Science • Technology • Quality • Regulatory • Community

PDA Letter

Volume XLVI • Issue #9

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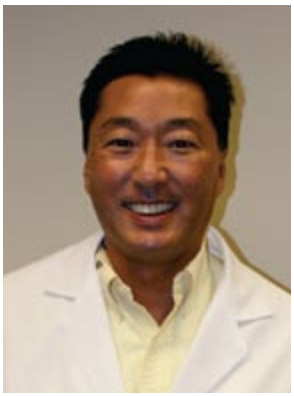
October 2010

In This Issue:

PDA® Parenteral Drug Association

Connecting People, Science and Regulation®

Meet TRI Instructor Dave Matsuhiro



Visit the PDA Training & Research Institute anytime, and there is a good chance you'll bump into **Dave Matsuhiro**, the lead instructor of TRI's Aseptic Processing course, a two week, hands-on class offered five times a year. Dave's been a faculty member for the course for a dozen years now. At his "day job," Dave is the Compliance Consultant/Founder at Cleanroom Compliance, Inc. He has worked as a consultant for Aseptic Solutions and KMI Systems, specializing in water, environmental systems and aseptic processing. He has also worked for Genentech in a variety of environmental control positions.

Besides PDA, Dave is a member of several professional associations, including: the American Society of Microbiology and the International Society of Pharmaceutical Engineers.

TRI's **James Wamsley** talked to Dave about his TRI course.

James: What is your background? How has it helped you in preparing for and teaching this course?

Dave: My background is in Microbiology and Engineering. I am very fortunate to be using my education in my occupation. I have also built an extensive network of business relationships, which I rely on when items come up that are out of these areas. In addition, this network has helped bring in many of the instructors for the class.

James: Why did you decide to become an instructor for PDA's Aseptic Processing Training Program? For example, what were the circumstances? Who contacted you? Why did you think it was a good idea?

Dave: In 1999, **Mike Korczynski**, the first Director of the Training and Research Institute, contacted me to participate in the first Aseptic Processing Training Program teaching the Airflow Study section. At the time, I was working for the consulting firm Kemper Masterson. I wanted to participate because it was an opportunity to help the industry learn and understand about airflow studies. By understanding airflow, companies could reduce the risk of contamination.

James: What makes you, in your opinion, the right instructor for this course?

Dave: My approach to training has various facets. I believe that people learn and

continued on page 19

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2010 PDA Europe Workshop + Training Course

Contract Manufacturing in the Pharmaceutical Industry

From Start-Ups to Big Pharma

30 Nov-1 December
Amsterdam, The Netherlands

Workshop, Exhibition, Training Course

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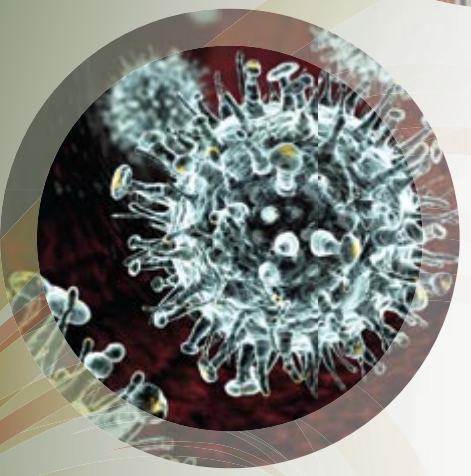
www.pda.org/ContractManu2010

Register by 1 Nov 2010 and SAVE!

Contract services, contract manufacturing, and outsourcing is common practice in many pharmaceutical companies. Meanwhile this has become true for the whole range of activities to develop and manufacture pharmaceuticals. Formulation and process development, environmental tests, analytical services, stability testing, clinical trial management or production of market products are some of the activities which might be taken care of by a third party company. What should be outsourced and what should you do in-house? What do sourcing strategies look like? What are legal and contractual aspects? What should quality agreements look like? How should regulatory issues be dealt with? The PDA Europe workshop will give the answers. Experts from pharmaceutical industry and service providers will share their experiences.



PDA/FDA Adventitious Viruses in Biologics:

Detection and Mitigation Strategies Workshop

December 1-3, 2010

Marriott Bethesda North Hotel
Bethesda, Maryland

This workshop has been developed to address current viral contamination events and is intended to **encourage modernization in industry with respect to viral detection and control measures**. Gaps in our current ability to detect, control and clear adventitious viruses; the availability of emerging technologies in areas where gaps exist; and CGMP expectations for adventitious virus detection and control, as well as consequences for noncompliance will be discussed.

This three day workshop will provide focus on:

- ☑ Current industry standards
- ☑ Review of viral contamination in biologics and case studies
- ☑ Gaps in overall testing strategies and emerging technologies for novel virus detection
- ☑ Best practices to mitigate virus contamination and evaluation of the risk to patients
- ☑ Barrier and inactivation strategies for control of raw materials
- ☑ Application of concepts presented in ICH Q7 and Q10 as they relate to the prevention and detection of viral contamination in production processes and approaches

Register before October 21
and save up to **$200!**

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Table of Contents

Volume XLVI • Issue #9 www.pda.org/pdaletter

Cover art:
PDA's Training and Research Facility has been in operation since 1997. Started by Mike Korczynski, TRI is dedicated to bringing hands-on and lecture-based training to pharma/biopharma professionals.

Coming Next Issue:
Top Stories from the PDA/FDA Meeting

Editor's Message

Celebrating TRI's Teachers: A Timely Decision

We decided over a year ago to dedicate a 2010 issue to the instructors of the PDA Training and Research Institute (TRI), and as events unfold in the industry, the timing couldn't have been better. One of TRI's main offerings is the Aseptic Processing course, and a number of firms have run up against warning letters and even stiffer FDA enforcement actions in relation to alleged failures to comply with GMPs for aseptic processing operations. We highlighted three well-known cases in the July/August issue of the *PDA Letter*, but since then, several other warning letters have been issued to big and small firms for similar violations, including one to Bristol-Myers Squibb in August.

Another trend surfacing in the compliance data this year is lack of training. I follow the LinkedIn group "FDA Inspections," and another member of the group routinely posts information on warning letters that include training issues. There have been several this year. The *PDA Letter* has taken a deeper look into training-related GMP violations in the past (see the April 2006 and April 2008 issues). Sound training, as we know, is part of a strong Quality System.

So it would seem a prime opportunity for PDA to tout the advantages of the world class training to be found at TRI, and we are. But it is always a good time to do that. What I think is equally as important is for our members—like those we highlight in this issue—to step forward and offer to teach! Students are just one-half of a good course, the other is a good teacher. When you read the interviews with the TRI faculty in this issue, you cannot help but see how dedicated and fulfilled the faculty is. Teaching for TRI is not a "volunteer" position, as our faculty is compensated, but that alone is not enough to keep people like **Dave Matsuhiro** at the TRI facility for a few months each year. His passion for teaching and dedication to the students and his field provides a larger incentive.

I also want to point out an article by *PDA Letter* Editorial Committee member **Miriam Estrano**, who writes "Challenges in Aseptic Production of Sterile Biologics" (page 26). This article received very good feedback from the committee, and the editorial staff enjoyed reading it as well. It is a timely piece in light of the aforementioned enforcement actions this year. We are proud to present it to our readers and hope you all enjoy it.

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2011 PDA Board of Directors Nominees

Jette Christensen works as the Aseptic Scientific Director at Novo Nordisk A/S in the Diabetes Finish Product section. Her responsibilities include setting directions and giving support within the following areas: Clean room design, classification and qualification, aseptic production including training in aseptic behavior and production microbiology. She works with sites located in Denmark, France, the United States, Brazil and China. She has a global view on the manufacturing processes, authority requirements and culture.

Jette has been an active PDA member since 1998 and has been involved in several activities: Annex 1 Committee (2005/2006); Member of Planning Committee for PDA's Annual Global Conference on Pharmaceutical Microbiology (2006-2008), Co-chair in 2008; Task force revising TR #13: Fundamentals of an Environmental Monitoring Program (2006–2010); Chair for the PDA European Conference on Pharmaceutical Microbiology (2010). In addition, she has presented at several PDA conferences.

She holds a Master Degree in Food Science from 1986 from University of Copenhagen, Denmark.

Personal Statement

As we all know, PDA today is the leading global provider of science, technology and regulatory information and education for the pharmaceutical and biopharmaceutical community. Of course, it should continue in this way to remain beneficial to the members. As the pharmaceutical and biopharmaceutical world develops, PDA must continue to lead this development by developing the right strategies and focusing on the right themes and issues.

If I am elected to the board, I will work for the successful implementation of the Paradigm Change in Manufacturing Operation (PCMO), a dossier prepared by PDA last year. Within these prioritized areas, I am especially focused on "Implementation of Quality by Design in Manufacture," "Capture of Knowledge Management during Commercial Manufacture," "Concepts for Training," "How to Improve Robustness of Manufacturing Processes" and "Risk-based Manufacturing." I believe that if we jointly work for preparing scientifically sound and practical technical information within these areas, it would be very beneficial to the PDA membership.

Furthermore, I would like to strengthen the relationship between authorities and PDA. This also applies to authorities other than the FDA and the European Medicines Agency, and here the BRIC countries (Brazil, Russia, India and China) are of growing importance.

Véronique Davoust, PhD, has over 20 years experience in the pharmaceutical industry, both in Regulatory Affairs and Manufacturing, for Pfizer Inc. In her current position she is responsible for the monitoring and analysis of European emerging regulations and guidelines, especially focussing on Good Manufacturing Practices and registration of the Quality section of Marketing Authorization dossier throughout the product life cycle. Furthermore, she ensures the communication and implementation of the guidelines and regulations within the firm, as well as the coordination of responses to competent authorities. Véronique is a pharmacist and earned a Doctorate in Pharmacy at the University of Rouen in Normandie, France.

Personal Statement

As a PDA member who participates in PDA's conferences and reads its publications, I recognize the high value and the great support offered by the organization. PDA's high scientific and technical level is recognized worldwide. I have been fortunate to be in the planning committee for the PDA/EMA Joint Conference since its creation in 2006 and continue to work diligently on the next edition planned for May 2011. I am also co-chairing the Paradigm Change in Manufacturing Operations (PCMO) Initiative, the goal of which is to drive the establishment of "best practice" documents and training events to aid pharmaceutical manufacturers with the implementation of ICH Q8, Q9 and Q10. The more I am involved with PDA, the more I appreciate the interaction with other PDA members, their great expertise, and the open discussions for exchanging scientific and regulatory information.

PDA has demonstrated that it is an excellent and effective forum for networking and sharing valuable experiences with colleagues from the pharmaceutical industry, making PDA a scientific partner of choice for regulators, especially in the United States and Europe, for establishing sound regulations and guidances. Therefore, it is a pleasure and a real honor to be nominated for a second term to the PDA Board of Directors. I look forward to contributing even more actively to the success and strength of PDA by enhancing PDA's activities in influencing regulations in the Quality/GMP arena, encouraging members' input to these developments and leveraging internal and external communication.

PDA Ballot Opens on Monday, October 18

Please visit eballot.votenet.com/pda to cast your ballot

John Finkbohner, PhD, is the Director of Regulatory Affairs for Investigational Vaccines at MedImmune, where he leads the regulatory team engaged in developing new viral vaccines. He previously spent 13 years in the U.S. FDA, where he performed CMC reviews for BLAs, conducted preapproval inspections and participated in policy development focused on biologics manufacturing. In addition to regulatory affairs, John is an expert in biopharmaceutical and vaccine production and is an accomplished speaker and author in these areas. He has taught for the PDA-TRI and is an adjunct on the graduate faculty at the Johns Hopkins University.

John is a long standing member of PDA. He currently serves as a member of the PDA Regulatory Affairs Quality Committee (RAQC) and actively participates in the PDA Vaccine Interest Group. He also continues in his eighth year as a member of the PDA/FDA Joint Regulatory Conference committee and served as the Conference Program Chair in 2008. John has presented a number of times at both the PDA/FDA and PDA Annual Conferences over the past 12+ years, and he was part of the core organizing group for the PDA/FDA Joint Vaccines Conference, which was held in May 2010.

Personal Statement

I am honored and delighted to be nominated to a position on the PDA Board of Directors. It has been a privilege to work with so many experienced and dedicated professionals through my PDA activities over the years. For many of us, the hallmarks of this great organization are the focus on sound science and the pursuit of actions that advance the efforts of the pharmaceutical community and regulatory health authorities to achieve our shared goal of efficiently getting valuable medicinal products to patients.

The depth and quality of the science found in PDA Technical Reports and other PDA publications inspired me to participate in PDA activities almost 18 years ago. PDA's success is driven by the broad pharmaceutical expertise and continued dedication of the many active members and the professionalism of the permanent PDA staff. It is this combination of knowledge, experience and member involvement that results in the highly-productive and effective organization we all look to as the leader in advancing pharmaceutical science.

We must continue to foster active dialogue with health authorities regarding regulatory science and public policy, while facilitating efforts to harmonize global regulatory requirements and to modernize production processes. I hope to bring my experience and regulatory perspective to the Board of Directors to enhance the ongoing dialogue with regulatory health authorities and to ensure that we maintain those aspects of the PDA that are so successful in meeting the needs of the members.

Lothar Hartmann, PhD, is the Head of Knowledge Management for the Global Quality Department of F. Hoffmann – La Roche.

Lothar has served as Plant Manager and in numerous functions such as Auditing, Quality Systems and External Relations in the Global Quality Department since 1988.

He has spent nearly 10 years as Vice Chairman for the Board of APIC/CEFIC. In this function, he was nominated for the ICH Q7a Expert Working Group. In this effort he received an award from the U.S. FDA. Lothar is currently a member of PDA's Scientific Advisory Board and the PDA Board of Directors. He also chairs the BioManufacturing Working Group of EBE (European Biopharmaceuticals Enterprises) and is chair of the Advisory Board of the GMP Manual. He is the co-author of various documents published by CEFIC/APIC and EBE.

He earned his degree in Technical Chemistry and his PhD from the Technical University of Berlin.

Personal Statement

It is an honor to be nominated for the PDA Board of Directors. PDA, for me, is the premier organization when it comes to combining science and manufacturing practices in our business and when talking about networking between authority and industry representatives. This broad spectrum enables PDA to take the lead in the "state-of-the-art" discussions. Today our industry is entering into a new phase of operation, a paradigm shift laid down in ICH (Q8, 9 and 10). Facilitating this change, PDA has established, under my leadership, a project called Paradigm Change in Manufacturing Operations (PCMO) with 19 working groups and several hundreds of PDA members. The United States, and European authority representatives are highly interested and engaged in this project; with that, we take full advantage of the resources and collective knowledge of PDAs membership and lead the discussions. Continuing this project is an important matter for me.

If I am elected to the Board, I will continue to promote initiatives which benefit our organization and the industry and help lead PDA through these interesting times. I will foster and support PDAs increasing globalization and assist in identifying harmonized manufacturing solutions based on science.

2011 PDA Board of Directors Nominees (Con't)

Stefan Köhler is a Director of Engineering, Maintenance and Utility for the Sterile, Aseptic Production of AstraZeneca. He started his working life as a senior-secondary school teacher, before becoming a technical design consultant for the pharmaceutical and process industry in Sweden in 1987. Stefan has had variety of leadership positions within technology and engineering at AstraZeneca Sweden Operations and has had extensive experience with both sterile and API production. At the start of 2000, Stefan established a new organization within AstraZeneca, focusing on clean room design and contamination control with respect to regulatory requirements and compliance. The new organization has developed a close collaboration with the Royal Institute of Technology. The collaboration has resulted in several research projects that are about to be published through PDA.

Furthermore, Köhler is a frequent speaker at PDA and at R3-Nordic conferences. He has spent the last 10 years in the pharmaceutical industry, specializing in the areas of manufacturing. Köhler is an active member within the PDA and the R3-Nordic.

Personal Statement

I'm pleased and honored to be nominated for a position on the board of PDA. For me, PDA has always been synonymous with science and professionalism, and I will do my very best to uphold these ideals by promoting and encouraging knowledge building and sharing between the organization and the industry. One of my fields of interest is the relationship between technology and regulatory demands. I believe we face many challenges today in this area, such as how to ensure that our technologies are focused in the right areas to ensure safety for patients.

From the broader, long-term perspective, the pharmaceutical industry will be challenged by many factors, including the impact we have on the environment. This, along with patient focus, will continue to be issues long into the future. I believe we need to maintain and increase open discussion and dialogue on these areas.

If elected, I will, from a strategically point-of-view, work to increase business for PDA and the value for the members from a global perspective

My key issue is to forge a greater harmony between regulatory demands and engineering design aspects, supported by clear technical guidelines and research. I will work to develop new technologies and to improve the existing ones into the future and pass that information to all PDA members in different meetings and journals.

Michael (Mike) Sadowski is a Director for Sterile Product Manufacture Support at Baxter Healthcare Corporation in Round Lake, Illinois. He is responsible for international sterility assurance programs in support of pharmaceutical products and medical devices. Mike has 25 years of experience with drug and device sterilization with a variety of sterilization methods including moist heat, ethylene oxide, radiation, and aseptic processing. In addition to participation on the Task Force to revise Parenteral Drug Association (PDA) Technical Report No. 1 on Moist Heat Sterilization, he is the Chairman of the Task Force for the revision of the PDA Technical Report No. 30 on Parametric Release, and serves on the PDA Board of Directors. Within these roles, Mike has successfully brought industry and agencies together to shape best practice and guidance. Mike continues to actively publish and give presentations and training sessions on moist heat sterilization and parametric release. He is actively sought as an expert speaker by industry and regulatory sterilization professionals across the globe. Mike received his B.S. Degree in Microbiology from Purdue University in West Lafayette, Indiana.

Personal Statement

It has been a great privilege and valuable experience for me to serve the PDA membership during my first term as Director. Despite challenging economic times, I believe that our organization has grown stronger through a strict focus on the quality of the products and services that distinguish the value that PDA brings to our membership.

The PDA Chapters represent a significant value proposition to our membership by providing an efficient local venue for the delivery and advancement of the critical knowledge base of science, regulation and technology that are at the core of PDA's mission. During my first term as Director, I collaborated with the talented leaders from the PDA Chapters with the goal of improving chapters through the sharing of best practices in support of PDA policy. One output of our team's effort is the PDA Chapter Handbook which is now being used by chapters across the globe.

PDA fosters the development and dissemination of scientifically sound and efficient practice which helps shape operations and regulations across our industry globally. In support of that endeavor, I have benefited both personally and professionally from the experiences that I have gained while contributing to and leading task forces, training sessions, conference planning committees and the Board of Directors. It would be an honor to continue to serve the PDA membership as a Board Member for a second term.

Please visit eballot.votenet.com/pda to cast your ballot

Susan Schniepp is Vice President of Quality for OSO BioPharmaceuticals Manufacturing, a contract manufacturing organization for sterile injectables. She has 30 years of industry experience in quality control and quality assurance. During her career, she has been responsible for complaints, labeling, investigations, compendial affairs, as well as other quality systems duties. As an active member of PDA, Sue has been a member of the PDA/FDA Joint Regulatory Conference since 2001, chairing the conference in 2007 and 2010. In addition to PDA/FDA, Sue is also a member of RAQC and the Membership Committees and has presented at many PDA venues. In 2009, Sue was the recipient of the PDA Gordon R. Personeus Award.

Personal Statement

It is an honor to be considered for the PDA Board of Directors. PDA is a unique organization because it connects people, science and regulation. I appreciate being part of an organization that accepts and values individual contributions and cooperative team efforts to achieve a common goal. I have been involved with a number of activities with PDA over the last 20 years and have had insight into the value of the organization to my professional career. I believe the organization helps people grow and achieve in a positive manner. In addition to providing a creative environment for its members, PDA also has its pulse on the scientific advancements and regulatory activities that play such an important part in our industry. PDA Technical Reports are some of the most quoted and respected scientific documents used by the industry.

It is because I believe in the activities and goals of the PDA that I wish to serve on the Board of Directors, so I can contribute to helping PDA maintain its uniqueness, while being a leader in addressing scientific and regulatory advances so critical to our industry.

It is refreshing to be part of an organization that accepts and values individual contributions and cooperative team efforts to achieve a common goal.

Glenn Wright is currently the Senior Director of Quality for Eli Lilly and Company's manufacturing and affiliate operations in Italy. He has over 20 years experience in the pharmaceutical industry in areas from development through commercial manufacturing, both for biologic and traditional small molecule products. Glenn received a Bachelors and Masters degree in Microbiology from Southern Illinois University. Prior to his current assignment he served as Director Manufacturing Science and Technology, Director Global Regulatory Affairs, as well as in various other QA and QC management and technical position at Eli Lilly and Company, Amgen Inc. and Pfizer Inc. From 1998 to 2003 he served on the PDA Board of Directors, and has also served on the PDA Science Advisory Board and PDA Program Advisory Board. In addition to these board assignments, Glenn has chaired various special industry working and task force groups for both PDA and PQRI (Product Quality Research Institute) as well as chairing several PDA meetings. In 1998 he received a distinguished service award from the PDA's Southern California chapter in appreciation for his efforts in founding and serving as the chapter's first president. In 2005, Glenn received the PDA's Fredrick J. Carleton Award for his significant contributions to the PDA Board of Directors.

Personal Statement

For me, PDA has and continues to be an organization of great importance built on the strength of its membership. Not only does it allow each of us the opportunity to connect, discuss, debate and work together to find solutions to the challenges facing our industry (providing the science-based answers to the important questions being asked). It also maintains our industry, providing the critical training needed for not only those new to the industry but for all of us, allowing us to keep in step with an every changing environment.

Ever since attending my first PDA meeting some 21 years ago in Washington, D.C., I have always believed that PDA is a unique and special organization with the noble mission of increasing and sharing the knowledge that sustains and improves our industry. Now, having lived and worked outside the United States for many years, I see it even more clearly as I experience first-hand work of PDA across Europe, Asia and the rest of the world. I have and continue to enjoy being an active member of PDA, sharing in its noble mission and working to find the answers to today's tough questions. Serving on the PDA Board of Directors would allow me the opportunity to directly work on ensuring we continue in our mission of shaping PDA's future to equal the success of its past, to always focus on the science and the needs of each of our members.

Science & Technology *Snapshot*

PCMO Risk-Based Manufacturing TF Leader Gives Update

Emma Ramnarine serves as the leader for the Paradigm Change in Manufacturing Operations (PCMO[SM]) task force on Risk-Based Manufacturing (aka, Task Force RO1), which formed late last year. The task force, a small part of the PCMO initiative that is "driving the establishment of best practices" in relation to ICH Q8, Q9, Q10 and Q11, is charged with putting out an approach for implementing quality risk management practices that are grounded on ICH Q9 principles. Emma started her career at Genentech 5 years ago, and earlier this year she took on the position as Head of Global Quality Risk Management for Roche. She has been a member of PDA since 2003.

The *PDA Letter* talked to Emma Ramnarine about her experience so far on the task force.

PDA Letter: Your current position as the Head of Global Quality Risk Management at Roche obviously fits in nicely with the work of this task force. How will the two roles complement each other?

Emma: My current position at Roche as Head of Global Quality Risk Management and the opportunity to lead the PCMO Task Force on Risk Based Manufacturing are mutually beneficial to each other. Since Quality Risk Management (QRM) is one of the newer elements of a Pharmaceutical Quality System, the PCMO effort affords an excellent benchmarking and knowledge sharing opportunity among different participating companies with varying levels of experience and expertise with QRM. As a corollary, my first-hand practical experience of deploying a global QRM program first for Genentech and now continuing for Roche, and that of others participating on the team, is allowing us to ensure that the deliverables generated by this risk based manufacturing task force provide actual practical implementation of QRM for manufacturing operations and as an enabler of the Pharmaceutical Quality System.

PDA Letter: Will you be sharing best practices at your company with the task force?

Emma: Risk management is not an exact science, nor is it a substitute for data. Therefore, there isn't a single right way of implementing risk management even though risk management concepts are fairly standard in the industry. This is both an advantage and a challenge for QRM implementation. Given this, there is tremendous value in participating in an effort like PCMO. The team membership ranges from small to global companies and regulators from the U.S. FDA and Europe. This diversity definitely provides the team a rich environment to

continued on page 13

Technical Report *Watch*

In Board Review: Following technical editing, TRs are reviewed by PDA's advisory boards (SAB, BioAB). If/when approved, the PDA Board of Directors (BoD) makes the final decision to publish or not to publish the document as an official PDA TR. Balloting at each level can take several weeks or longer, depending on the questions posed or revisions required.

- *Technical Report No. 22: Process Simulation Testing for Aseptically Filled Products* **(BoD)**
- *Technical Report No. 3: Validation of Dry Heat Processes Used for Sterilization and Depyrogenation* **(BoD)**
- *Technical Report No. 13: Fundamentals of Environmental Monitoring* **(SAB)**
- *Guidance for Good Distribution Practices (GDPs) for Pharmaceutical Supply Chain*

In Publication: TR is approved and ready for publication.

- *Technical Report No. 51: Biological Indicators for Gas and Vapor-Phase Decontamination Processes: Specification, Manufacture, Control and Use*

Journal *POV*

Our new Snapshot is Journal POV, or point-of-view, which we will be running regularly. PDA Journal Editor **Govind Rao** and his team of associate editors have been providing and obtaining interesting editorials, and we feel it is worth reprinting them in the *PDA Letter* to make sure no one is missing them. To see this and other editorials in the PDA Journal, go to journal.pda.org.

Biosimilars

Anurag Rathore, PhD, Indian Institute of Technology

Biosimilars, also referred to as the follow-on protein products in the U.S., can be defined as biotech drugs that have been shown to have comparable quality, safety and efficacy to the original product. Discussion and resolution of the various scientific and regulatory factors behind approval of biosimilars is perhaps one of the most significant events in the last decade for biotechnology.

There is a strong push for laying out a regulatory path for approval of biosimilars. Healthcare is already one of the largest expenses for developed societies (U.S., Europe and Japan) and is slowly becoming a concern for emerging economies as well. As per one published estimate, the cost of biotech therapies is expected to steadily grow about 30 percent (an approximately 20 fold increase in 10 years) by 2016. Another published study puts the financial savings by the European health care providers from approval of the first wave of biosimilar products at $2 billion. The financial case for biosimilars will continue to serve as the engine for laying down the regulatory framework that facilitates approval of biosimilars in the U.S.

There are some key aspects that make the task of approval of biosimilars more challenging than the traditional small molecule generics, for which the regulatory path is clear and accepted:

- Capital investments (including the operating costs) associated with manufacturing of biosimilars along with the risk of failure for biosimilars are significantly higher than that for small molecule generics. The result is a relatively smaller discount for biosimilars compared to the small molecule generics.
- Seemingly minor changes in manufacturing process have been known to cause significant change in efficacy or immunogenicity of the drug in the clinic.
- Biosimilars are larger and more complex molecules with associated structural heterogeneities when compared to their small molecule counterparts. This is the reason that biosimilars cannot be completely characterized analytically.
- The exact manner in which the numerous product quality attributes of a biosimilar impact the safety and efficacy of the product in the clinic is generally not known completely. In particular, immunogenicity assessments of novel and

continued on page 14

In *Print*

Training Personnel in Micro Labs

The following is excerpted from the chapter, "Training Personnel in the Microbiology Laboratory," by Michele M. Conway, Vectech Pharmaceutical Consultants. The chapter appears in the recently published PDA/DHI book, Laboratory Design: Establishing the Facility and Management Structure*, edited by Scott Sutton. References have been removed for this excerpt, but can be found in the book.*

Evaluating Training

21 CFR Parts 210 and 211 clearly state that training is very important for all personnel working in a cGMP environment, and that includes microbiology laboratory personnel. The next item to consider for the laboratory training program is how to measure the effectiveness of the training program, and how to document employee proficiency with the training material presented.

As working in the microbiology laboratory is a dynamic function, training evaluation should include some type of physical evaluation, such as a demonstration of the skills learned by the trainee. This type of evaluation can be accomplished in a number of ways, but two popular methods are written examination and a hands-on demonstration of proficiency.

Written examinations are simple in concept and are easy to prepare. The trainer can develop the exams from the training materials and then use them repeatedly until the SOPs are updated, at which time the exam would need review and updating as well. Written exams can be saved as a paper file, or can be scanned and saved electronically for employee training records. Written exams though, can only capture what the trainee can remember from reading or from discussion. Hands-on training, in addition to or in place of written examination, can indicate more clearly to the trainer the proficiency of the training candidate.

A hands-on approach to microbiology laboratory training is valuable because microbiology is a hands-on science. Proficiency can be demonstrated by physical performance of tasks required by the microbiologist, with a qualified trainer at hand during the proficiency exercise. Another way to quantify proficiency is to test employees in a number of laboratory functions using an outside source for proficiency examination for routine microbiology skills, such as plate counting, identification, Gram staining, basic math skills, Most Probable Number (MPN), etc. Using an outside source for proficiency testing can be beneficial, too, because the employees do not just physically train on the internal SOPs. In addition, the firm can evaluate the usability of its procedures simultaneously.

The National Registry of Microbiologists (NRM) is a professional branch of the American College of Microbiology within the American Society for Microbiology (ASM). The NRM has

a proven program for certification of professional microbiologists that measures the competency of educated, skilled scientists. A microbiologist can become certified through registration of college courses taken, work experience, and by passing a written exam. The *PDA Technical Report No. 35, A Proposed Training Model for the Microbiology Function in the Pharmaceutical Industry*, makes this point clear by stating that critical to a company's training program is the demonstration of competency in appointed tasks. Proficiency and competency can be achieved by proficiency certification, written examination, and maintenance of current technical and regulatory knowledge through continuing education.

An example of the importance of hands-on microbiology training can be seen in the following example.

Company B is finding coliform bacteria in its Purified Water system. Company B launches an internal investigation to try to determine the cause of the problem. The water system is re-evaluated from end to end, additional system flushing and sampling is performed by engineering and the quality control (QC) technician, duplicate tests are run, and coliform bacteria is still being found. After months of frustration, Company B is feeling pressure to solve the coliform investigation and calls Pharma Consultant M to come and take a look at sampling procedures, testing practices, and so. Consultant M notices that the water sampling program does not have written procedures. In conjunction with Company B, ConsultantMdrafts procedures for PurifiedWater sampling and testing. Consultant Mperforms PurifiedWater sampling side by side with the QC technician so that the sample results can be compared.

After requisite incubation, the QC technician calls Consultant M and reports that coliform colonies are still being detected on the growth media! Consultant Masks, "What color are the colonies on the media? Are they green with a shimmery sheen?" At this point, it becomes clear that the QC technician was never properly trained on the reading of the specialty media, so Consultant M returns to look at the incubated plates.

The "coliform" colonies that were seen on the specialty media were not, in fact, coliform colonies at all. The colonies were reddish-pink with no shimmery sheen, which indicated a typical waterborne microbe routinely seen in Purified Water systems. The Company B QC technician was not trained to read and report results from specialty growth media, and therefore Company B spent a lot of time and money investigating a problem they never actually had.

Training itself is mandatory and just plain necessary for smooth laboratory function, but the recording and documentation of training is just as critical. Several citations have been made with regards to training in *GMP Trends, Inc.*, a semimonthly subscription that focuses on excerpts from actual FDA 483 observation reports by the Food and DrugAdministration (FDA). Listed below are a few examples of recent FDA 483 observations excerpts.

- Employees are not given training in the particular operations they perform as part of their function
- Procedures for identifying training needs were not implemented
- Employee training is not fully documented. Specifically, your firm does not have documentation that employees have received training in all tasks and functions being performed
- Employees are not given training in written procedures required by current good manufacturing practice regulations
- GMP training is not conducted with sufficient frequency to assure that employees remain familiar with cGMP requirements applicable to them
- Employees are not given training in current good manufacturing practices. In addition, cGMP training is not conducted on a routine basis (i.e., at a minimum annually)
- SOP training based on review of applicable written procedures was recorded in some cases to have covered a very large number of written procedures in one day, but there is no documented evaluation to demonstrate adequate proficiency with those procedures

As stated previously, training and training documentation are critical for compliance to cGMPs. As one would expect proper training and training documentation in the production area, formulation, packaging, etc., one would also expect that proper cGMP training in the microbiology laboratory be part of the every day function of the laboratory employees.

Ongoing Training

Training when a new employee enters a new laboratory job function seems pretty obvious. What is also important, and critical, is ongoing training when, for example, new methods become available. Ongoing training and refresher training are key to continued compliance to cGMPs with regard to training requirements. Continuous learning and appropriate documentation of the learning is expected in the laboratory where new methods are being explored, new materials are being introduced, testing is continually improved, etc. Refresher training on updated SOPs is mandatory. If during an FDA inspection, a lab technician performs a testing method using an outdated SOP or has not been properly trained on the changes to the older version of the SOP, the result could be an FDA 483 observation of noncompliance. It is the responsibility of every laboratory manager or supervisor to maintain current and relevant training documentation for each employee working in their lab. The laboratory manager and/or supervisor must also maintain a current training status for continued compliance. Training built in to the laboratory schedule helps to ensure that the training is being updated on a regular basis and that employees remain current in their technical abilities.

Tracking ongoing training with Continuing Education Unit (CEU) based training courses results in guaranteed standards for the provider and ease for the user. CEU-based courses are widely used because they provide evidence of completion

of continuing education requirements mandated by certification bodies and professional societies, and also provide employers with records of the training. A wide variety of CEU-based training courses are available for pharmaceutical microbiologists and laboratory personnel in general through the many professional societies associated with the pharmaceutical and regulated industry fields.

Laboratory Specific Training

The microbiology laboratory typically functions as many smaller subsets of sampling and testing activities. Some lab employees conduct compendial product and process testing, some conduct environmental process control testing in the drug manufacturing area, some train others on gowning techniques, some specialize in microbial identification, etc. For each type of job function in the microbiology laboratory, a written training program should exist with details

continued on page 32

PCMO Risk-Based Manufacturing TF Leader Gives Update, continued from page 10

share their respective experiences, perspective, approaches and QRM program deployment strategies. Everyone on the team, industry and regulators, are very engaged and open in sharing both their best practices and challenges. There is an understanding that we are working towards a common objective of delivering an output from the task force that takes the best of all our experiences and puts out an approach for implementing QRM that is not only grounded on ICH Q9 principles but is pragmatic and scalable such that it can be implemented just as well for a small company as it would for a global company.

PDA Letter: The group started in 2010, what would you count among the accomplishments of the task force since you have headed it? What are your goals for the group?

Emma: The Risk Based Manufacturing Task Force is made up of four distinct teams that are working on multiple deliverables that include implementation details for a QRM program for manufacturing operations and specific case studies. All teams are very active and have made great progress towards these deliverables. The most significant goal and accomplishment of the task force is developing a framework for QRM implementation that brings ICH Q9 concepts to the "executable" level; the case studies will further "demystify" QRM implementation for manufacturing operations through realistic and relevant examples that can be leveraged for different types of manufacturing operations.

PDA Letter: What are the deliverables PDA members can look forward to? Timelines?

Emma: As you might be aware, the current PDA Technical Report No. 44 provides an excellent case study for aseptic processes. The PCMO Task Force R#01 on Risk Based Manufacturing is expanding the concepts presented in *PDA Technical Report No. 44: Quality Risk Management for Aseptic Processes* (2008). The new content will provide "how to" details for implementation of an integrated QRM program for manufacturing operations. The team is making excellent progress and is working towards having a completed draft by the end of this year and getting it published in 2011.

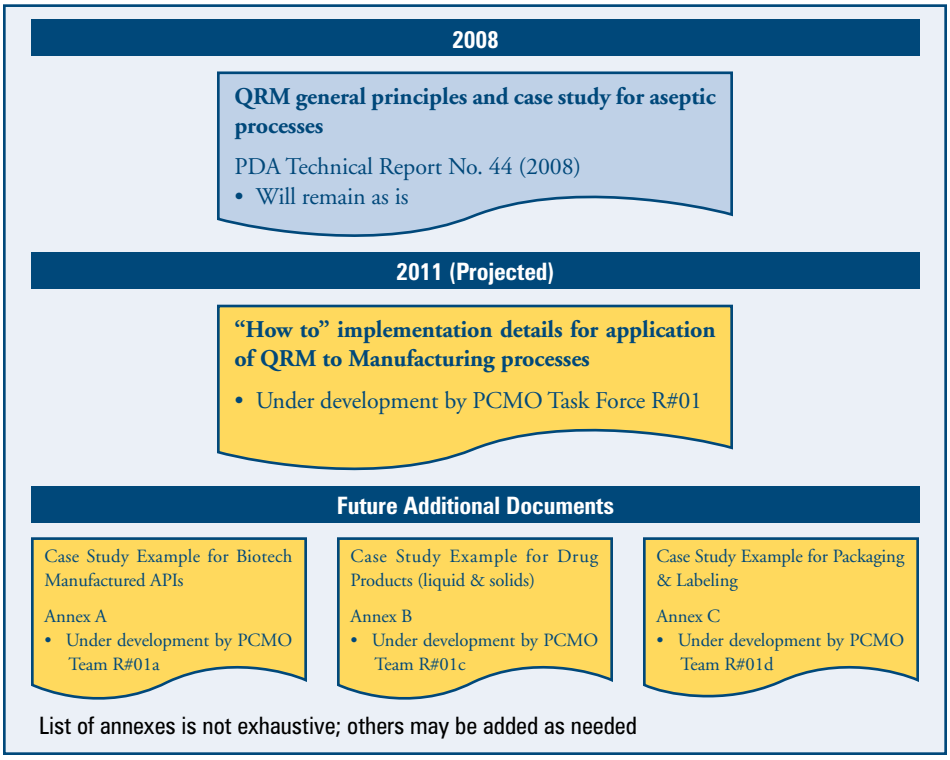
Additionally, there are three supporting teams that are developing specific risk assessment case studies for biotech manufactured APIs, drug product (liquids and solids) and packaging & labeling. The case studies will utilize the concepts discussed in the QRM implementation document and have been selected to illustrate the use of various risk assessment tools for different types of manufacturing operations.

The deliverables from the Risk Based Manufacturing Task Force teams is illustrated in the following graphic.

[Editor's Note: The pathway for publishing these documents, i.e., as Annexes to TR 44 or as separate, in dependant Technical Reports, is still being determined.**]**

PDA Letter: The whole concept of PCMO was developed as PDA's way to help industry implement ICH guidelines. How do you feel the PCMO is doing in

Deliverables of the PCMO Task Force on Risk Based Manufacturing



general meeting those needs so far? How do you feel that your particular task force has done?

Emma: The various task forces under the PCMO initiative have been very thoughtfully designed to develop an "implementable" framework for various aspects of the ICH guidelines. The task forces are still at the stage of developing these implementation details, so it is a little early to determine how the objective of the PCMO in helping the industry implement the ICH guidelines is being met. But I have no doubt that once the deliverables from PCMO have been completed, the industry will have an excellent guide on how to execute on the concepts from the ICH guidelines. For the Risk Based Manufacturing Task Force, this has remained the basic focal point: Deliver a roadmap for implementing QRM per ICH Q9 and integrating QRM into the Pharmaceutical Quality System per ICH Q10. The work from the task force continues to stay true to this focus.

PDA Letter: Where do you think your group fits in with in the other groups? Does your work need to be completed before other task groups work on their projects or would you say that you work in collaboration with the other groups?

Emma: The Risk Based Manufacturing Task Force has identified interdependencies with the deliverables from several other task forces such as establishing a quality management system, technology transfer, process validation to process verification, improving robustness of a manufacturing process, etc. Though none of these interdependencies are pre-requisites to each other and can be developed in parallel, we need to ensure that key concepts contained in the deliverables from these task forces are aligned and leverage each other adequately and appropriately. Identifying these interdependencies in the early development of the QRM implementation document framework has helped our task force in determining the touch points with other teams so we can reach out and collaborate with them at appropriate stages during the development of our respective deliverables.

Biosimilars, continued from page 11

biosimilar products still heavily depend on clinical studies.

In view of the above discussion, it is clear that the regulators have the daunting task of keeping the balance between the financial benefit from allowing approval of biosimilars and the safety of the patients. The European Medicines Agency (EMA) has done a commendable job of successfully creating the regulatory framework that allows for review and approval of biosimilars. This has led to approval of recombinant somatropin, recombinant human epoetin alfa and recombinant filgrastim in Europe. Now that the U.S. Congress has passed a law allowing biosimilars, we look forward to a timely but responsible creation of a regulatory process that can bring them to the U.S. market.

Recent Sci-Tech Discussions: Presence of Mold in Grade C Rooms

The following unedited remarks are taken from PDA's Pharmaceutical Sci-Tech Discussion Group, an online forum for exchanging practical, and sometimes theoretical, ideas within the context of some of the most challenging issues confronting the pharmaceutical industry. The responses in the Sci-Tech Discussions do not represent the official views of PDA, PDA's Board of Directors or PDA members. Join at www.pharmweb.net/pwmirror/pwq/pharmwebq2.html.

Questioner: Hi Forum Members,

Is the presence of mold acceptable in a Grade C room, and what is the acceptable action/alert level? Is the SDA plate needed for environmental monitoring or will a TSA suffice to monitor the total count?

Respondent 1: The amount and presence of mold cannot be easily identified, as it depends upon the type of process you have, what caused the mold, and so forth. Humans carry molds on them and having some mold present at times is not unusual. However, mold also can indicate poor housekeeping practices and that is unacceptable.

Did you originally recover the mold on the TSA?

Respondent 2: As far as I know, the guidelines for monitoring do not differentiate between bacteria, yeasts and molds. If this is the first time that you observed the presence of a mold in your clean room, I would be alert. It could be an incident, but it could also indicate poor hygiene, insufficient cleaning and disinfection, etc. I would not change the monitoring procedure because of this incident but rather take is as proof that your monitoring system is capable of detecting molds.

Respondent 3: I agree, a one time incident is possible. Watch for trends though. If you isolate molds somewhat periodically, there could be a potential problem brewing (HEPA filters, too much humidity or hygiene).

Trends tell the story much better than a single incident.

Respondent 4: Mold spores are a routine and continual problem from a contamination control perspective in clean rooms. Aspergillus and Penicillium spores, for example, can be brought into a clean room on bags, boxes, intervention equipment, raw materials and personnel as part of routine clean room operations. Some molds can be toxic as well, so limits need to be set for mold in the clean rooms based on real time environmental monitoring data and trending. A couple of recent articles on biocidal products that are effective and may be useful are:

Carol Bartnett, Jim Polarine, and Paul Lopolito, "Control Strategies for Fungal Contamination in Cleanrooms Controlled Environments," *Controlled Environments*, September 2007

Jim Polarine, John Macauley, Peter Karanja, Dan Klein, and Abigail Martin, "Evaluating the Activity of Disinfectants Against Fungi," *Cleanrooms*, February 2009, Vol. 23, No. 2

Respondent 5: If the products are terminally sterilized with or even without a bioburden approach, the D-value of fungal spores should be evaluated. That would be of more concern rather than their presence alone.

Respondent 6: In most clean rooms the limit for fungus is "zero" cfus and a limit of cfus is supposed to be for only bacteria. If you get a fungal colony on your settle plate, active agar strip or on the surface monitoring plate; there should immediately be an alarm. Production is stopped, area is disinfected with glutaraldehyde, mincare or similar H2O2/Ag containing aerosols, monitored for 3 days (absence) and then released for production. If your cfu limit is say 10 and if you even get 9 bact colonies and 1 fungus, you are in trouble!

Respondent 7: Sorry, but the cfu applies equally for bacteria, yeast, mold and soybean-casein digest agar routinely passes growth promotion testing for each case of organisms.

Although fungal spores may be transient, the concern is that porous building material with water activities greater than 0.7 may harbor fungal growth leading to chronic fungal contamination

Respondent 8: Sorry for joining a bit late in this discussion. If you repeatedly find mold in your class C, it is just a matter of time before you find it in your B and A critical areas. Find the source and eradicate it. It could be something as hidden as a poorly insulated air duct on which condensation forms and drips onto the ceiling or in the walls of the class C area. You may have quite the mushroom patch growing, I have seen this in several state-of-the-art facilities.

Join the discussion at www.pharmweb.net/pwmirror/pwq/pharmwebq2.html

PDA Interest Groups & Leaders

PDA Interest Groups are divided into five sections by subject matter. This aligns them for improved effectiveness, supports increased synergies and provides the opportunity for Interest Group members to play a more active role in Task Forces. The five sections are Quality Systems and Regulatory Affairs, Laboratory and Microbiological Sciences, Pharmaceutical Development, Biotechnological Sciences and Manufacturing Sciences. PDA's goal is for each group to have co-leaders from the three major regions in which the Association is active: Asia, Europe and North America. Any PDA member can join one or more Interest Group by updating their member profile (www.pda.org/volunteer). Please go to www.pda.org/interestgroups for more information.

SECTION TITLE

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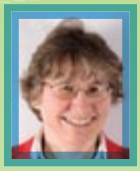

Leesa McBurnie, Senior Microbiologist, *Meissner Filtration Products, Inc.*

Terry Munson, Technical Vice President, *Parexel Consulting*

Mike Sadowski, Director, Sterile Manufacture Support, *Baxter Healthcare*

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Meet TRI Instructor Dave Matsuhiro, continued from cover

comprehend in different ways. This class enables me to use a visual, audible and a hands-on approach. One of the aspects to teaching is to listen, watch and learn from the students. No two classes are the same because of the various backgrounds of the students. It is very important to instruct at the level of the students to keep them attentive and interested.

James: How has your role changed over time?

Dave: For the initial class, I was asked to stay the entire week to assist with several other sections associated with microbiology, environmental/personnel monitoring and gowning. After the first class, I assisted in refining the curriculum. In addition, I was asked to teach various other sections based on my background in the industry, microbiology and engineering. At the end of 2000, Mike Korczynski stepped down as the Director of the TRI, and I became a Co-Lead Instructor. In 2007, when TRI moved to Bethesda, I became the Lead Instructor for the Aseptic Processing Training Program.

James: What do you hope the students take home with them?

Dave: The intent is to provide the students the how's and why's of aseptic processing and to help them understand the concepts, so they can apply them at their facilities.

James: As a consultant, do you feel the problems you see in companies are being addressed by this course? How?

Dave: I believe companies provide sufficient training per SOP for personnel to perform their job functions; however, most people do not have the basic knowledge to thoroughly understand the process. The Aseptic Training Program covers various aspects of the process which gives them a broad base of knowledge in which to build upon. The issues that companies have are very similar, and I believe the class addresses these areas. One of the most important aspects is that the companies do not really understand the problems and implement "band aid" corrective actions as opposed to fixing the root cause.

James: How have the students changed over time?

Dave: The students seem to be more knowledgeable. I think previous Aseptic Processing students were taking the information back to their companies and disseminating the information. Now, those people who learned from those students are coming to TRI and learning.

James: How has the U.S. FDA Guidance for Aseptic Processing impacted the industry and this course since its release in 2004?

Dave: The guidelines are an enhancement from the previous version but still leave a lot for interpretation. This makes it difficult because companies have to deal with various regulatory agencies. The industry has been talking about regulatory harmonization for a long time. This is extremely difficult because within each regulatory agency, auditors have a different interpretations of the requirements.

James: What have you learned while teaching this course that you've taken with you in your role as a consultant?

Dave: Many companies have systems in place; however, they do not really understand the overall aseptic process. Each department has their experts, but very few people comprehend the various pieces to the aseptic puzzle. I try to put myself into their situation and look through their eyes. This enables me to see the big picture, as well as the small details of the process.

James: What do you feel is unique about this course?

Dave: The class was the brainchild of Mike Korczynski. His vision was to develop a Training and Research Institute in which people could learn through kinesthetic training. Prior to this class, there were few, if any, hands-on training for the pharmaceutical industry.

James: What trends do you see across the industry that prompted you to change the content of the course? How did you address these trends?

Dave: The class has evolved significantly since the first one in 1999. As new guidance documents are issued, the class keeps up with all the new requirements. As for trends, the biggest issues are brought about by the regulatory agencies themselves. I refer to it as "Regulatory Creep." Many times, agencies issue observations without really understanding the problem, and a favored outcome becomes an expectation of the agencies, though the initial way the firm behaved was acceptable. I believe that companies should not always accept the observation but challenge them if warranted, as long as companies use good scientific rationale to defend their case.

Also, regulatory agencies want the industry to move in the direction of RABS and isolators based on the risk to the product. I firmly believe that a basic fill line similar to the system used by the PDA Training and Research institute can produce product with the same sterility assurance as the new systems. The caveat being that each

In 12 years of teaching the Aseptic Processing Course, Dave has seen new regulations, new methods, new students and a new TRI facility. Dave lecturing at the facility at the University of Maryland (left); Dave demonstrating smoke studies at in the new cleanroom in Bethesda (right).

company needs to thoroughly understand their process based on airflow, contamination control and aseptic techniques.

James: What is the most rewarding aspect of teaching for PDA?

Dave: The most rewarding for me is when the light bulb goes on for the students. This usually occurs during the second week of the class. They demonstrate, through the media fill process that they understand all the concepts that have been taught over the two-week class. In addition, the students also have a better understanding and appreciation of the overall process and not just their specific area of expertise.

About the Instructor

David Matsuhiro,is the president of Cleanroom Compliance, Inc. Matsuhiro has worked as a consultant for Aseptic Solutions and KMI Systems, specializing in water, environmental systems and aseptic processing. He has also worked for Genentech Inc. in a variety of environmental control positions. Matsuhiro is a member of several professional associations, including PDA, The American Society of Microbiology (ASM) and The International Society of Pharmaceutical Engineers (ISPE). He received BS degrees in Microbiology and Chemical Engineering from San Jose State College. He has taught the following training programs at PDA's TRI:

- Basic Microbiology for Aseptic Processing
- Quality Systems for Aseptic Processing
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Olivia Henderson, Principal Scientist, Container Closure Group, *Biogen Idec*
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Meet the Instructors!

Good teachers are memorable. Good, committed teachers make a difference. Good, committed and expert teachers are why PDA's Training and Research Institute has helped train a generation of industry professionals in aseptic processing techniques, microbiology testing, and a host of other topics. With this issue, the *PDA Letter* begins highlighting TRI faculty. On the cover, we start things off with David Matsuhiro, the driving force behind TRI's well-known aseptic processing course. Below, a sampling of interviews with **Anne Marie Dixon, Frank Kohn, Kirby Farrington** and **Trevor Deeks** to appear in upcoming issues.

Trevor Deeks

PDA Letter: How do you measure your impact on the students you try to help?

Trevor: Sometimes I get follow up from my students, not so much for my philosophy. That is nice to have. People come back and ask for advice, because it means that you've had the right kind of impact. If someone comes to you for advice, it means they respect what you've got to say and that can't be a bad thing. I get a lot from being able to impart my knowledge and my opinions and having people recognize and appreciate it.

PDA Letter: You must be quite dedicated to teaching. Besides your work with PDA in the classroom, you have authored and peer-reviewed books and many papers.

Trevor: I like to think that if I can't influence things in any other way, I can influence people with what I write. The pen is mightier than the sword.

Kirby Farrington

PDA Letter: So you've been involved with PDA Education for quite a long time. That's great! So we've noticed that you teach a number of courses including antimicrobial preservative systems, pharmaceutical water systems, pharmaceutical microbiology and HAACP, which I guess is sort of a newer topic. What about these topics do you, obviously your background is in a number of these, but what excites you about these topics, and why do you teach them in a professional setting?

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 of 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 microbiology contamination control, that type of thing originated in foods to begin with.

PDA Letter: So you come in 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 learned? Was that part of your job?

Kirby: Well, yes. Education is big part of it. I came into Schering Plough right after the merge 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-based automotive products. So I got in there and they said, 'Hey, you are starting a microbiology department.' I said. 'Okay.'

PDA Letter: Have the students changed over time with the available technology or when the get into the little classroom, are they the same?

Kirby: They are still the same. Everybody is still wondering about what is required and how do I do it. Again, the message is you are not alone. You are not floating out there. There are other people doing the same thing you are or trying to do, everybody has the same problems. They have the same questions. Some are a little more experienced, some are working for bigger companies with more resources; but, in the end, everybody has the same objectives they have to meet.

Anne Marie Dixon

Letter: How have you seen the students and the issues you have to address with them change over time?

Anne: Because I have been in the field of training for so long, I'm seeing it revert to the same level of questions that were asked when I started training. The new hires do not have the historical perspective of clean rooms and associated environments, as it relates to design, regulations, operations, etc. This dramatic change in the knowledge base has occurred in the last three years, because we have lost so many senior people in industry through retirement. Some of the mentors that we had within organizations are gone today, so companies are going to be looking at outside consultants and groups like PDA to help fill that gap.

Letter: There is a lot of flux in the industry—companies merging, people with a lot of experience let go, in some cases, and a lot of new people coming in, as well as reduced staff. How am I as a new professional in the field, going to keep up with all of this? How do they go about their daily jobs, as well as keeping up with all of the standards and understanding all of them?

Anne: I think it is very critical that people belong to an organization such as PDA. People will benefit from attending networking sessions and reviewing the technical reports that societies like PDA issue. Another important point is networking—staying connected to other colleagues in other companies. But, today we have severe controls on travel. Many people can't leave their offices. Staffing has been cut and most scientists and engineers do not have time to attend meetings, but web-based training can help fill some of those gaps.

Education is critical in these economic times—we are seeing a result of poor or missing training and education in the quality issues and concerns stated in 483's and warning letters.

Frank Kohn

PDA Letter: You have been a consultant and trainer for about eighteen years, what have you learned during those years that you have applied to your TRI courses?

Frank: I've been teaching classes on various topics related to microbiology quality and manufacturing. I've been in the biopharm/vaccine industry for approximately 28 years and as a consultant for the past 10 years, I believe that you get a lot of different views from being a member, from both participating and teaching classes. You learn just as much from the class many times as you do when you are lecturing. Also, as a consultant, you get the opportunity to see your clients' problems and issues from a practical scientific quality standpoint without any bias. It's their problem and you are trying to work within resolving their problem. By using these experiences, I've been able to integrate this practical experience into my classes, case studies and working with discussion groups.

[Editor's Note: A photo of Frank Kohn was unavailable at time of press.**]**

Authors Wanted!

The PDA Letter is looking for authors for the following topics:

Issue	Topic	Articles Due
January	Advances in Cold Chain Technology	November 12
February	The Latest News on Parenteral Technologies	December 1
March	Knowledge Management	January 1
April	Process Validation – The New FDA Guidance	February 1
June	Top 5 Supply Chain Solutions	March 1
May	Internal Investigations – Finding Out What Went Wrong and What to do about It	May 1
July/August	Sterile Products/Aseptic Processing	June 1
September	Pharmaceutical Microbiology	July 1
October	Cross-Over Moves: Insights from Recent Industry Recruits from FDA and FDA Recruits from Industry	August 1
Nov/Dec	Reports from the PDA/FDA Joint Regulatory Conference	October 1

Send articles to Emily Hough, hough@pda.org.

Need Training? Give TRI a Try

Emily Hough, PDA

Developed in 1997, the PDA Training and Research Institute facility was created in Baltimore, Md. by former PDA President **Mike Korczynski**, PhD, to give hands-on, intensive, job-focused training that could be brought home and applied on the job. It offered a broad curriculum designed for students to enhance their professional development. Now, 13 years, and roughly 19,000 students later, the only difference is that the PDA TRI facility has moved to Bethesda, Md.

TRI boasts over 100 instructors, who are all subject matter experts in the fields in which they teach

The training and education at TRI is done on a global level, and fosters career-long learning and professional development. Customized training has been provided to agencies all over the world, including the U.S. FDA, the European Medicines Agency, the Irish Medicines Board, the MHRA, the Italian Inspectorate, the Kazakhstan Ministry of Health, the Russian Ministry of Health, PIC/S, as well as individual pharmaceutical companies and company executive management.

According to **Bob Dana**, Senior Vice President Quality and Regulatory Affairs and PDA Training and Research Institute, "[The facility] is a replica of a commercial clean room where our students can learn in a risk free environment. No product or commercial facility is at risk, as the students get to learn new skills and practice them. We also have supporting laboratories and equipment which allow us to provide hands-on learning in aseptic processing technology, biotechnology, environmental monitoring, filtration, microbiology, quality/regulatory affairs, training, validation and specialized topics such as Visual Inspection and Cold Chain."

A fundamental part of TRI is the courses it offers. TRI's broad curriculum was designed for students to enhance their professional development and is large enough to be effective, but small enough to tailor its courses to a group's needs.

TRI's courses are unbiased since they conform to the standards set by the Accreditation Council for Pharmacy Education (ACPE). New courses are planned by regularly monitoring the landscape of the pharma/biopharma industry to see what the hot topics are. Dana said, "We often survey our members to solicit their ideas and recommendations. They are out there where the rubber meets the road, so to speak, and see first hand where there is a need for more education to help the industry address emerging technological or regulatory issues."

The TRI staff tries to plan courses at PDA Conferences that are consistent with the theme of the conference. Dana said that this strategy provides people attending a conference the opportunity to stay on for a day or two and take advantage of the learning opportunities, while saving their company money–two benefits in one.

TRI offers over 120 courses covering topics in:

- Aseptic processing
- Biotechnology
- Environmental monitoring
- Quality/Regulatory
- Training
- Validation
- Specialized areas, such as Lyophilization, Prefilled Syringes, Transportation of Temperature-Sensitive Pharmaceutical/Biopharmaceutical Products and Visual Inspection

TRI boasts over 100 instructors, who are all subject matter experts in the fields in which they teach. Instructors are picked to teach courses byPDA's Advisory Boards, (BioAB, RAQC and SAB) and Interest Group leaders recommendations. Existing faculty provides recommendations for new instructors and course topics as well. In addition, **Rich Levy**, Senior Vice President, Scientific and Regulatory Affairs for PDA, is asked for suggestions and recommendations from the various Science and Technology task forces who are preparing PDA Technical Reports.

"We are very fortunate to have a cadre of subject matter experts (SME) to serve as our faculty," Dana said. "These people are out doing the work in the subjects they teach on a daily basis. They have 'been there, done that, got the tee shirt' and are most anxious to impart their knowledge and the lessons they have learned to the students they teach. We are fortunate to be able to draw on their experience as faculty members."

Dana concluded, "I would just stress to all our members and prospective students the importance of continuing their education on a regular and ongoing basis. I've been around this industry for a long time and I understand the importance of economic drivers. However, I also know that with the fast paced growth of technology and the expansion of our industry into new areas, education and knowledge is critically important to ensure long term success. The next time you are in the Washington, D.C. area, give us a call. We are proud of our facility and would love to have the chance to show it to you. Better yet, think about enrolling for one of our courses and experience what TRI has to offer first-hand. I look forward to seeing you soon."

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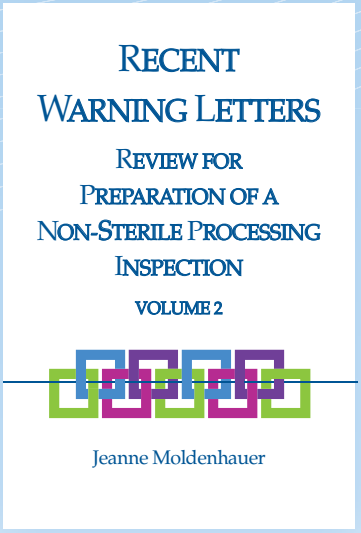
New Release at the PDA Bookstore



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By Jeanne Moldenhauer

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- Equipment Design, Size and Location
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Challenges in Aseptic Production of Sterile Biologics

Miriam Estrano

In the ideal parenterals manufacturing world, thousands of units are filled in an isolator by an automated robotic arm. The units are then terminally sterilized in a validated, well controlled load configuration and transferred using a conveyor belt for second packaging, labeling and distribution. Quality Assurance (QA) reviews the batch records, environmental monitoring data, sterilization data and release tests. For product release, QA may wait to receive sterility test results or apply an alternative such as parametric release. In this ideal scenario, QA is able to release the batch with a 10-6 sterility assurance level (SAL).

For most biologic parenterals, the production process is considerably more complicated than this ideal scenario in terms of sterility assurance levels. By their nature, most if not all biologicals cannot undergo terminal sterilization, since the currently available processes would result in denaturation or destruction of the active substance. Furthermore, biological starting materials are inherently variable with regard to their quality characteristics and often represent potential microbial food substrates. As such, these types of products provide unique challenges with regard to designing a production process that provides an acceptable and reproducible sterility assurance level.

Biologics are substances used in the prevention, treatment or cure of diseases or injuries of man and are prepared from or with the aid of a biological process rather than a chemical one. The first step in production of many biologics involves the use of living material, such as cells and tissues. Downstream steps may include isolation, purification and final formulation of the bulk drug substance (the active pharmaceutical ingredient) into finished drug products. These processing steps introduce special challenges in contamination control of the biologic product and careful planning to detect and prevent, mitigate or eliminate contamination risks is required. The drug product must be sterile and within specified limits for microbial components, such as endotoxins, particulates and other official compendia tests. Contamination in a parenteral product is catastrophic to manufacturers, as patients may be harmed, the product can be recalled and regulatory actions may follow.

Ideally, manufacturers implement a complete interrelated contamination control plan that includes facility and equipment design, qualification, maintenance and sanitization or sterilization to provide sterile, aseptically processed biologics for the patient and comply with regulations. Some of the controls and systems included in this plan are:

- Environmental monitoring
- Aseptic process simulations (e.g., media fills)
- Disinfectant qualification using isolates from the facility and process
- Cleaning validation
- Qualification of training of operators in aseptic manipulation skills.

Some firms fail to provide a complete, interrelated contamination control plan where systems interact to reduce contamination risks and where process and product understanding is evident. This lack of oversight may cause inadequate control and consequent production failures. These deficiencies often result in additional regulatory scrutiny and actions including product withdrawal from the market and warning letters.

Challenges

One obvious challenge in contamination control of biologic parenterals is that most biologics are adversely affected by heat and will not withstand the high temperatures (> 121°C) necessary for removing microbial contaminants by terminal sterilization.

Sterility assurance level is a term used to describe the probability of a single unit being non-sterile after the sterilization process. These levels of sterility assurance are observed in validated terminal sterilization processes.

Since most biologics cannot withstand being terminally sterilized, they are processed aseptically. The acceptable SAL for aseptically filled product is 10-3, meaning that the probability of 1 out of 1,000 filled units may be contaminated.

Another challenge in preventing microbial contamination is that the growth medium (such as DMEM) used in cell culture contains nutrients to support cell growth. As such, it is also supportive of contaminating microbial agents' growth.

Long processing times complicate microbial contamination control further. Continuous cell culture may take several weeks, and in some cases months, where perfusion methods are involved and contamination may be introduced during manipulations or via contaminated feed lines.

Many biologics production processes require human intervention and sometimes involve open manipulations. Automation, such as isolators or restricted access barrier systems (RABS), may not be cost effective when the process involves small batch size.

Additionally, a short shelf life is a characteristic of biologic drug products. In some instances, such as with Dendreon's cellular therapy sipuleucel-T, the product may have as little as an 18-hour expiration. USP/EP sterility tests require a 14-day incubation period; the results of these compendial drug product sterility tests will not be available prior to batch release.

All of these challenges contribute to the most critical obstacle in aseptic production of parenteral biologics–preventing contamination and assuring sterility of the final product.

Solutions

Some straight forward solutions to the individual challenges listed above include the use of:

1) Closed systems that are free from human intervention during processing ➤

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2) Rapid microbiology methods (RMM) to assess product sterility (see **Table 1**)

Table 1 Challenges in Production of Sterile Biologics and Possible Solutions

Challenges	Solutions
Short shelf-life: pharmacopeial test results not available prior to batch release	RMM, cryopreservation, parametric release
Heat sensitivity: inability to achieve 10-6 SAL by terminal sterilization	Isolators, RABS, Blow-Fill-Seal
Long processing times: higher risk of contamination	PAT, closed systems
Intensive manual interventions: higher risk of contamination	Isolators, RABS, Blow-Fill-Seal

However, to ensure a unified approach to contamination control, it is important to use a systems-based approach.

The regulatory authorities and industry have progressed a long way in their approach to cGMP, moving away from product-based quality control to process-based quality assurance. In the former approach the focus is on defect detection, whereas today's approach focuses on defect prevention. More recently, the U.S. FDA introduced a new system-based approach to product quality where the focus is on science based risk management (see **Figure 1**). This new paradigm is called Pharmaceutical cGMP's for the 21st Century and was introduced in 2002.

Figure 1 Changes in approach to cGMP.

The focus shifts from product-based quality control (defect detection) to a process-based quality assurance (defect prevention) to a science-based risk management quality system.

Imagine a house of cards (see **Figure 2**); the bottom row represents quality systems, the second row are environmental factors, the third row, operations, and the top row makes up product quality.

The first step in contamination control of an aseptic process is to understand the individual elements of the manufacturing process and to design quality into the process. When designing these systems, it is essential to take account of environmental factors and operational requirements. This three-layer model is the basis for product quality conforming to its sterility assurance requirements. Just like a house of cards, which is very fragile, the failure to maintain any single element of an aseptic processing control strategy can bring down the entire structure; the results are much different, however, because the latter failure results in a non-sterile product and severe harm to the patient, as well as economically damaging the responsible company.

Systems that promote process understanding include Quality by Design (QbD) and Process Analytical Technology (PAT). QbD requires that process and product characteristics are designed to meet quality specifications and quality attributes, respectively. Using PAT, the process is continuously monitored and analyzed. The process may be adapted to allow for consistent quality throughout the product life cycle. At the present, the principles of QbD and PAT have been slow to be accepted and adopted by biologics manufacturers, mainly because of the challenges presented by the complexity and inherent variability of biologics that hinder the identification of those process and product characteristics that impact product quality. For example, there may be lack of linkage between bioactivity measurement and chemical potency.

When applying the principles of QbD and PAT to biologics, it is imperative to use risk management. A few methods to identify risks include Failure Modes and Effects Analysis (FMEA), Hazard Analysis and Critical Control Points (HACCP) and Fault Tree Analysis (FTA). FMEA, as well as HACCP, identifies potential failure modes based on past experience with similar products or processes, while FTA is used to analyze a single fault event.

Risk identification complements the development and improvement of quality into both the process and product by enabling manufacturers to focus on individual process steps with a higher risk of contamination. Risk is a function of the severity of impact (S), the probability of occurrence (O) and the probability of detection (D). It can be described in the following formula: Risk = SxOxD. Therefore, to mitigate risk, efforts should focus on reducing the severity of impact, minimizing the probability of occurrence and increasing the capability of detection. However, for biologics, as for all parenteral products, the impact of contamination is always severe. It is a go/no-go acceptance criterion, since detection of only one microorganism will result in product rejection.

As a result, minimizing the probability of occurrence and increasing capability of detection is required and can only be achieved ➤

Figure 2 House of cards model

Quality systems are the foundation for product quality. Important contributors to product quality are environmental factors and human interventions and these must be assessed and included in the quality systems.

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Table 2 Risk Rating

Rating	Severity (s)	Occurrence (O)	Detection (D)
1	No impact on safety/ effectiveness	Low probability	Will be detected prior to release
2	May impact safety/ effectiveness	May occur	May be detected
3	Impacts safety/effectiveness	High probability	Will *not* be detected prior to release

with complete process understanding and continuous monitoring of quality attributes. Process and product understanding, coupled with risk assessment and risk management is a powerful tool that can be used to increase quality and sterility assurance level of biologics produced by aseptic processing. Refer to Tables 2 through 4 for an example of risk management at a biologics production facility.

In **Table 2**, the company assigns risk rating. In **Table 3**, the company assesses risks and calculates Risk for each identified hazard. In **Table 4**, risk mitigation is applied to each identified hazard.

Table 3 Risk Assessment

#	Potential Hazard / Failure Mechanism	Potential Cause	Potential Source	Severity (S)	Occurrence (O)	Detection (D)	Risk (S*O*D)
D1	Cell culture contaminated during scale up	Media was contaminated	Contaminated media feed bottle	3	3	2	18

Unique Challenges for Implementing Quality Systems

Aseptic processing of biologics has a number of associated special challenges. These include sensitivity to sterilizing heat, long processing times, short shelf-life and increased sensitivity to microbial contamination. As such, these types of products provide unique challenges with regard to designing a production process that provides an acceptable and reproducible sterility assurance level.

The cGMP regulations require implementation of quality systems intended to prevent and control contamination. Failure to use process and product understanding in the design of these systems may result in limited and inadequate contamination control. Risk management is essential in complementing process and product understanding. Unfortunately, there can be no universal solution to the challenges of contamination control confronting biologics manufacturers. It is essential to understand the process and product and to assess critical process parameters and their impact on quality attributes, to allow for better control of the production process. While some biologics manufacturers have employed advanced technological solutions such as isolators, RABS and robotics, others continue to operate with systems such as biosafety cabinets, which provide a lower degree of sterility assurance levels. In the past few decades, several systems have been introduced to facilitate better process and product understanding such as QbD and PAT. Unfortunately, the applicability and implementation of these systems to biologics have not been broadly embraced despite the potential for improvements on process control and enhanced sterility assurance in products.

Table 4 Risk Mitigation

#	Severity (S)	Risk Management- Mitigation & Verification	Residual Risk			
			Occurrence (O)	Detection (D)	Risk (S•O•D)	Accept Code
D1	3	Decrease dirty hold times Increase CIP/SIP frequency PAT – add PH check points	2	1	1	6

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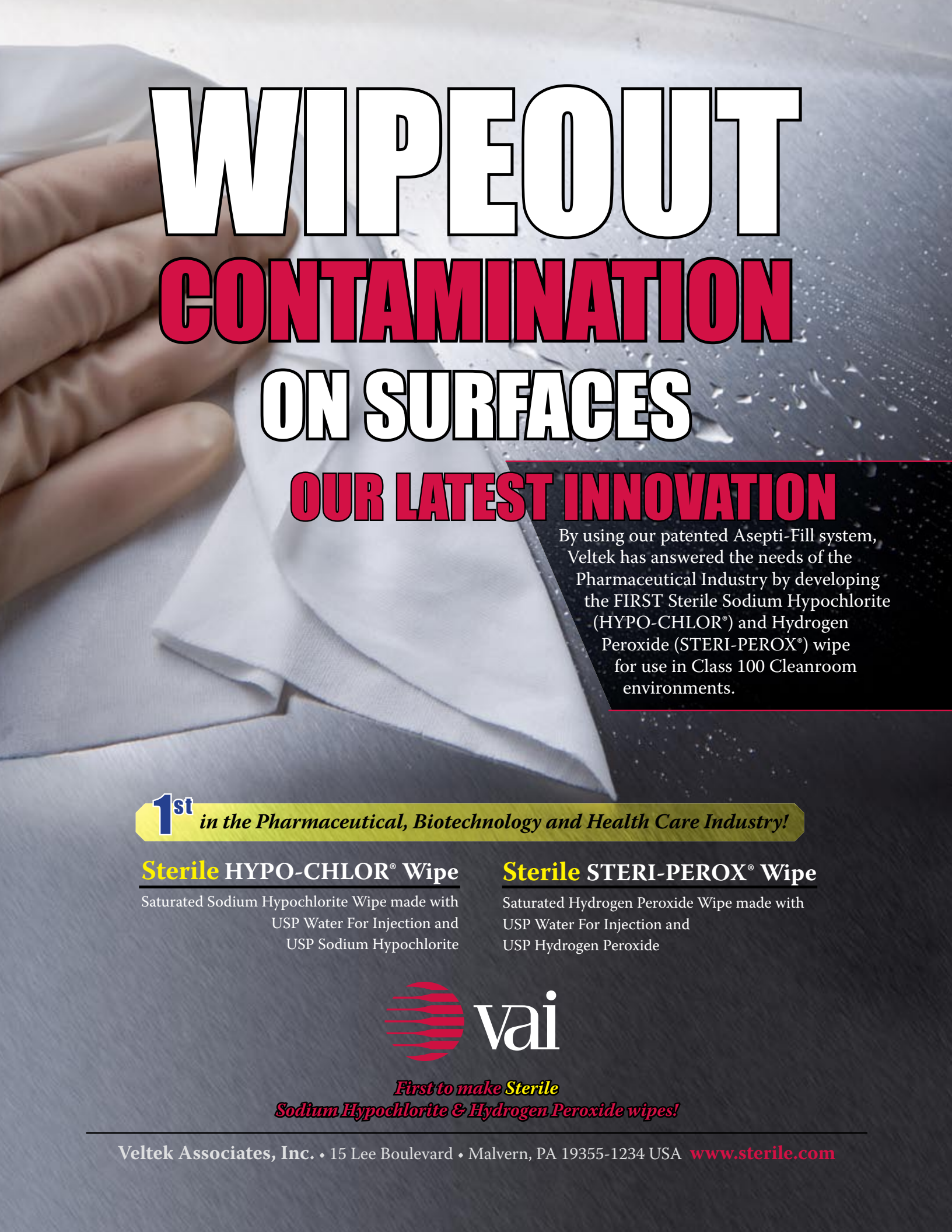
About the Author

Miriam Estrano works Medtronic's Spine & Biologics Orthobiologics Compliance division as a Compliance/Audit Specialist. She previously worked at TiGenix as the Head of Quality Assurance and Quality Control. She is also on the *PDA Letter's* Editorial Committee.

Miriam would like to thank Mike Parker, her mentor and good friend, for his continuous support and guidance.

The views expressed in this article do not necessarily reflect the views of Medtronic.



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PDA Requests Scientific Discussion on CMC Draft Guidance

For the comments grid, visit www.pda.org/regulatorycomments

31 August 2010
Katerina Bursikova, Scientific Administrator
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European Medicines Agency
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Reference: Guideline on the Requirements for Quality Documentation Concerning Biological Investigational Medicinal Products in Clinical Trials, draft
(EMA/CHMP/BWP/534898/2008, 18 February 2010)
Deadline for comments: 31 August 2010

Dear Dr. Bursikova,

PDA is pleased to provide comments on this important draft CMC guidance. Our comments were prepared by an expert committee of members with practical expertise in the science, development and manufacture of biological products. We have attached a table in the EMA format that lists both our general and specific comments. Our general comments cover four concerns including: level of information, phase related information, use of prior knowledge, and storage time vs. shelf-life of drug substance. Please see the table for supporting details.

PDA proposes to have a scientific discussion with EMA representatives on the setting of re-test date/expiry date for biotechnological/biological drug substances/drug products. Such a discussion will allow consideration of the complex technical issues related to this topic. Please see the comment table for supporting details.

Again, we appreciate the opportunity to support the development of high quality CMC guidance. PDA is ready to provide support for any activities or discussions that are helpful in furthering the usefulness and interpretation of this guidance. For questions, or to pursue a scientific discussion on re-test date/expiry dates, please contact myself or James C. Lyda of the PDA Staff (lyda@pda.org).

With very best regards,
Georg Roessling, Ph.D.
Senior VP, PDA Europe

Training Personnel in Micro Labs, continued from page 13

on what types of written and hands-on proficiency testing shall be conducted before the employee is allowed to perform those functions for cGMP applications. Cross-training is very important, too, for laboratories running on a low headcount. Any employee who could conceivably cover for another scientist in the lab shall perform the requisite training to be able to perform that function. This training shall be properly documented, and shall be performed before the need to switch functions is presented. Training "on the fly" in the laboratory is not an acceptable practice. Proper planning and regularly scheduled training in the laboratory should help to make that type of situation avoidable.

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 http://www.pda.org/regulatorynews.

North America

Agency Releases Annex 11, 12

The U.S. FDA has released two guidances that recognize the interchangeability between the local regional pharmacopoeias. The two guidances are entitled: *Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 11, Capillary Electrophoresis General Chapter* and *Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 12: Analytical Sieving General Chapter.*

Agency Draft Guidance Recommends Residual Solvents Limits in New Animal Drugs

A U.S. FDA draft guidance entitled *Residual Solvents in New Veterinary Medicinal Products, Active Substances and Excipients (Revision) VICH GL18(R)* recommends acceptable amounts of residual solvents in new animal drugs for the safety of the target animal, as well as for the safety of human consumers in the case of those animal drugs intended for food producing animals.

The draft guidance updates a final guidance on the same topic and was prepared for veterinary use under the auspices of ICH.

Comments should be submitted by October 18.

Bill to Strengthen Manuf. Quality Standards, Enhance FDA Power

A bill has been introduced (S. 3409) that strengthens manufacturer quality standards, enhances FDA's ability to protect Americans through improved tracking of foreign manufacturing sites, and gives the FDA authority to recall potentially dangerous drugs.

The *Drug Safety and Accountability Act of 2010*, sponsored by Senator Michael Bennet, D-Colorado, would provide FDA with additional recall power, as well as other enforcement options to respond appropriately to violations. The bill would provide tools such as:

- Granting FDA the authority to assess civil penalties for violations of the Food, Drug and Cosmetic Act and to subpoena documents and witnesses;
- Facilitating exchange of information between the FDA and other regulatory agencies
- Protecting industry whistle-blowers that wish to bring information to the FDA

These tools would allow FDA to investigate threats to drug quality and safety.

Europe

MHRA Requiring Inspectors to Assign Risk Rating to Sites

The MHRA is starting to require inspectors to use inspection outputs and a number of other factors to identify a risk rating for a site. This rating will determine future inspection frequency. The process is being introduced on a rolling basis, and it will be two to three years before all sites will have been formally assessed.

Risk ratings can change following inspection resulting in either increased or decreased risk. Inspection risk ratings will not be published by the MHRA and there will be no formal process of appeal against risk ratings and future inspection frequency. However, any rating that results in an increased inspection frequency from the previous standard will be peer reviewed before conclusion by a GMP Operations Manager or a GMP Expert Inspector.

The MHRA does have a formal complaints process if sites wish to log an issue, however any concerns regarding the inspection process should be raised with the inspector in the first instance.

Questions or comments on risk-based inspection should be addressed to your inspector in the first instance.

Key Regulatory Dates

Comments Due:

October 18
Comments should be submitted for the Agency draft guidance on residual solvents limits in new animal drugs

EMA and U.S. FDA Seeking Candidate Companies for Joint GMP Inspection Pilot Program

The European Medicines Agency (EMA) and the U.S. FDA are seeking potential candidate companies for a joint GMP inspection pilot program for manufacturers of medicinal products.

The overall objective is to see whether greater international collaboration can help to distribute inspection capacity by allowing more manufacturing sites to be monitored and reducing unnecessary duplication.

Companies that have submitted in parallel two equivalent marketing authorization applications for the same medicinal product to both the EMA and FDA can request to participate in the pilot program for joint pre-approval inspection should such an inspection be considered necessary by both agencies.

Companies can also participate in the pilot exercise by hosting a single join re-inspection (routine surveillance) where both the EMA and the US FDA have separately planned routine surveillance inspections (re-inspections) to take place within a similar time period at a manufacturing site of a medicinal product authorized in the United States and in the European Union.

Companies that wish to participate should contact either gmp@ema.europa.eu and/or CDERInternationalGMP@fda.hhs.gov.

PDA TOOLS FOR SUCCESS

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Go to www.pda.org/careers for the latest opportunities.

The Art of Finding More Time

TIME is money. We've all heard it before, but these days it bears repeating. Yes, it's *always* been important for workers to make sure that they're doing the right things and staying on task, but in shaky economic times it's a matter of survival (your own, career-wise, as well as your company's). Yet nearly all of us are guilty of sabotaging our performances to some degree because we fail to go on the offensive against two specific threats: disorganization and poor time management.

Well, that's true, you might agree. *I know that I sometimes get my priorities mixed up, and that I lose one minute here and there. But I'm just a regular Joe—not an efficiency or organizational expert. How can I improve the way I spend my time?* There's no doubt about it: organization and time management are essential for job stability, career advancement and contribution to your company's well-being.

Here are some ideas to help you take control of your time and boost your own hourly value:

Learn to Live by the 80/20 Rule

Generally speaking, only 20 percent of the things you spend your time doing produce 80 percent of the results you want to achieve. Yes, you read that correctly! To maximize your productivity, you need to identify the key 20 percent activities that are most effective and prioritize them.

To get started, take a look at how you currently use your time. What do you spend most of your day doing? How many things on your to-do list get checked off? Then, identify what you'd *like* for your 80 percent—your results—to look like. Once you know where you stand and where you'd like to go, reflow your priorities and focus the first fruits of your time and energy on achieving them.

Prioritize, Prioritize, Prioritize!

Prioritizing definitely falls into the "easier said than done" category. After all, there are so many responsibilities that have to be met and so many "what-ifs" are involved in each decision. It's enough to give anyone a headache, so most of us simply manage by putting out the fires that are burning brightest instead of drawing up battle plans for tomorrow, next week and next year.

If you want to tap into your productivity's full capacity, though, you've got to know exactly what's in front of you and what's coming—and you also need to know in no uncertain terms which ones should be done in which order. In that way, you can progressively work through all the minor tasks that lead to the greater steps that, in time, lead you to achieving your goals.

Divide (And Conquer!) Your Documents

For many workers, the amount of papers and emails that cross the desk on a daily basis is nearly overwhelming—and figuring out how, when and if you should address them can take up more time than the actual tasks themselves. To make sure that you don't drown in a sea of memos, directives, spreadsheets and more, you need to figure out immediately what to do with each one.

Whether you're dealing with physical papers or electronic documents, you have four options to consider whenever something new comes into your possession: *Act on it, file it away to be acted on later, delegate it to another* or *toss it*. That's it. Make it your goal to touch (or click on) each document only once before putting it into one of these categories. This will ensure that you handle each item as quickly, efficiently and accurately as possible. (And guess what? The boldest move you can make is to be honest with yourself about what you can and will make time for—and then having the courage to pitch everything else.)

Make Your Desk a "No Parking" Zone

This may come as a shock, so brace yourself: your desk isn't a storage area or a catch-all… it's a workspace! Remember, less is more. The more pictures, notes, boxes, tools and so on that park themselves on your desk, the greater your odds of being distracted. What's more, a topsy-turvy desk translates into greater stress and the misleading feeling that you have all the time in the world to complete your projects. And let's face it: clutter is never conducive to good thinking.

Be brutal. Remove everything that isn't absolutely necessary from your desk. Put family photos on your credenza or bookcase. Store your stapler and tape in a desk drawer. And don't be afraid to pitch what you don't use. If you haven't touched something in a year and it doesn't have sentimental value, get rid of it. You'll be amazed by how much a clear workspace promotes a clear mind!

Ask Very Specific Questions

We've all experienced data overload—you might have felt as though your head would explode if you tried to cram one more number, date, spec, or explanation into it! Sometimes this avalanche of data finds you regardless of what you've done… but other times, you invite it

through a lack of specificity. When you ask a vague question—or one that does not include the salient details—the answer is likely to come back in a variety of forms, most less than helpful.

Specificity cuts out confusion and extraneous detail. When you ask a question, make sure to communicate precisely *why* you need to know the answer, and what its purpose is. For example, instead of asking, "What is our company's current payroll burden?" you might ask, "What is the average monthly amount we're paying in pretax salaries (no benefits) in all our U.S. operations? I don't need a breakdown, just one number." You'll find that one number much easier to deal with than a 92-page listing of employees and a breakdown of their salaries and benefits!

Guard Your Domain Against Time Encroachers

Being successful in time management means adhering to your schedule… which happens through controlling interruptions. Essentially, you need to think of your workday as a fortress to which *you* control access. No, you shouldn't become a hermit… but you *should* be on your guard against people and situations that pull you away from your goals, dreams, objectives, and schedule.

So, how do you discourage "invaders" from coming around? Try closing your office door for starters or putting a post-it on your cubicle that reads, "Busy—do not disturb!" Also, be proactive in choosing the ground on which you engage others. Reach out to coworkers and collaborators so that they don't drop in on you. Schedule as many meetings ahead of time as possible. Discipline yourself to check your email once every hour (if realistic) instead of every five minutes. Remember—it's *your* time… so make sure you're in charge and not at the mercy of others!

Make Preemptive "Appreciation Strikes"

Unless you work in a vacuum, you'll inevitably have certain clients or contacts who suck up a lot of your time and energy because they want to be involved in every step of the process or because they're just friendly by nature. To cut down on their well-meaning but workflow-disrupting interruptions, employ a preemptive appreciation strike!

Send a handwritten thank-you card for their business or for their birthdays. Make a (brief!) call to them on a regular basis. Deliver added value for your services by, for example, forwarding articles of personal or professional interest. Most likely, you'll find that these individuals will be quite content with your relationship—and they won't be constantly pestering you in order to improve it.

Plan your procrastination

You've known how disastrous procrastination can be since grade school. If you leave something to the last minute, you're stressed, and your task may not be accomplished satisfactorily… or at all! Nevertheless, it's a stark fact that you can't do everything at once—some things you simply have to put off.

The secret to successful procrastination is to do it deliberately, based on the time you have and the status of the tasks. Take a look at what's on your plate and choose the tasks that are the least time-sensitive and least at-risk and then postpone them for a bit. In other words, allow yourself to procrastinate—but give yourself a deadline by which to complete those tasks. Taking your time can sometimes be a good thing—decisions made in haste or tasks completed under pressure might result in a damaging outcome.

Capitalize on the Carrot-Or-Stick Principle

Remember when you were a kid and you had a chore to do? "Clean your room now, and you can stay up and watch a movie," your mom said. "If you don't, you're going straight to bed after supper." Well, that approach still works today. The nature of humans is to move away from pain and toward pleasure, so when you're setting up a prioritized plan, use the carrot-or-stick approach to motivate yourself toward accomplishment.

When you feel the urge to procrastinate, what you need is an incentive (the carrot!) to keep pressing on. For example, promise yourself a latte and a scone *after* you turn your proposal in to your boss—or on a larger scale, plan a Caribbean vacation as a reward for completing your freelance writing project! On the other hand, don't forget about the stick. Failing to meet your responsibilities always has consequences. They may be immediate or delayed, but they'll always come—so figure out and remind yourself of what they are.

Check in With Yourself Every Friday

One way to determine how effectively you're managing your time is to check your results by tracking them on an ongoing basis. Each Friday evening, perform both a weekly review that focuses on the past week and a periodic review of where you stand in relation to your overall goals.

This is a time for you to replay the tape of the week, looking at the highs and lows. What problems and distractions did you face? What made you want to pull your hair out? On the other hand, what worked well? Which days proceeded smooth as silk? And most importantly, what were the differences in those days besides the outcome?

As for the periodic review, look back over your job description, key responsibilities, and the ways in which your performance and success are measured. Then ask yourself how well (or if!) you're meeting those responsibilities and expectations. In spite of side tasks that pop up and tangents that present themselves, it's essential to remember why you're "there" in the first place.

In the end, we all have the same amount of hours in our days—but we don't all use that time equally well. However, if you take control of managing your time and organizing your resources, you'll be assured of using them in a way that you really want to—and you'll reap a return that fulfills your life and attracts successes. It all boils down to this: know what your time is worth. And invest it wisely!

About the Book

Thriving in the Workplace All-in-One For Dummies® is available at bookstores nationwide, major online booksellers or directly from the publisher by calling (877) 762-2974.

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Volunteer Spotlights

www.pda.org/spotlight

Daikichiro Murakami, Advisor, Taikisha

PDA Join Date: 1994

Areas of PDA Volunteerism (Years of Participation): PDA Japan Chapter (more than 16 years); Medical Device Committee Chair (2006-present); Compendial Conference in Frankfurt Co-chair (2008); the Visual Inspection Conference in Berlin Chair (2009).

Interesting Fact about Yourself: I have been interested in regulatory and technological subjects on Pharmaceutical Process Engineering and Electronic Records and Electronic Signatures (ERES) on 21 CFR Part 11. Therefore, I became a Chair of the ERES committee during 2002-2005, when ERES was a hot issue in Japan; and I became a Chair of the Kansai Study Group (KSG) committee during 1998-2001, as well as within the PDA Japan Chapter. Both committees have been focused in technological discussions from the aspect of Pharmaceutical Process Engineering, which is my main expertise.

Why did you join PDA and start to volunteer? To deeply understand GMP and enlighten younger engineers in aseptic processing.

Of your PDA volunteer experiences, which stand out the most? My proposals to the "Guidelines" for terminal sterilization and aseptic processing, as well as on pharmaceutical waters for the pharmacopoeias. Next, my experiences being the committee Chair of the KSG, ERES and Medical Device Committees within the PDA Japan Chapter have stood out. I would have to say Co-chairing the Compendial Conference in Frankfurt in 2008, Chairing and speaking at the Visual Inspection Conference in Berlin in 2009, and giving more than ten speeches at various meeting including the PDA Japan Chapter Annual Meeting have also made an impact to me in my volunteering experience.

How has volunteering through PDA benefited you professionally? It has allowed me to have the contacts in order to have tripartite technical discussions with international friends. As a PDA member, I have acquired and accumulated worldwide information of pharmaceutical science and technology from the regulatory, industry and academic viewpoints. Information gleaned in such a manner helps me in my activities in the above volunteer operations, which has also contributed to the Japanese guidelines on the revisions of Pharmaceuticasl Waters of JP, Aseptic Processing for Manufacturing Products and Terminal Sterilization, as does being a member of the study groups under Ministry of Health, Labour and Welfare.

Which PDA event/training course is your favorite? The PDA/FDA Joint Regulatory Conference and the PDA/EMA Joint Conference.

What would you say to somebody considering PDA membership? By joining, you'll receive key international and information sources that are easily exchanged with highly professional people.

Ano Xidias, Senior Consultant, PharmOut Pty Ltd

PDA Join Date: 1996

Areas of PDA Volunteerism: Joined PDA Australian chapter committee (2006-present); Current PDA Australian Chapter President (2010-present)

Interesting Fact about Yourself: I come from the land down under (Australia), where there are many strange animals and sports we call our own. One such sport is cricket, which I have played since I was very young. I have played at the same club for 40 years and am currently still playing; we'll see for how long. I am proud to be the club's president and provide opportunities to people of all ages and abilities to participate and enjoy the game.

Why did you join PDA and start to volunteer? Having been introduced to the pharmaceutical industry over 20 years ago as an enthusiastic microbiologist, there was a huge learning curve for me to gain knowledge of the industry, regulations and guidance that were present and developing at the time. I was fortunate to have people willing to educate and mentor me, which provided opportunities to me to ask questions and learn. PDA was another source of relevant, leading-edge information and opportunity to continue to learn and meet quality people. Volunteering is an opportunity to continue the learning process and meet people; but more importantly, it helps provide similar, up-and-coming enthusiastic individuals another avenue to learn.

Of your PDA volunteer experiences, which stand out the most? Without question, the recent Quality Risk Management two-day workshop in May 2010 that was held in Australia. It took six months and a dedicated team to bring it together. Over 200 delegates, presenters, including 16 TGA (Australian) regulators of which seven were also presenters. The opportunity to co-host and participate at the event was a tremendous highlight.

How has volunteering through PDA benefited you professionally? It has provided me the opportunity to meet people of various backgrounds and knowledge of the industry with differing opinions or perspectives. Not right or wrong, just different. Volunteering continues to provide a chance to learn from many other sources.

Which PDA event/training course is your favorite? I have been extremely fortunate to be a part of the QRM workshop in Australia. The PDA Annual Meeting in March 2010 in Florida was *the* event. Meeting PDA representatives, people from around the world with common professional interests and attending the various presentations over the course of the event was special.

What would you say to somebody considering PDA membership? You have a wealth of global knowledge and information available at your finger tips. Press that button and join today. No regrets.

Recipients of the 2009 Honor Awards

www.pda.org/2009honorawards

The honor awards have been presented to esteemed PDA members since the first award was given in 1958. It is our intention to highlight each of the 2009 Honor Award Winners (announced at the 2010 Annual Meeting in March) in each upcoming issue of the *Letter* until the 2011 Annual Meeting. This month we have chosen to spotlight the individuals who were awarded the Frederick J. Carleton Award.

Frederick J. Carleton Award

Presented as a tribute to lifetime contributor Fred Carleton, this award is designated for a past or present Board member whose services on the Board are determined by his/her peers as worthy of such recognition.

Vince Anicetti

Vince has been active as a leader in PDA for many years, serving first as President of his local chapter (the West Coast Chapter), and more recently, as a Director and finally as the Chair of the Board of Directors. He has long been a champion of local chapters and worked diligently to increase their visibility and importance within PDA. This has proved to be a significant benefit in connecting with our membership and developing our future leaders.

During his term on the Board of Directors, Vince played a key role in bringing stability to our association. He helped to refocus the organization on its core strengths of science and regulation and rebuild a strong financial foundation.

Yoshihito Hashimoto

Yoshihito is a Senior Consultant at Chiyoda Corporation, Japan. He has been a director of PDA for six years since 2003. He is one of the four members who established PDA Japan Chapter in 1991. Since then he has organized the Technology & Education Committee in Japan Chapter for 18 years with Dr. Morikawa, National Institute of Public Health, and Dr. Hiyama, National Institute of Health Sciences.

Enhance Your Job Search Through PDA's Career Center

Hassana Howe, PDA

Did you know that the PDA Career Center can provide tools and services that can help you enhance your job search?

On this site, you can:

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- Sign up for personal job alerts. These help notify you by email of new jobs that match your search preferences. Create one now and never miss an opportunity!
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Please visit all the career resources and tools at www.pda.org/career.

The Parenteral Drug Association presents:

2010 Pharmaceutical Freeze Drying Workshop

Current Science and Technology of Lyophilization

NOVEMBER 15-18, 2010

SHERATON SAN DIEGO HOTEL & MARINA | SAN DIEGO, CALIFORNIA

Lyophilization technology has permitted the development of many drugs and diagnostic reagents that cannot be commercially produced and distributed in aqueous solutions because of required quality standards for performance, safety and shelf life. **As a result, this has driven the health care industry to develop and implement lyophilization to produce quality and user friendly products with robust and efficient process in a rapid and dependable manner.**

To carry this out, the type of development, practitioners of lyophilization development and implementation must be skilled in the adaptation of a wide range of scientific, engineering and quality principles. Gain these skills at the *2010 Pharmaceutical Freeze Drying Workshop!*

Confirmed speakers include:

Enrico Corona, Formulation and Process Development Manager, *Patheon Italia S.p.A.*

Fred Lim, PhD, Principal Engineer, *Genentech Inc.*

David Doleski, Team Leader, CBER, DMPQ, *FDA*

Edward Trappler, President, *Lyophilization Technology, Inc.*

Shanker Gupta, PhD, Program Director, Pharmaceutical Resources Branch, NCI, *National Institute of Health*
Sharon Thoma, PharmD, National Expert Pharmaceutical Investigator, *FDA*

Plenary sessions include:

- Advances in Lyophilized Health Care Products: Past, Present and Future
- Product and Formulation Design
- Aspects of Process Development
- Industrialization of Lyophilized Products
- Quality of Lyophilized Products
- Current Regulatory Expectations

PDA's Training and Research Institute will be hosting a pre-workshop course, *Fundamentals of Lyophilization* on November 15-16.

Register by **October 7** and save **$200**!

www.pda.org/freezedry2010

PRE-WORKSHOP COURSE NOVEMBER 15-16 **WORKSHOP** NOVEMBER 17-18 **EXHIBITION** NOVEMBER 17-18

Chapter Contacts

The following is a list of the PDA Chapters, organized by the regions of the world in which they are located. Included are the Chapter name, the area(s) served, the Chapter contact person and his or her email address. Where applicable, the Chapter's website is listed. More information on PDA Chapters is available at www.pda.org/chapters.

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James Aldrich, Aldrich Group
Beverly Asbury, Genentech
Renata Assis, New England Student Chapter
Donald Balogh, Sanofi Aventis
Garth Bennett
Paul Bezy, Genentech
Jeff Boesiger, NNE Pharmaplan
Derek Bruce
Oz Cabiri, LaModel
Philippe Callegari, Merck Sharp & Dohme
Michael Cane, Westwood + Wilshire
Maritere Carattini, Pfizer
Merri Carlson, ALK Abello Source Materials
Edward Catton, Eli Lilly
Joanne Challinor-Rogers, Dentsply
Geraldo Chua, Alk-Abello Pharmaceuticals
Russell Ciliento, Pfizer
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Shannon Coleman, Hach Company
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Matthew Eggers, W L Gore & Associates
Abigail Eyer, GlaxoSmithKline
Jason Fernandez, Pfizer
Thomas Fisk, Alpha Insights
Monica Frechette, Shire HGT
Pamela Froelich, Eli Lilly
Koichi Fujiwara, Clean Mechanical
Takayuki Fukuyama, Mitsubishi Tanabe Pharma
Taro Furukawa, Shin Nippon Air Technologies
Fernando Gallegos Sola, Biomerieux
Hector Garcia, Particle Sciences
Melvin Gaskins, United Therapeutics
Valeria Giannelli, Pfizer
Ruth Gould, Gilead Sciences
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Reenie Jackson, Genentech
Claudia Jacobs, Eli Lilly
Tiffany Jenneke, Paddock Laboratories
Christopher Johnson, Genentech
David Jones, Eli Lilly
David Alan Kapitula, Roche Technical Operations

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Scott Kellogg, Jabil

Joe Keoghan, Elan Drug Technologies

Ian King, Pfizer

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Shankar Kunjir, Genzyme

Hiroshi Kyogoku, Clean Mechanical

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Meng Lip Lim, Schering-Plough

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Robert Magina, Sanofi Pasteur

Karen Marshall, Avid

Tom Martin, 3M

Kimura Masako, Senju Pharmaceutical

Anthony Massina, New England Student Chapter

Hajime Matsumura, Takeda Pharmaceutical

Jennifer McCann, Baxter Healthcare

Paul Metz, Agilent Technologies

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Pascal Van Der Cruyssen, Baxter

Darren Varney, Genzyme

Paul Villanueva, Genentech

Douglas Wachtmann, Parker Hannifin

Toby Walrath, GlaxoSmithKline

John Wass, Commissioning Agents

Jane Wastl, Eli Lilly

Stephanie Winstead, Sandoz

Kalvin Yim, PharmAthene

Lloyd Yu, Planet Biotechnology

Jean Pascal Zambaux, Disposable-Lab

Audrey Zaweski, Lachman Consultants

Katherine Zipfel, Eli Lilly

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

Knowledge Management Focus of 2011 Annual Meeting

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

Meeting Co-chairs Christopher J. Smalley, PhD, Merck and Marsha Hardiman, Avrio Biopharmaceuticals

Many of us have received training in how to *protect* intellectual property, but how do we develop, nurture, record and share our intellectual property to be more efficient and more effective to make a better quality product or improved process?

Your best performing people are hungry to perform better. Hanging around the coffee pot to swap experiences and lessons learned is being replaced with tweets and other techniques. We all know how good people can make a poor, even a bad, process work, and they are sharing this information to achieve this. But how do we ensure that the organization captures this information or perhaps more importantly the interpretation of this information?

Join us for several beautiful spring days along the River Walk in San Antonio, Texas from April 11-15, 2011, as we hear well-researched and presented papers by experts in the topic of knowledge management, share experiences with colleagues who are confronted with the same issues as you, visit with vendors that are designing solutions to these issues, and network across organizations to expand your knowledge and understanding.

Session topics will include:

- **Development Science:** Advances in dosage form delivery systems, automated sterilization technologies, contamination control/facility management control, cell culture/line development.
- **Manufacturing/Process Science:** Aseptic processing, automated manufacturing systems, barrier/isolators/RABs/blow fill seal/robotics, building management and control.
- **Quality Science:** Compliance monitoring and trending, environmental monitoring, LIMS and lab management systems, microbiological methods and trends.
- **Outsourcing:** Quality contract and agreement development, transfer of critical information and knowledge, audit of suppliers, supply chain integrity.

This program will also have something entirely new!

The program committee prides itself on obtaining breakthrough and innovative presentations on leading "hot" issues that are advanced and sophisticated. But, we recognized that many organizations are in transitions, with lead operations,

supervisors and managers who may be new to their roles and responsibilities. So we have created a module that will be presented on Tuesday, April 12 that will consist of **Basics and Fundamentals**. Topics will include sterilization, aseptic processing, cleaning, contamination control, microbial/analytical testing, documentation.

The exhibition will be held April 11-12, and PDA's Training and Research Institute will be offering courses in conjunction with this meeting on April 14-15.

We hope to see you at the meeting! For more details about the *2010 PDA Annual Meeting*, and to register, please visit www.pda.org/annual2011.

Best Practices for Moist Heat Sterilization Presented

Chicago, Ill. • December 6-7 • www.pda.org/moistheatworkshop

Mike Sadowski, Baxter Healthcare Corporation

The leaders from PDA's moist heat sterilization task forces have developed a workshop that will summarize best practice and essential content from three technical reports that were developed as companion documents to PDA's flagship sterilization reference, Technical Report No. 1, (Revised 2007), *Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Qualification and Ongoing Control.* This workshop presents a unique opportunity for sterilization professionals, as well as professionals from other supporting functional competencies to gain first-hand knowledge from the experts on the contemporary moist heat sterilization concepts. The workshop program and format was assembled to provoke active group discussion with a focus on the sharing of best practices and experiences from regulatory and industry perspectives.

Moist heat sterilization processes are the oldest and most dependable processes that have been used in sterilize pharmaceuticals and medical devices for many years. Accordingly, regulatory authorities across the globe not only prefer moist heat sterilization processes, but also further acknowledge its superiority by formally recognizing and approving moist heat parametric release programs that do not require the 14 day sterility test for sterile product release. The program content for this workshop will highlight the fundamentals of a scientifically sound moist heat sterilization program that can be utilized to support parametric release.

The workshop will commence with a review of the critical principles addressed in TR-1to set a foundation of science that will be steadily leveraged in subsequent sections of the program. This session will summarize basic and advanced microbiological and engineering concepts to ensure alignment between these important disciplines in the development and operation of a moist heat sterilization program.

Based on the scientific foundation provided in the opening, the essentials of a parametric release program will be discussed. In addition to the industry perspective presented in this session, **Terry Munson**, Technical Vice President, Parexel and an invited U.S. FDA speaker will provide invaluable insight on this topic with support from many years of regulatory experience.

Important considerations in the development of user requirements will be stressed to ensure that moist heat sterilization process equipment, which includes both autoclave and Steam-in-Place systems, is properly designed and capable. Strategies for the development of the moist heat cycle will be presented followed by a summary of verification and validation approaches used to confirm that moist heat process efficacy requirements are met. To address the age-old concerns regarding sterilization of filter configurations, **Leesa McBurnie**, Senior Microbiologist, Meissner Filtration Products, will provide her expertise in a focused discussion aimed at overcoming this challenge. This section also will emphasize the fundamentals of maintaining the validated state of SIP or autoclave systems and processes.

The workshop will conclude with a presentation on Post-Aseptic Fill Lethal Treatment, which has been added to the program to provide background and up-to-date information from a recently-commissioned PDA task force. This presentation will address an emerging approach to further reduce sterility risks associated with aseptic processes.

A panel discussion will occur at the conclusion of the conference providing an additional opportunity for attendees to further interact with the speakers ensuring that all questions have been answered.

If your job responsibilities include direct or indirect support of moist heat sterilization programs, and you want to keep up-to-date on current best practices and evolving topics on this widely practiced methodology, our workshop has been developed to meet your specific interest. In addition to the value proposition of the content from this highly interactive workshop, attendees will also discover that December is one of the best times of the year to experience all that the great city of Chicago has to offer.

On behalf of the program planning committee and speakers, I would like to invite you to attend and look forward to your participation in the *PDA Technical Report Workshop on Moist Heat Sterilization* in Chicago on December 6-7. To learn more about the workshop and to register, please visit www.pda.org/moistheatworkshop.

Learn About Energy Efficient Pharmaceutical Manufacturing

Web Seminar • December 1 • www.pda.org/webseminars

A web seminar on how liquid desiccant dehumidification systems protect product integrity and property assets at pharmaceutical facilities will be presented by **Peter G. Demakos**, President, Kathabar Dehumidification Systems, and **Brian Demers**, Lead Applications Engineer, Niagara Blower Company on Wednesday, December 1, 2010 from 1–2:30 p.m. EST.

The presentation, entitled, *Energy Efficient Temperature, Humidity, and Microbial Control for Pharmaceutical Manufacturing with Liquid Desiccant Dehumidification Systems* will be given as part of the PDA web seminar series.

The presentation will cover how liquid desiccant dehumidification systems can deliver clean, temperature and humidity controlled air for applications, including, capsule forming & drying, hard shell filling, pan coating, sterile filling, spray & powder drying, tablet compression and product packaging. It will also cover how dehumidifiers provide critical bacterial control by capturing most airborne bacteria, viruses, and mold.

For more information or to sign up, visit www.pda.org/webseminars.

Mitigate the Risk of Adventitious Viruses

Bethesda, Md. • December 1-3 • www.pda.org/adventitiousvirusworkshop

Program Planning Committee Member Sherri Dolan, Sartorius Stedim

The *PDA/FDA Adventitious Viruses in Biologics: Detection and Mitigation Strategies Workshop* is currently being organized as a result of recent viral contamination events, which have occurred in the biopharmaceutical industry. This workshop is intended to encourage modernization in industry with respect to:

1) Viral detection and control measures
2) Gaps in our current ability to detect, control and clear adventitious viruses
3) Availability of emerging technologies in areas where gaps exist
4) CGMP expectations for adventitious virus detection and control, as well as consequences for noncompliance

The workshop will provide an engaging forum for regulatory, industry and academic colleagues to discuss and integrate current and emerging strategies for controlling virus contamination for product safety. It will be held on December 1-3 in Bethesda, Md., and will discuss current and updated manufacturing practices and processes designed to mitigate the risk of adventitious virus contamination in biologics. It will also highlight the U.S. FDA's regulatory expectations for product quality and purity with respect to adventitious agents.

Anthony Lubiniecki, Senior Fellow, Large Molecule Portfolio Management, Centocor R&D, will give the keynote presentation on the historical perspective of viral contamination in biologics. He will discuss the need for reevaluation of existing assays and consideration of emerging technologies and mitigation strategies for assuring safety in biologicals.

The workshop will have sessions on current regulatory approaches, case studies of viral contamination to emerging technologies in viral testing. There will also be a session on process design strategies for prevention of viral contaminations. This session will describe the application of the concepts described in ICH documents Q8, Q9, and Q10 to the control of adventitious viruses

In addition, two important aspects of adventitious virus control will be addressed during the workshop at the facility control and GMP expectations session. It will clarify CGMP requirements and enforcement actions available to the Agency designed to ensure that manufacturing standards for the control of adventitious viruses are met at the time of approval and over the product's life cycle. It will also describe approaches for the control of adventitious virus contaminations

There will be a wrap up session on lessons learned throughout the workshop; a moving forward session on best practices to mitigate the risk of virus contamination of parenteral products; and a "Ask the Experts" panel discussion for any outstanding issues participants still have questions on.

In order to delve deeper into specific areas of interest, six breakout sessions are planned where there will be a panel of experts to moderate the discussions. Session topics include:

- Elimination or treatment of high risk of raw materials
- Regulatory Expectations for CGMP
- Current Virus Detection Methods
- Emerging Technologies for Virus Detection
- Case studies of viral contamination
- Decontamination Methods

The *PDA/FDA Adventitious Viruses in Biologics: Detection and Mitigation Strategies Workshop* Program Planning Committee has planned a information packed workshop where there is a unique opportunity to hear from the regulatory agencies regarding topics of interest in mitigating the risk of viral contaminations. Every professional in our industry

involved with the development, manufacture, testing, and improvement of biopharmaceutical products should find the discussions engaging and relevant to current events.

For more information, visit www.pda.org/adventitiousvirusworkshop.

Aseptic Processing Issues and Approaches

Bethesda, Md. • November 15-16 • www.pda.org/asepticprocessingworkshop

Conference Co-chair James Agalloco, Agalloco and Associates

The production of sterile products using aseptic processing is one of the more complex and technologically challenging of sterile in the healthcare industry. Products manufactured in that manner receive the closest scrutiny from both producers and regulators. Changes in regulatory expectations and the resultant technological responses have begun to change the way in which aseptic processing is performed. The changing paradigms of the more novel production methods have made it difficult at times to reconcile them with existing and emerging regulatory expectations. A continual exchange of information between industry, suppliers and regulators is essential to ensure the best possible outcome for the patient. PDA has supported this dialogue with meetings and conferences where participants discussed the ramifications of the changes in methods and goals that we have all been faced with.

PDA's last targeted effort in this area was in May of 2008, in Bethesda, Md., on *Aseptic Processing and Risk Management*, which provided an initial look at the issues and concerns. That meeting highlighted the many challenges facing our industry related to the mitigation of risk associated with the manufacturing of sterile drug products by aseptic processing. The meeting included presentations from industry and regulatory thought and opinion leaders to review means for enhancing patient safety through innovation in aseptic production methodologies and risk control. Numerous issues were identified and discussed relative to the application of novel technologies for aseptic processing. The conference introduced aseptic processing risk assessment and mitigation as a critical component for fostering further improvements in operating methods. The conference concluded with much agreement, but there was a general consensus that additional conferences would serve to benefit all in understanding the challenges that lie ahead of us.

PDA has developed the *2010 PDA Workshop on Aseptic Processing: Issues and Approaches* that will be held November 15-16 in Bethesda, Md. to further the dialogue that was begun. This second meeting will provide a contemporary perspective on aseptic processing practices, include several new topics and emerging concerns. The sessions will include presentations by regulatory and industry experts; however, the emphasis will shift towards technological solutions as opposed to problem identification. The meeting will include presentations on parametric release, post aseptic lethal treatments, sterility by design, control of interventions, quality systems, aseptic process simulations and validation, manual aseptic processing, modeling and other topics.

This meeting will review the approaches needed to improve aseptic processing methodologies using technology and procedural refinements to better match the ever tightening expectations for patient safety. It will also restart the dialogue that began in 2008 between industry and regulators on the measures needed to advance aseptic processing practices and ensure patient safety. The areas this meeting will explore include:

- Aseptic process designs that will fully satisfy the CGMP requirements of 2010 and the next decade
- The impact of FDA's draft Process Validation Guidance with respect to the validation of aseptic processing
- The use of post aseptic-fill lethal treatments for sterile products that can't tolerate more aggressive terminal sterilization processes
- Methods for the evaluation of operator interventions on aseptic processing
- The proper execution of manual aseptic processing to best assure product sterility
- Emerging technologies and concerns issues that impact can sterility assurance

We have added breakout sessions on aseptic processing technologies, process simulation and process monitoring & testing. These give the attendee an opportunity to provide their insights and suggestions in these critical areas. The breakouts will be repeated to allow attendees the opportunity to hear two different discussions.

It is essential that industry and regulatory professionals play a cooperative role in continuing to improve the means for aseptic processing. For this to happen, regulatory expectations and production capabilities must be aligned to assure maximum performance with minimum risk. It is our joint responsibility to assure that future methods are as robust and as consistent as possible to assure patient safety without undue requirements. This meeting is an excellent opportunity to become aware of the emerging ideas, technologies, issues and future direction. Your attendance and active participation can help ensure a better capability for aseptic processing than previously possible.

For more details on the workshop and to register, please visit www.pda.org/asepticprocessingworkshop.

New Courses Still Available in Final Months of 2010

James Wamsley and Stephanie Ko, PDA

While the end of the year in approaching, the PDA Training and Research Institute is offering new lecture and laboratory courses to offer in the last two months of 2010.

Two new biotechnology courses can be found in our upcoming New Brunswick Course Series; there are five total lecture courses to choose from. Or, if you prefer a more in-depth, hands-on course, visit us at our training facility in Bethesda, Md., for the new five-day laboratory course, "Quality Systems for Aseptic Processing."

At the completion of this two-day course participants will be able … to participate in developing a risk mitigation program

The New Brunswick training courses will be held at the Heldrich Hotel from November 16-18 in New Brunswick, New Jersey and will feature a range of lecture classes from microbial issues to APIs. The laboratory course, "Quality Systems for Aseptic Processing," will take place in Bethesda, Md. from December 6-10.

Taught by experienced TRI instructors, the New Brunswick training course series offers five courses:

- "cGMP Training for Sterile Manufacturing" (New Course)
- "A Risk Based Approach to Technology Transfer" (New Course)
- "Principles of Effective Quality Auditing"
- "Microbiological Issues in Non-Sterile Manufacturing"
- "Active Pharmaceutical Ingredients – Manufactures and Validation"

Frank Kohn, President, FSK Associates, will be teaching the two new courses, "cGMP Training for Sterile Manufacturing," and "A Risk Based Approach to Technology Transfer." Kohn's course on sterile manufacturing will provide sterile manufacturing personnel the knowledge and skills required to understand not only the specific GMP regulations governing sterile production but an understanding of the reasons and scientific principles behind the regulations.

Kohn's other course on technology transfer will focus on the various risk analysis techniques, methods, and tools for optimizing a successful technology transfer program. Specific examples such as transferring products from site-to-site and global locations will be discussed. At the completion of this two-day course participants will be able not only to describe the value of using risk analysis methods to identify risk issues in manufacturing processes; analyze the value of risk analysis; master using risk analysis tools for future use, but will be able to participate in developing a risk mitigation program.

Judith Torres, Global Quality Consultant, Eli Lilly, will teach the "Principles of Effective Quality Auditing." This is an introductory course for new auditors who are or will be involved in performing quality assurance audits of quality systems. Torres' class will teach the auditing cycle with a step–by–step guide to "putting the pieces of the puzzle together" using different technical tools.

The next two-day course will be taught by **Dan Gold**, President, D.H. Gold Associates, on "Active Pharmaceutical Ingredients – Manufacture and Validation." His in-depth course is designed to give the participant a thorough foundation in manufacturing operations related to the production of APIs. In the course, every aspect of plant operations will be covered, including how to manage the relationship with the regulatory authorities. Attendees will take away the ability to discuss the regulatory and compliance issues associated with the manufacture of APIs; analyze and improve the organization of their process development, personnel training and manufacturing programs, as well as to demonstrate use of several tools to formulate the validation programs commonly required for the manufacture of APIs.

The final course in the series, "Microbiological Issues in Non-Sterile Manufacturing," will be taught by **Kirby Farrington**, Coordinator Microbiology Teaching Labs, Biological Sciences, Auburn University. This one-day course will discuss various issues in non-sterile manufacturing including setting of specifications, process development, holding times, reservation, cleaning, sanitization and approaches to evaluating recovered organisms.

Following right behind the New Brunswick Course Series, a new five-day laboratory training program, "Quality Systems for Aseptic Processing," taught by **Hal Baseman**, Chief Operating Officer and Principal, ValSource, **David Matsuhiro**, President, Cleanroom Compliance and other industry leading experts with over 100 years of combined experience, will offered at TRI in Bethesda, Md. This course will give tools that are necessary to optimize Quality Systems associated with Aseptic Processing. This course combines the three modes of learning; Visual, Auditory and Kinesthetic with almost 50% laboratory interaction to maximize information retention. Risk management; sterility by design; troubleshooting and solving sterile filtration issues; investigations and CAPA; and how to effectively implement change within a structured regulated environment will be covered in this course.

For information on these and other TRI offerings, visit www.pdatraining.org.

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Upcoming 2010 Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

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October 2010

14-15: Biennial Training Conference Course Series
Baltimore, Maryland | www.pdatraining.org/BiennialCourses

20-21: PDA's Universe of Pre-filled Syringes and Injection Devices Course Series
Las Vegas, Nevada | **www.pda.org/Pre-filled2010**

26-29: Contamination Control
Bethesda, Maryland | **www.pdatraining.org/Contamination**

26-27: Fundamentals of D, F and z Value Analysis
Bethesda, Maryland | **www.pdatraining.org/DFandZ**

Register for both courses and save $500

28-29: Validating a Steam Sterilizer
Bethesda, Maryland | **www.pdatraining.org/VSS**

28: PDA's 5th Annual Global Conference on Pharmaceutical Microbiology Course Series
Washington, D.C. | **www.pda.org/Microbiology2010**

November 2010

3-4: Bioassay Development and Validation
Bethesda, Maryland | **www.pdatraining.org/BioassayVal**

4: Developing a Robust Supplier Management Process
Bethesda, Maryland | **www.pdatraining.org/SupplierManagement**

15-16: Fundamentals of Lyophilization
San Diego, California | **www.pdatraining.org/Lyophilization**

16-18: 2010 New Brunswick Course Series
New Brunswick, New Jersey | **www.pdatraining.org/NewBrunswick**

17-19: Practical USP Microbiological Test Methods
Bethesda, Maryland | **www.pdatraining.org/USPTestMethods**

December 2010

6-10: Quality Systems for Aseptic Processing
Bethesda, Maryland | **www.pdatraining.org/QSforAseptic**

14-16: Fermentation/Cell Culture Technologies Training Workshop
Bethesda, Maryland | **www.pdatraining.org/Fermentation**

Course held at the PDA TRI facility in Bethesda, Maryland.

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**

Recent Developments in Parenterals Discussed at Conference

Berlin, Germany • October 26-28 • www.pda.org/europe

Conference Co-chairs Friedrich Haefele, Boehringer Ingelheim and Nik Seidenader, Seidenader Maschinenbau

The target of the Parenterals 2010 conference is to give examples on how to practically integrate most recent developments in process, technology and regulatory trends into parenteral manufacturing. The topics discussed at this meeting are of vital interest and crucial to biopharma and pharmaceutical companies.

The *PDA Europe Conference on Parenterals 2010* will be held in Berlin, Germany on October 26–28. From around the world this conference will bring together regulators, production and validation professionals from the biopharma and pharma industries, component suppliers and equipment vendors. The Parenterals 2010 conference will feature nine sessions that have an impact on those industries operations, such as:

- Regulators and industry members points of view
- The future of parenteral manufacturing
- Packaging components and their impact on quality
- Manufacturing flexibility and control
- Innovative plants
- Monitoring technologies and devices
- Medical and application devices
- Regulatory trends

Speakers are coming from international regulatory authorities, i.e., U.S. FDA, Swedish MPA, French AFSSAPS and German authorities, as well as industry experts from the global pharmaceutical and biotech industries. They will provide insight into advanced aseptic manufacturing technologies, parametric release concepts and case studies of innovative plant operations. The impact of primary packaging components on quality of parenteral products will be addressed from regulators', industry experts' and vendors' perspectives.

Industry experts will share their wealth of experiences on 100% leak detection of lyophilized vials and the added value of such operations. Solutions for innovative filling equipment of small and mid-size batch production and perspectives to enlarge capabilities for complex formats like nested syringe fillers using liquid cartridge filling technology will be provided. Recent trends in application device development, i.e., autoinjectors and pens and their regulative boundaries are presented. Attending this will allow you to benchmark practices and to review potential practical solutions suitable for your situations.

Finally, regulators from the United States and Europe will illustrate their expectations and experiences on various fields including virus detection and inspection trends in sterile and biologics manufacturing. This gives you a chance to understand most recent cGMP trends in Europe and elsewhere, specifically on Annex1 to the EU GMPs and its practical implementations.

Take home benefits are:

- Comprehensive overview on compliance issues, trends and expectations given by leading health authority representatives
- Impact of primary packaging components on quality of parenteral products and how to address improvement
- Achievement of operational excellence in the production process of parenterals through plant design, manufacturing environment, line equipment and controls
- Outlook on future trends in manufacturing of sterile and parenteral products

The agenda is designed to encourage discussion and networking with colleagues in our industry as well as key component and equipment suppliers and regulators. The conference will provide practical information that you can apply immediately upon returning to the workplace. I hope you will attend this educational opportunity that will help secure your company's future success. For more information, visit www.pda.org/europe.

New Perspectives for Analytical Methods & Validation Procedures

Vienna, Austria • November 11-12 • www.pda.org/europe

Volker Eck, PhD, PDA

Does this sound familiar?

- You have not established and documented the accuracy, sensitivity, specificity and reproducibility of test methods as required by 21 CFR § 211.165(e).
- The test methods performed for XXX USP have not been verified to ensure suitability under actual conditions of use. Specifically, you have failed to conduct adequate verification of USP compendial test methods as applied to the production of your firm's XXX.
- Furthermore, our investigators found that numerous products were tested using analytical methods, provided by outside sources, which had not been validated/verified according to SOP XXX and SOP XXX to determine these methods suitability for their intended use.
- Method validation documentation did not include appropriate data to verify that the analytical method produced accurate and reliable data.

Analytical Method/Procedure Validation insufficiencies still are a frequent observation by inspectors. This is complex if you think of the Analytical Method/Procedure Validation process under the auspices of Quality by Design (QbD). Terminology is the least of one's problems in this case, but no doubt there is confusion about what is meant by analytical procedure, as described in the ICH Q2 documentation and analytical methods.

An article published in *PharmTech* in early 2010 discusses the implications and opportunities of applying QbD principles to analytical measurements. This article encourages improving robustness in and applying continuous improvement concepts to analytical methods. The claim is "that the steps, tools and approaches developed for application of QbD to the manufacturing processes (and described in ICH Q8, Q9, and Q10) have analogous application to the development and use of analytical methods." In analogy to the quality target product profile that leads to defining critical quality attributes (CQA), an analytical target profile (ATP) is proposed. The ideas and concepts conveyed in this article are the outcome of a joint effort of the Pharmaceutical Research and Manufacturers of America (PhRMA) Analytical Technical Group and the European Federation of Pharmaceutical Industries and Associations (EFPIA) Analytical Design Space Topic Team.

An ATP would be defined in the same way that the process control strategy is defined, and, in the same manner, CQAs requiring measurement are identified. The development of appropriate analytical methods is, however, fundamental to establishing product and process control (in a traditional- or a QbD-development approach) and in the overall control strategy. Having defined the ATP, the principles of QbD can be used during method development and evaluation to ensure that an appropriate analytical-measurement technology is selected and that the analytical method is designed to meet its intended performance requirements.

The conclusion of the article states that, "in the desired future state for a QbD-approach based submission, the focus of the analytical-measurement portion of the submission will be to demonstrate a thorough understanding of the requirements for measuring the drug substance/product and process CQAs used to define the design space of the process and describe how this understanding is translated into an ATP. The commitment the company makes will be to ensure that any method used to measure CQAs and quality assurance meets the registered ATP, but there should be no commitment to follow the detailed analytical methodology provided as an example." This would be a radical

change to the situation today, as changes to methods are are sometimes difficult to implement, although they might be most beneficial to control and assure the quality of the product. It would allow the registration of multiple alternative methods and "as multiple methods (alternative methods) may be in use and may be available for regulatory authorities, tools to compare the performance of these alternative methods with others and ensure equivalency will need to be established." It can be concluded that a reduced volume for validation studies would be necessary, so introducing alternative methods might also go along with less validation work for each method.

As in any design and development, a QbD approach can be utilized for the systematic development of analytical methods. Information and knowledge gained during analytical method development and validation from sample analyses and stability data, as well as knowledge from prior experience, pre- and post-approval trend analysis and other sources define a design space for the analytical method. Modifications to the method within the design space would not be considered a change to the method under internal quality systems, whereas modifications outside the design space would be a change with appropriate regulatory disclosure.

At the PDA Workshop on Analytical Method Validation in Vienna, Austria, **Anne Warner**, PhD, Senior Research Advisor, Analytical Sciences, R & D, Eli Lilly and **Shanthi Sethuraman**, PhD, Head, Manufacturing Science and Technology-Statistics, Eli Lilly, will introduce statistical thinking, planning and techniques for designing and analyzing the validation data and design space.

Rosario LoBrutto, PhD, Group Head, Pharmaceutical and Analytical Development, Novartis, will discuss the difference between a traditional validation concept based on characteristics and how to transform this in a QbD approach to method validation, what remains in its traditional form, as well as what changes and how in a QbD perspective. In addition, benefits and limitations of such an approach will be presented using a case study. **Phil W. Nethercote**, PhD, Head of the Analytical Center of Excellence, GlaxoSmithKline, will present drivers for change. He will speak about some issues with the current approach to method validation and expand on to the topic of method transfer, how QbD concepts can be applied to analytical methods and how a transition from a "life cycle" approach to method validation looks like. Case studies, current status and future plans for these concepts will be illustrated.

This and other new and emerging regulatory trends will be, discussed and explored in more detail at the PDA Workshop on Analytical Method and Procedure Validation in Vienna, Austria on November 11-12. To learn more about this event, please visit www.pda.org/europe.

PDA Parenteral Drug Association

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PDA Europe Workshop, Exhibition

Analytical Method Validation

11-12 November, Vienna, Austria

Workshop, Exhibition

For more information see:
www.pda.org/AnalyticMethod2010

Register by 15 Oct 2010 and SAVE!

This Workshop will provide participants with an in-depth review of the laboratory and documentary standards providing guidance on validation requirements for Chemical, Pharmaceutical and Physical Methods and Procedures used in product development and release testing. It will explain what is meant by an analytical method versus a procedure and give examples about their use. The workshop will review the recommendations for appropriate validation for these methods and procedures by looking at ICH, Pharmaceutical and Regulatory Documents. It will embark in illustrating how to define Design Space in an implemented control strategy under the Quality by Design paradigm. Also, aspects for analytical methods and procedures that do not fit into the ICH frame as well as biological and biotechnological based methodologies and procedures will be presented.

PDA's 5th Annual Global Conference on Pharmaceutical Microbiology

Advances in Microbial Control and Product Quality

October 25-28, 2010 • Capital Hilton • Washington, D.C.

The agenda will include discussions on topics such as objectionable microorganisms, investigations of microbial data deviations, manufacturing and product attributes impacting sterility assurance, new technologies and more!

The keynote addresses are:

Mitigating Microbial Risk during Spaceflight Missions
C. Mark Ott, PhD, Chief Microbiologist, Habitability and Environmental Factors Division, *NASA Johnson Space Center*

Practical Regulatory Guidance on Risk Assessment for Microbial Controlled Issues
Thomas Arista, Investigator and National Expert Pharmaceutical/Biotechnology, ORA/ORO, Division of Field Investigations, *FDA*

New this year! A third half day featuring a partnership with US Pharmacopeia (USP) with sessions related to Rapid Microbiological Methods.

Popular sessions to attend include the:

- **Ask the Experts Panel Discussion** where representatives fromglobal regulatory agencies, standards-setting authorities and thepharmaceutical industry present their latest perspectives on themicrobiological challenges that are faced related to aspectof drug manufacturing.
- **Urban Myths** session where industry experts dispel commonlyheld myths in pharmaceutical microbiology.

For details and to register, visit
www.pda.org/microbiology2010

What is PDA?

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

www.pda.org/join

CONFERENCE OCTOBER 25-27 **EXHIBITION** OCTOBER 25-26 **COURSES** OCTOBER 28