, Vice Provost, Provost Office, UMBC

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

Tom Pringle, Industry Consultant and Educator, Pharmaceutical and Biomedical Temperature Controlled Transport Packaging

James Wamsley, Sr. Manager, Laboratory Education, PDA

Editor's Page

New Year, New Look…Same Letter

So you might be holding the January issue of the *PDA Letter* and asking yourself, "Where's my *PDA Letter*?" But rest assured, this is it! Due to the capable hands of publication designer **Katja Yount**, we began experimenting with some of the design features of the Letter, which have remained virtually unchanged since our last major redesign back in 2004 and decided it was time to update, refresh and recast a few things, though we have not gone so far as a complete redesign.

We also took the opportunity to reorganize the Departments to match PDA's new Strategic Plan, which you can read all about in an article on p. 6. Not only have some of the Departments been renamed (for instance, "Membership Resources" is now "People"), we shuffled their positions in the Letter to better reflect the goals of the Association.

Most notable of all the changes is the new-look cover. We've elected to take all content off of the cover in order to provide a larger canvas for Katja to work with and to allow her creations room to shine. Inside, we updated the Table of Contents page to give it room to breathe. We added much needed white space to the interior pages by eliminating the blue bar in the headers and shrinking the colored "Department" tabs. Also, we've update the look of the Chapter Contacts list, and, we will have a new-look for the Interest Group page which we'll unveil soon.

So here's my message, nestled safely in the back of the issue. I hope readers find it and take the time to read it, but if pressed for time, I'd much rather see readers spend time with the great feature articles we work so hard to publish. Our cover story by **Emilio Frattaruolo**, a packaging engineer, offers sound advice on the design and selection of packaging systems for temperature-sensitive products.

The report from the Microbiology Conference was pulled off of the blog written by longtime PDA member **Michael Miller**, who did an admirable job posting highlights throughout the meeting. We thank him for sharing his insights with us and for allowing us to republish them here.

I think PDA's **Volker Eck** is making a bid to join the *PDA Letter* staff, based on his crack report from the Parenterals meeting in Berlin. His comprehensive coverage, complete with quotes, will run in two parts. If you missed what looked to be a fantastic event (as I did), Volker has provided a great alternative.

We were pleasantly surprised to receive the summary of the *2010 PDA Biennial Training Conference*, and thank author **Joyce Winters** for preparing it. I attended sessions of the Biennial Training Conference for the first time and really enjoyed them. Look for an in-depth article on "Quality Near Hits," discussed at the conference by a team from Talecris, in an upcoming issue.

Speaking of upcoming issues, we are looking for articles on the following topics for future issues:

- Process Validation – The New FDA Guidance
- Top 5 Supply Chain Solutions
- Internal Investigations – Finding Out What Went Wrong and What To Do About It
- Compliance and Sterile Products/Aseptic Processing
- Pharmaceutical Microbiology

Email me (morris@pda.org) or **Emily Hough** (hough@pda.org), if you'd like an opportunity to be published.

PDA Letter

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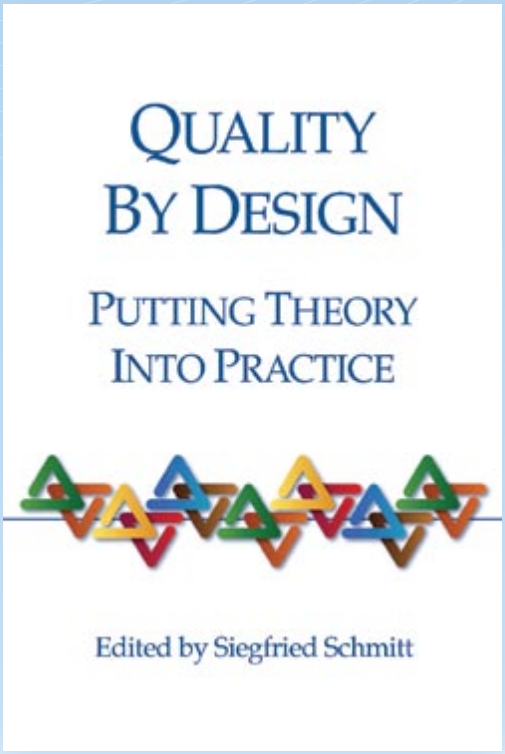

Quality By Design: Putting Theory Into Practice

Edited by Siegfried Schmitt

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

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

- Proactively address regulatory trends
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- Drastically reduce recalls
- Achieve leadership in the industry

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

www.pda.org/QualitybyDesign

The PDA Bookstore's December Top 5 Best Sellers

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

2 **Laboratory Design: Establishing the Facility and Management Structure**
Edited by
Scott V. W. Sutton
Item No. 17294
PDA Member $ 280
Nonmember $349

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

4 **Recent Warning Letters Review for Preparation of a Non-Sterile Processing Inspection, Volume 2**
By Jeanne Moldenhauer
Item No. 17295
PDA Member $280
Nonmember $349

5 **Cleaning and Cleaning Validation, Volume 1**
Edited by
Paul L. Pluta
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