Science • Technology • Quality • Regulatory • Community

PDA Letter

Volume XLII • Issue #8

September 2006

In This Issue…

PDA Parenteral Drug Association

Connecting People, Science and Regulation℠

Times are Changing: The Role of the Qualified Person in the 21st Century

Joyce Ramsbotham, Solvay Pharmaceuticals (ret.)

The Qualified Person (QP) in Europe forms the backbone of the quality assurance system, ensuring that quality medicines reach the patient. However, the development and manufacturing environment in the pharmaceutical industry is changing rapidly, and one has to wonder if the current concept of the role and responsibilities of the QP also need to change. We are moving from "quality by testing and inspection" to the concept of "quality by design," where quality is built into the product and process during the development phase. We are moving away from traditional specifications to a concept of monitoring quality during processing, with suitably chosen in-process controls and continuous verification, which is also going to replace traditional three-batch validation. This, in turn, is also going to allow real-time or parametric release of batches, instead of end-point testing. Assuring the quality and continuing supply of medicines to the patient requires not only individual batches to be within specification, but also processes that are robust and reliable. Process understanding, quality risk management and continual improvement are becoming the cornerstones of the quality paradigm. Risk-based and science-based decisions are now expected instead of compliance-based decisions. Also, the logistics of our supply chain are becoming more complex, as we move away from local stand-alone processes to complex international supply chains, and as we move away from only supplying local markets to supplying multiple international markets from strategic manufacturing facilities. We are also seeing an increase in the number of—and the time spent on—inspections, not just from our own local inspectorates, but from many other inspectorates from the markets which we supply around the world, who all expect us to comply with their own local GMPs.

In this rapidly changing environment, the traditional role of the QP that focuses on the certification of each individual batch seems outdated. Surely there are better ways to protect the patient than focusing on individual batch release. This paper will examine some of the changes mentioned above, and how the role and responsibilities of the QP need to be adapted to respond to these new concepts.

Quality by Design and Process Understanding

There is no disputing the concept that the QP remains responsible for the quality of the product released to the market. But as we see more reliance placed on building the quality into the design of the product and the design of the

continued on page 20

PDA
Parenteral Drug Association

Connecting People, Science and Regulation℠

Featuring innovative Pharmaceutical Biotechnology courses, plus focused Quality Assurance/Quality Control training!

PDA Training and Research Institute

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- Biopharmaceutical QA/QC for Senior Management
- Design of Experiments for Efficient and Practical Assay Development and Validation
- Managing the Microbiological Quality of Non-Sterile Pharmaceutical and OTC Drug Products
- Minimizing the Legal, Quality & Compliance Pitfalls of Contract Manufacturing
- Overview of FDA QSR Requirements for Medical Device Inspection Approaches
- Preparing for an FDA Pre-Approval Inspection
- Risk Management in Thermal Validation
- What Every Biotech Startup Needs to Know About CMC

www.pda.org/calendar/courses/bostontraining

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PDA Parenteral Drug Association

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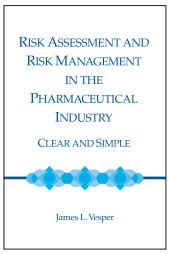
Bestsellers



Risk Assessment and Risk Management in the Pharmaceutical Industry: Clear and Simple

by James L. Vesper

Explores the history, definitions, and how we think about risks and hazards, offering an overview of the risk management process and commonly used risk assessment methods and tools. It also examines the phases of the risk management process in detail and examines how the various tools can be applied in identifying hazards and evaluating their potential impact and affects. There are examples throughout the book that illustrate how the tools can be applied in "real life".

Item No 17219 PDA Member $210 Nonmember $260

Pharmaceutical Filtration: The Management of Organism Removal

by Maik W. Jornitz and Theodore H. Meltzer, PhD

Offers a deep, comprehensive understanding of the all connections between the different aspects of the filtration universe.

Item No. 17235 PDA Member $225 Nonmember $279

Environmental Monitoring, Volume I, Volume II and Protocol CD

edited by Jeanne Moldenhauer, PhD

Describes methods for developing and operating an appropriate, sustainable microbiological program both in the lab and during production. Numerous useful protocols are included on the CD.

Item No. 17239 PDA Member $480 Nonmember $599

Encyclopedia of Rapid Microbiological Methods, Volume I, II, III

edited by Michael J. Miller, PhD

Focuses on regulatory and compendial initiatives currently in place that help pharmaceutical microbiologists and managers implement RMM in their facilities.

Item No. 17252 PDA Member $660 Nonmember $815

Technical Report No. 42, Process Validation of Protein Manufacturing

Focuses on validation of biopharmaceutical processes used to manufacture therapeutic proteins and polypeptides produced from recombinant or non-recombinant cell-culture expression systems.

Item No. 01042 PDA Member $75 Nonmember $150

Risk-Based Software Validation: Ten Easy Steps

by David Nettleton and Janet Gough

This book offers a systematic, ten-step approach, from the decision to validate to the assessment of the validation outcome, for validating configurable off-the-shelf (COTS) computer software that generates data or controls information about products and processes subject to binding regulations.

Item No. 17256 PDA Member $200 Nonmember $249

PDA Archive on CD-ROM – PDA Archive Retrieval Index (2006 version)

Fully-searchable four disk CD-ROM archive includes all PDA Journal articles, Technical Reports and Monographs, Technical Bulletins and select Conference Proceedings.

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Steam Sterilization: A Practitioner's Guide **20% OFF**

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The Manager's Validation Handbook: Strategic Tools For Applying Six Sigma To Validation Compliance

by Siegfried Schmitt, PhD

Modern methodologies and tools that deliver the best validation practice processes and results, while achieving compliance with regulatory requirements or the healthcare industry.

Item No. 17234 PDA Member $225 Nonmember $279

PDA Technical Report No. 27, Pharmaceutical Package Integrity

The information provided in this guideline is intended to assist users in developing integrity assessment strategies for use during the phases of product life.

Item No. 01027 PDA Member $75 Nonmember $150

Pocket Code of Federal Regulations GMP Guide – 2006 Edition

21 CFR Part 210-CGMP in Manufacturing, Processing, Packing, or holding of drugs; general. 21 CFR Part 211-CGMP for Finished Pharmaceuticals. Reproduced in pocket size by PDA. 2006, 68 pages.

Item No. 13004 PDA Member $4 Nonmember $10

Volume discount and booklet with customized logo is available, please contact PDA for price quote.

To Order: +1 (301) 656-5900 www.pda.org/bookstore

Table of Contents

Cover art: In October, PDA will help bridge industry and the EMEA at the first annual PDA/EMEA Joint Conference in London (Tower Bridge shown).

Coming Next Month... Pharmaceutical Development

[**Editor's Note:** The article on Biopharm. Manufacturing Capacity will appear in a future issue.]

2006 PDA/EMEA Joint Conference

London, England

Training Courses
10-11 October 2006

Conference and Exhibition
12-13 October 2006

Understanding the European GMP Environment

Mark your calendars for the opportunity to meet European Regulators in person! Continuing its tradition of service and leadership, PDA is proud to celebrate its 60th anniversary by partnering for the first time with the European Medicines Agency (EMEA) to offer the *PDA/EMEA Joint Conference: Understanding the European GMP Environment.* This is a unique opportunity to interact and network directly with top European health authorities and industry representatives in a neutral, science-based forum.

The aim of this conference is to increase understanding and awareness of GMP trends and expectations in Europe. Participants will include representatives from EMEA, member state health authorities and industry, who will share their expertise on recent developments in European GMPs and be available to meet and discuss topics with conference attendees.

Save the Date... Join us in London in October 2006 for the first ever **PDA/EMEA *Joint Conference!***

For further information please go to
www.pda.org/pdaemea2006

MEET THE REGULATORS!

This is a unique opportunity to interact and network directly with those people who enforce regulation in the European Union.

PDA℠ Parenteral Drug Association

emea

Celebrating 60 Years: Ed Fry, PDA's Regulatory Ambassador

As we continue to recognize influential PDA leaders of the last 60 years, we want to acknowledge Ed Fry as one of our most outstanding leaders who reached out to regulatory authorities around the world and help grow PDA's membership from 2000 to over 10,000 in a decade.

Most PDA members recognize that science is the cornerstone of PDA. Yet, few may know or be around to remember that PDA was formed partly in response to the passage of the Federal Food, Drug and Cosmetic (FD&C) Act by the U.S. Congress. It was the burgeoning regulatory demands of those early years that drove parenteral manufacturers to seek access to technological and scientific information, a dynamic that continues to exist today. The early PDA leaders meeting this need set the model of PDA reaching out to the regulators to help industry better understand the new requirements and, in turn, to help the regulators better understand the scientific and technical challenges associated with industrial pharmaceutical manufacturing.

Over the ensuing years, many PDA members worked to facilitate meaningful and productive dialogue between government and industry. The establishment of the first cGMPs in 1963 by the U.S. FDA invigorated another generation of PDA leaders to reach out to the regulators. During this time, the focus of PDA's annual meetings expanded to include topics on regulatory compliance, and a growing contingent of U.S. FDA and USP representatives began speaking at the annual meetings.

With a solid foundation of regulatory dialogue and education already in place, Ed Fry took PDA to a higher level. Ed's leadership from 1991-2003 helped cement PDA's reputation as the foremost organization for *Connecting People, Science and Regulation*[SM].

Through the hard work and leadership of Ed Fry, PDA has built very strong relationships with regulatory bodies worldwide, particularly in Europe and the United States, to the benefit of the membership and the industry at large. The channels of dialogue between government officials and industry that Ed helped open fostered the creation of scientifically sound regulations and guidances and advanced the desirable goals of regulatory harmonization.

Of course, we cannot overlook the fact that Ed served under a like-minded and equally committed Board of Directors, including Chairs **Michael Korczynski, James Akers, Clarence Kemper, and Raymond Shaw,** each of whom worked hard to help build strong relationships with regulators worldwide. In addition, Ed's predecessor, **Frederick Carleton,** worked with the PDA Board to launch the very first PDA/FDA Joint Regulatory Conference, first held in 1990—an event that symbolizes PDA's role as a connector of people, science and regulation. Fred also played a large role in recruiting Ed.

Ed's experiences in both the field and the headquarters at FDA during a 27-year career provided him perspective on both the challenges facing manufacturers and the public health goals of the Agency. In his early career with FDA, he served in a number of district offices, including Puerto Rico, New Jersey and New York. In 1972, he became the Supervisory Investigator in the San Francisco District, and in 1976 was elevated to Director of Investigations in the Kansas City District. For the final 11 years of his FDA career, Ed worked in CDER's Office of Compliance as the Director of the Division of Manufacturing and Product Quality, and he had a hand in the development of a number of key guidelines, regulations and policies impacting PDA members. Among the numerous and challenging topics addressed in FDA guidelines developed under Ed's direction were process validation, aseptic processing and the inspection of active pharmaceutical ingredients. Ed also oversaw a special enforcement group involved in investigating fraud in the generic drug industry (the generic drug scandal) and in overhauling FDA's drug inspection program. Representing FDA abroad as liaison to the Pharmaceutical Inspection Convention and the World Health Organization, Ed gained the experience necessary to manage an organization about to expand significantly into Europe.

When Ed started with PDA in the summer of 1991, the Association was implementing plans that would ultimately grow the membership rapidly. Already, PDA had launched its first chapters in the United States and was looking to organize local groups of members in Europe and Japan. Ed's international experience and knowledge of the key regulatory challenges of the day provided impetus to these initiatives to keep them moving in a positive and productive direction.

Ed's leadership in regulatory issues reached more and more industry professionals throughout the 1990's, as PDA's membership grew at a stellar pace. His grasp of the issues was a strength, as was his ability and willingness to communicate with the membership in each issue of the *PDA Letter.* Ed's column in the Letter quickly became a reliable source for information and analysis on important regulatory developments.

The relocation of PDA to Bethesda, Md.—right in FDA's front yard—provided Ed an opportunity to interact with Agency officials in a manner that has reaped benefits to PDA unparalleled in any other era. Soon, Ed was reporting in the Letter on meetings between PDA and FDA officials here in Maryland.

continued on page 8

Past Leader Spotlight: Fred Carleton, President 1977-1979, Executive Director 1988-1991

For 30 years, one PDA member played a central role in every major meeting, training event and recruiting effort at PDA: Fred Carleton.

Fred joined PDA in 1960 while working for Pfizer Inc. His career with Pfizer would extend for 29 years, ending in 1988, as the Manager, Scientific Affairs for the company's domestic facilities (seven in total). Fred joined Pfizer as a radiological biochemist, with degrees from City College, Purdue University and the Oak Ridge Institute of Nuclear Studies. He was one of the first experts in the industry trained to work with radioactive compounds. Fred also was an adjunct professor at the Fairleigh Dickinson University (1960-1970) where he taught biochemistry and radiochemistry.

Fred's first experience with PDA was at the National Meeting (now called the Annual Meeting). After attending for the first few years, the educator in Fred came out. He approached the PDA Board of Directors in the mid-1960's and proposed a number of changes to enhance the conference. Impressed with his ideas, PDA named Fred to the planning committee for the national meeting. In 1971, Fred became a member of PDA's Program Committee, on which he served until 1991. In those two decades, he participated in planning every event PDA sponsored!

Fred by no means wants to take all the credit for PDA's phenomenal success in that period of time. He acknowledges the hard work and dedication of those who served with him. "I was a member of a team," he says. "I'm a team player."

In the late 1970's, Fred and other PDA leaders of the time, started looking to develop better educational offerings. Fred helped recruit experts to teach courses for PDA at no fee. Dr. **Irving Pflug** was one of the early educators brought on board to lead PDA courses. Fred personally invited two members of the Pfizer staff to teach courses on computer programming, PDA's first foray into the world of IT!

Two important events happened to bolster PDA's education mission during Fred's tenure as President. First, the Association received accreditation from the American Council on Pharmaceutical Education, the strongest possible endorsement of PDA's educational qualifications at the time. Second, the Association created the PDA Foundation for Pharmaceutical Sciences, Inc., to support research and education in parenteral sciences and technology. Fred joined with other PDA volunteers, including **Nina Demuth, Jack Cole, Nathan Kirsch and Leon Lachman** to launch the venture.

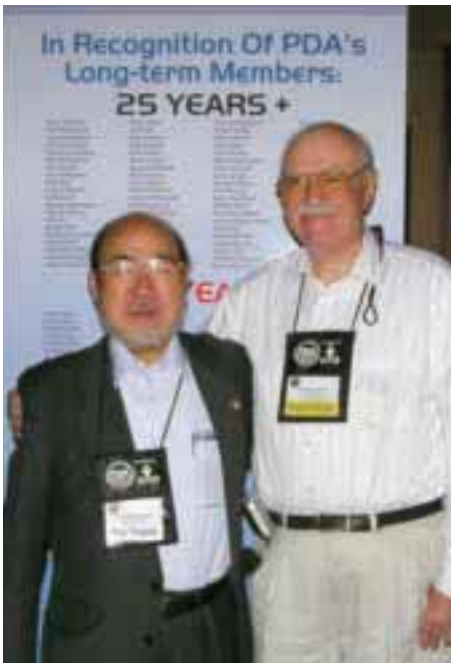
Perhaps none of Fred's contributions can outweigh his role as top cheerleader and recruiter. His honest dedication to PDA helped him recruit many of its foremost leaders during his 30 years of active involvement.

Upon Fred's retirement as PDA Executive Director in 1991, PDA President **Michael Korczynski** provided perhaps the best summary of Fred's role ever written (*PDA Letter* vol. 27, no. 7):

Fred's contributions and activities during his 30-year association with PDA are almost too numerous to count. He has either chaired or been a principal member of every major committee or activity within the Association. Fred has been instrumental in identifying and encouraging talented individuals in the pharmaceutical industry to participate in PDA....Fred exemplifies PDA.

Former PDA Chair **James Akers** describes Fred's devotion to PDA as infectious:

"He had an enormous love of PDA which manifested in an untiring effort to recruit talented volunteers. Fred was directly responsible for recruiting half of the people who served on the Board of Directors in the late 1980's and 1990's. Without Fred's persistence, I probably would not have gotten as involved with PDA, for which I am very grateful to have done!"



Honorary Members: Fred Carleton (r) poses with Kunio Kawamura at the 2006 PDA Annual Meeting. Kunio joined Fred as a PDA Honorary Member this year.

The Frederick J. Carleton Award was created in recognition of his hard work and dedication. It is awarded to past or present Board members whose services on the Board are determined by his/her peers as worthy of recognition.

When asked why he gave so much to PDA, Fred replies simply, "The thing I loved was PDA. I mean it. It has been a love affair for me."

PDA is fortunate to have had a leader like Fred involved for so many years!

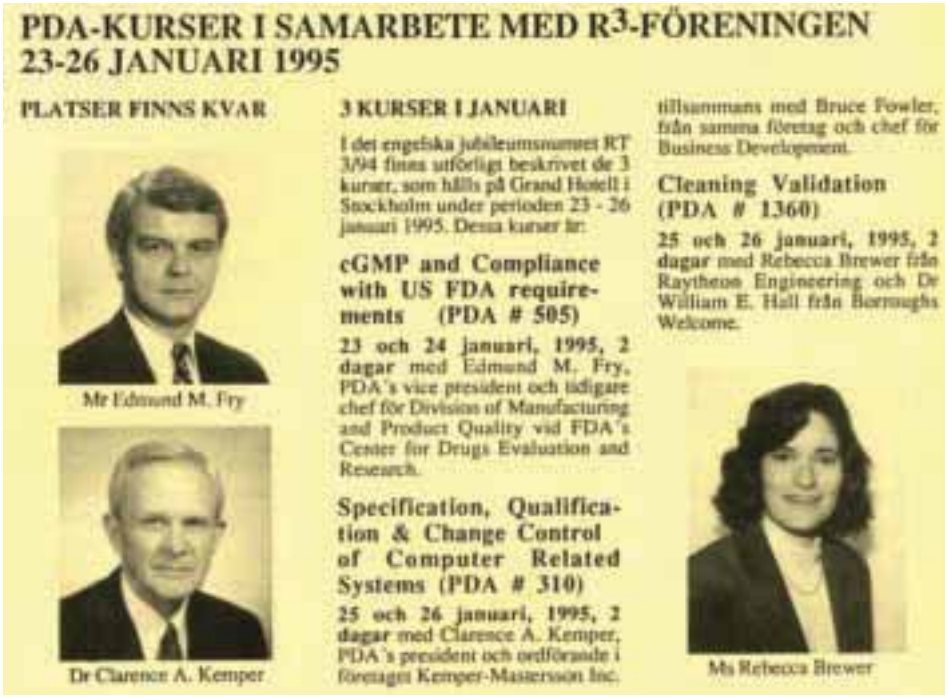
Celebrating 60 Years: Ed Fry, PDA's Regulatory Ambassador, continued from page 6

In the wake of the famous Barr decision, Ed provided a series of articles analyzing the Court's ruling and the impact it had on the industry. Ed also expanded his coverage to international regulatory developments, and by 1995 was providing frequent contributions to the international regulatory news coverage in the *PDA Letter.*

As a former career FDAer, Ed grasped from the start of his PDA tenure that reasonable and worthwhile regulation must come from industry. As such, he was a strong advocate of industry's needs. Only two years into his new role as PDA's top employee, Ed asked "Who's In Charge?" (*PDA Letter,* vol. 29, No. 7). In response to a question posed by a UK inspector about who should drive up good manufacturing standards, Ed wrote words that ring true to this day:

I doubt that many would disagree that the industry must lead; FDA doesn't make drugs, the industry does. The industry has the knowledge, the expertise and the responsibility to know what is feasible and valuable. The problem is that all too often the focus of discussion is on what FDA's future requirements might be, rather than on the science and technology. Research, data-gathering and information-sharing (typical PDA activities) are the things that will shed light on what is feasible and valuable, and these must come from industry.…The focus should be on what is right *rather than on what the minimum rules might be in the future. After all, who's in charge?*

On top of using his pen to educate and inform the membership, Ed used his voice. He was an effective and authoritative speaker at PDA events around the globe, often providing expert presentations on the FDA inspection process, the inner workings of the Agency and how to respond to inspection observations. Harmonization of regulatory and pharmacopeial standards for cleanrooms and aseptic processing was another topic Ed frequently spoke on at meetings over the years.



PDA-KURSER I SAMARBETE MED R3-FÖRENINGEN
23-26 JANUARI 1995

PLATSER FINNS KVAR

Mr Edmund M. Fry

Dr Clarence A. Kemper

3 KURSER I JANUARI

I det engelska jubileumsnumret RT 3/94 finns utförligt beskrivet de 3 kurser, som hålls på Grand Hotell i Stockholm under perioden 23 - 26 januari 1995. Dessa kurser är:

cGMP and Compliance with US FDA requirements (PDA # 505)

23 och 24 januari, 1995, 2 dagar med Edmund M. Fry, PDA's vice president och tidigare chef för Division of Manufacturing and Product Quality vid FDA's Center for Drugs Evaluation and Research.

Specification, Qualification & Change Control of Computer Related Systems (PDA # 310)

25 och 26 januari, 1995, 2 dagar med Clarence A. Kemper, PDA's president och ordförande i företaget Kemper-Mastersson Inc. tillsammans med Bruce Fowler, från samma företag och chef för Business Development.

Cleaning Validation (PDA # 1360)

25 och 26 januari, 1995, 2 dagar med Rebecca Brewer från Raytheon Engineering och Dr William E. Hall från Burroughs Welcome.

Ms Rebecca Brewer

Ed was a frequent speaker on FDA topics at conferences. Here he was on the agenda of an R³ Nordic conference in 1995.

No PDA event or publication testifies to Ed's lasting impact on the relationship between PDA and the FDA than the PDA/FDA Joint Regulatory Conference. During Ed's tenure, the PDA/FDA conference grew into not only PDA's most important meeting, but one of the few "must attend" events for regulatory affairs, manufacturing and quality control professionals. The number of FDA speakers at the conference has grown—averaging more than 20 annually—as has total attendance—now drawing over 1000 attendees, speakers and exhibitors.

It did not take FDA long to recognize Ed's influence. At the 1995 PDA/FDA conference, Ed was awarded the FDA Commissioner's Special Citation in recognition of his "outstanding performance in promoting cooperation between the Food and Drug Administration and the Parenteral Drug Association in developing educational programs for the pharmaceutical and biopharmaceutical industries." FDA Deputy Commissioner for External Affairs Sharon Smith Holston, in presenting the award, stated: PDA "made our communications easy, and our joint programs were, for us at FDA, a source of pride." Not bad after only four years on the job!

Earlier this year, Ed was recognized by PDA for all his remarkable contributions when he was awarded PDA's Distinguished Services Award.

PDA owes Ed a debt of gratitude for his years of dedicated service to our Association and the industry. We look forward to seeing Ed at our conferences for years to come!

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Parenteral Drug Association

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upcoming sessions

Managing the Microbiological Quality of Pharmaceutical Excipients

September 19 / 1:00 p.m. – 2:30 p.m. EDT

The microbiological quality of the pharmaceutical excipients used to manufacture pharmaceutical and over-the-counter drug products may significantly impact the outcome of individual processing steps and the microbiological attributes of the final drug products. Unlike active pharmaceutical ingredients, managing excipients' microbiological quality is less straight-forward. This presentation discusses the qualification of suppliers, excipient production methods, compendial standards, regulatory control, and microbial limits testing of excipients. Emphasis is given to the risk assessment necessary for the implementation of reduced incoming testing programs.

Speaker: Dr. Anthony M. Cundell, Director, Pharmaceutical Science, Microbiology, Schering-Plough

Replication Competency: How Market Leaders Stay Ahead by Rapidly Identifying and Spreading Best Practices

September 21 / 1:00 p.m. – 2:00 p.m. EDT

"Insanity in any business is doing the same things over and over and expecting better results." In the case of multi-location pharmaceutical companies, business insanity is too often "reinventing the wheel over and over" due to the lack of effective knowledge and experience sharing across organization lines. Learn how to uncover the hidden discipline of Replication Competency and quickly and efficiently find and spread best practices to drive continuous performance improvement by turning great ideas into common practice.

Speaker: Mr. Rick Tucci, President and Founder, Leap Technologies, Inc.

Design Space: DoE Basics for PAT and ICH Q8

October 4, 2006 / 1:00 p.m. – 2:30 p.m. EDT

The FDA has released two new "Guidance for Industry: Process Analytical Technology, PAT, and Q8, Pharmaceutical Development." Both contain the concept of quality by design and process understanding. An additional concept in Q8 is that of "Design Space," This presentation reviews the application of designed experiments to PAT and quality by design. It also presents an operational definition of Design Space and discusses how statistically designed experiments can be used to quantitate product and process Design Space.

Speaker: Lynn D. Torbeck, President Torbeck and Associates, Inc.

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www.pda.org web seminars

PDA's Prefilled Syringes and Injection Devices Interest Group

Georg Roessling, PDA

In 2004 a group of PDA members in Germany initiated a conference on prefilled syringes and formed the PDA Interest Group on the topic.

Since this is a very important and dynamic field for the pharmaceutical industry, many people showed interest and participated in the first "The Universe of Prefilled Syringes" conference in Hanover, Germany. The Interest Group decided to hold a second conference on the topic in Munich in 2005; over 200 industry professionals attended.

The Interest Group has been very active in driving the content of these meetings. PDA members in North America who are interested in the IG and in the topic will have a chance to participate on their side of the Atlantic in October, when PDA holds its third "The Universe of Prefilled Syringes and Injection Devices" (www.pda.org/prefilled). This conference will be the ideal platform to share information and to meet with people from all disciplines of importance to the development, manufacturing, packaging and handling of syringes and injection devices. At the conference there will be presentations on technologies, materials, processing, case studies and on regulatory issues.

Thomas Schoenknecth, Gerresheimer

Glenn Thorpe, Becton Dickenson

Also, it will be the ideal time to join the Interest Group. The scope of the interest group is to provide a forum for open discussion where the various aspects of the technologies can be discussed. Information exchange is encouraged. It is a place where people share their experiences, ask questions and discuss scientific, technical and regulatory issues relevant to this topic.

The two leaders—**Thomas Schoenknecht,** PhD, Gerresheimer (European Branch), and **Glenn Thorpe,** Becton Dickenson (U.S. Branch)—are assisting PDA by organizing conferences alternating in Europe and the United States. Additionally, they are planning for the IG to meet at other PDA conferences, such as the Annual Meeting.

If you would like to get involved contact the leaders or inform PDA. Also, go to www.pda.org/science/IGs.html for more details.

PDA is very proud to have members who actively lead our Interest Groups. We look forward seeing you in Bethesda on October 23-25.

PDA Awards Special Grant for Global Pharmaceutical Science Education

During this year's Graduate Student fellowship competition, PDA received a series of three applications from the University of the Witwatersrand in Johannesburg, South Africa, that the review committee recommended for special consideration. The applicants included two students from the Democratic Republic of Congo and a Nigerian national, all of whom have demonstrated an extraordinary drive and determination to make a meaningful contribution to medical sciences. PDA decided to award each of these students a two thousand dollar grant in support their efforts toward graduate training in pharmaceutical technology. Therefore, a special award for global pharmaceutical science education will be made in the name of the following three students of **Eberhard W. Neuse,** Professor of Macromolecular Chemistry, to the University of Witwatersrand: **Diakanua Nkazi, Hembe E. Mukaya,** and **Blessing A. Aderibigbe.**

PDA
Parenteral Drug Association

Conference	Training Courses	Exhibition
13-15 November	16-17 November	13-14 November

2006 PDA Asia-Pacific Congress

Connecting People, Science and Regulation℠

Overview

The 2006 PDA Asia-Pacific Congress will provide important information on current and emerging regulatory, scientific and technical issues. Key health authority and expert industry speakers will present updates of regulatory requirements, including the revision of the Japanese Pharmaceutical Affairs Law and practical examples of quality systems, microbiological topics and manufacturing processes. The Congress will be a multi-track format focusing on new regulatory developments, pharmaceutical manufacturing, and microbiological issues relevant to the global pharmaceutical and biopharmaceutical industries.

Topics to Include:

- Revisions to Japan's Pharmaceutical Affairs Law – and Implementation
- Quality by Design
- 21st Century GMPs
- Pharmaceutical Harmonization
- Process Analytical Technology (PAT)
- Novel Manufacturing Processes
- Aseptic Processing
- Risk Management
- Rapid Microbiological Testing
- Viral Safety
- Active Pharmaceutical Ingredients (APIs)
- Computer Validation
- Disposable Technologies
- Environmental Monitoring
- Pharmaceutical Water
- GMPs During Clinical Development

Featuring:

- Regulatory updates and implementation strategies for Japanese and worldwide delegates
- New presentations by health authority leaders from U.S. FDA, EMEA, Japan and China
- First-time sessions on practical applications of revised Japan's Pharmaceutical Affairs Law
- Case studies examining novel manufacturing processes, new developments in microbiology, disposable technologies, PAT and more

Visit **www.pda.org/apcongress** for the full program

Interactive Training Courses

Presented by the PDA Training and Research Institute

Fundamentals of Pharmaceutical Filters and Filtration
Maik Jornitz, Group Vice President, Product Management, Sartorius Corp.
Theodore Meltzer, PhD, *Capitola Consulting*
16-17 November

Quality Programs – The Road to Continuous Improvement
Daniel H. Gold, PhD, President, *D.H. Gold Associates, Inc.*
16-17 November

Risk Assessment in Manufacturing
Hal Baseman, Chief Officer and Principal, *ValSource LLC.*
16 November

GMP Requirements for the Manufacture of Clinical Trial Materials (CTM's)
Robert Dana, Vice President of Quality and Regulatory Affairs, *PDA*
17 November

For complete course descriptions, visit **www.pda.org/apcongress/courses**

Tokyo, Japan

13-17 November 2006

Venue

Tower Hall Funabori
Tokyo, Japan
Hotel information available at
www.pda.org/apcongress

Registration

See registration form on reverse for full details, or visit
www.pda.org/apcongress

Full Congress and One Day registrations available!

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Exhibition and Sponsorship Opportunities Available!

For more information, contact:
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Feedback Workshops for 2006 Revision of PDA TR-1

2006 Revision Task Force Travels to Cork, London, Pavia and Bethesda

Richard Levy, PhD, PDA and Genevieve Lovitt-Wood, G.I. Lovitt and Associates

The PDA Task Force charged with finalizing the revision of Technical Report No. 1: *Moist Heat Sterilization* began feedback workshops in Europe in an unprecedented effort to gain broad input during its development**.** Thanks to the efforts of **Georg Roessling,** PhD, PDA, steam sterilization leaders from the European regulatory agencies and industry representing both pharmaceutical manufacturers and vendors met with the group in Ireland, the United Kingdom and Italy in June. Additional workshops were held in the United States in Bethesda, Md., in July.

Some of the Cork workshop participants posed for a photo: (l-r) Tom Hodgkinson (Genzyme Waterford), Teresa Coen (Wyeth Biopharma), Rich Levy (PDA), Coleman Casey (School of Pharmacy, UCC), Alice Redmond (Consultant), Frank Hallinan (Wyeth Biopharma), Stan O'Neill (IMB), Genevieve Lovitt-Wood (Project Manager), Kris Evans (U.S. FDA), Georg Roessling (PDA)

Cork, Ireland

The TR-1 tour began with a well-attended meeting that was the largest held by that Chapter to date thanks to the well-coordinated efforts of Anne-Marie Duggan and Alice Redmond of Project Management Group. Irish Chapter President, Frank Hallinan, PhD (Wyeth Biopharma, Dublin) opened the day-long conference welcoming the packed room.

Technical Report 2006 Revision Task Force Chair, Rich Levy, opened the discussion of TR-1 giving a historical perspective on the development and organization of the document as well as the proposed disposition of those sections that have been excised from the previous draft.

Kristen Evans, Guidance and Policy Development, CDER Office of Compliance, U.S. FDA, guided the attendees through the science of sterilization as well as ongoing process control. Evans pointed out that the report provided information so users can develop their own sterilization process. Rather than creating a sterilization process for readers, it provides a fundamental scientific foundation for them to develop their own. As a part of qualification, he went on to state the importance of documentation during development in order to gain process knowledge for ongoing control.

Cycle development and qualification of a sterilization cycle were presented by **Nigel Halls,** PhD, Executive Director, Science and Technology, IAGT. Dr. Halls discussed the technical report's emphasis of the importance of both biological and physical qualification of sterilization cycles. He also noted that a well-designed and developed sterilization process should exhibit an agreement between the physical and biological performance parameters.

Stan O'Neill, Senior Inspector, Irish Medicines Board, gave an elucidating presentation called "Typical Inspectional Issues around Moist Heat Sterilisation Processes" for terminal sterilisation, aseptic processing and steam-in-place. All participants found useful the opportunity to compare and contrast PDA TR-1 with current regional regulatory expectations.

London, U.K.

The second stop for the Team was London where the subject matter drew steam sterilization experts from the United Kingdom and United States, industry end-users and vendors as well as the MHRA. Opening remarks were given by U.K. Chapter President **Frank Talbot** (FT Pharmaceutical Services), who also organized the event. A day of stimulating roundtable discussion drew much excitement from all attendees as they participated in an intense review of the report comparing and contrasting U.S. and EU perspectives. Of particular interest to the U.K. attendees were the following topics:

- Definition of equilibration time
- Methods of air removal detection
- Importance of load orientation
- Data capture from the pre-exposure phase for validation
- Agreement between $F_{physical}$ and $F_{biological}$
- Worst case load.

Paul Hargreaves, Unit Manager, Technical & Operations ➤

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Co-ordination in the Inspection & Enforcement Division, U.K. Medicines and Healthcare Products Regulatory Agency (MHRA) was quite encouraged by this last revision of TR-1, and he agreed with, in particular, differentiation between temperature and heat. **Andrew Hopkins**, GMP Inspector, Division Inspection and Standards, MHRA, gave a presentation called "Moist Heat Sterilization, the MHRA Perspective." Again, interested attendees were given an opportunity to review and discuss current regional regulatory expectations in light of the technical report and to engage in discourse on where they are in approximate alignment (expectations and standards for steam quality and the need for adequate air removal) and where they differ (importance and use of BI's versus thermometric studies).

Pavia, Italy

The Task Force traveled to Pavia, Italy to present TR-1 at the world headquarters of the Fedegari Autoclavi S.p.A. This well-attended event drew attendees from Sweden, Germany, Spain, France, Romania, Belgium, the United Kingdom and the United States due to the effective efforts of **Volker Eck**, PhD, now with PDA, **Barbara Sambuco**, Bristol-Myers Squibb and **Giuseppe Fedegari,** Fedegari Autoclavi S.p.A. PDA Italy Chapter President, Dr. **Gabriele Gori** (Bausch & Lomb) welcomed the attendees and gave opening remarks.

PDA President **Bob Myers** and **Mike Sadowski**, Manager, Sterile Product Development, Baxter Healthcare, both joined the Task Force in Italy. Myers gave a historical perspective on the development of the report leading to the current formation of the 2006 Revision Task Force. Sadowski gave a presentation on cycle development wherein he discussed EU expectations for lethality (e.g., 121°C for 15 minutes) in contrast to use of 12 F_0 Overkill as a base for cycle development as stated in the Technical Report.

Paul Hargreaves joined the discussion again in Pavia and gave insightful comments on TR-1 as well as an enthusiastic presentation titled, "Regulatory Aspects of Autoclave Validation," that focused on steam sterilization of equipment in porous load (vacuum) autoclaves. **Vittorio Mascherpa**, Fedegari Autoclavi, then gave a forward-thinking presentation entitled, "Technological Innovations in Moist-Heat Sterilization for Current and Future Processes and Performances."

Gilberto Dalmaso, GlaxoSmithKline Parma site, presented "Parametric Release for Terminally Sterilized Ampoules," which included a case study on parametric release. **Dr. Lorella Chiappinelli,** Agenzia Italiana del Farmaco—AIFA (Italian MoH), gave attendees the European health authority perspective on regional expectations regarding moist heat sterilization.

Attendees noted in all three conferences the lack of prescription in Version 18 of Technical Report No. 1. One of the goals of the 2006 Revision Task Force is to develop a technical report that stimulates sterilization science by providing sound science-based approaches while not prescribing acceptance criteria and limits that tend to discourage greater process understanding.

Bethesda, Md.

The fourth leg of the TR-1 tour included gaining input from the United States. Two meetings were conducted in Bethesda, Md., the first was hosted by PDA Headquarters for previous authors and contributors to Technical Report No. 1, Version 17. In this meeting, PDA's goal was to provide prior authors and contributors with a clear understanding of the decision process that led to the current version and the proposed disposition of the excised portions of Version 17.

The Bethesda workshop was open to the general membership and drew attendees from across the United States. In his discussion of process development, **Kevin Trupp**, Manager, Sterilization Engineering, Hospira, garnered feedback from attendees on thermocouple placement (what is actually being measured), equilibration time, defining heat penetration vs. temperature distribution, and the possible use of a process challenge device in lieu of a worst case load for requalification runs. Trupp stated that he is conducting a study to evaluate the effect of thermocouple placement when measuring process parameters such as equilibration time and load heat-up time. The study focuses on evaluating various surface measurement (heat penetration) techniques and compares those measurements to various heating media/environmental (heat distribution) measurements.

Irving Pflug, PhD, Professor, University of Minnesota, and **Keith Shuttleworth,** Keith Shuttleworth & Associates Ltd, both contributing authors to Version 17 of the revised monograph, attended both Bethesda conferences and gave insightful comment and recommendations for clarification on the current version.

Further Feedback

To facilitate continued feedback from the PDA membership and attendees of the workshops, PDA has also developed an Online Review Tool for Technical Report No. 1. Reviewers can now log on to the web-based review tool and either download a draft technical report ready for comment, save it to their hard drive and upload their edited document; or, insert their comments directly in to the tool. This tool will help to track Reviewer's comments as well as increase communications between members. The 2006 Revision Task Force is taking in to consideration all feedback received and expects to have a finalized version by year-end.

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Recent Sci-Tech Discussions: Validating Cleaning Practices and Microbiological Count Tests for Disinfectant Solutions

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.

Does anyone use visual inspection of equipment (post cleaning) as the sole criteria for the validation of cleaning procedures? I have read a couple of articles by Richard J. Forsyth suggesting the applicability of visual release limits to cleaning and cleaning validation. Does anyone practice this kind of policy? In my experience, it is possible to have a "visual failure." but after sampling, the sample passes the calculated analytical release limit (based on standard L1, L2, L3). This makes one question why we use a less sensitive analytical method (TOC, UV or even HPLC) over a more sensitive visual inspection (if it can be proven so). Again, does anyone use visual inspection as the only spec for equipment cleanliness (including during validation)? If so, what kind of qualification process do you use for the residue(s)?

Respondent 1: This topic has been kicking around for 10-15 years. I am unaware of anyone who has based a cleaning validation on visual alone. You can make a good argument on visual, but what about the unusual shape of equipment, marginal lighting in manufacturing areas, etc.? Destin LeBlanc also had a paper on visual cleanliness a few years ago. You may be an innovator if you do visual without any chemical testing in a cleaning validation.

Respondent 2: I'm curious to see how many people will leap up to admit using this technique. But let me be the first (if not the only one...). I believe this is a very valuable validation tool that is unwarrantedly maligned by many in our overly conservative industry. Some years ago I worked for a company where I pushed to start using visually clean, and I was met with supercilious smirks from people who all seemed to feel that cleaning their glasses while discussing it with me was sagacious and humorous. After I pointed out that all of their equipment was released after cleaning by operators and then by QA inspectors based on a "visual inspection," the chuckling subsided. A program to start "certifying" the operators and inspectors using "visual standards" was started. We used a company called Pharmaceutical Resource Associates that makes such standards. Coupons were created with varying concentrations of product, and the operators and inspectors were certified to see residues down to a certain level. There was a product whose residues were visible far below its acceptance limit, and a cleaning validation was performed using "visually clean" only as the method of analysis. This was for a packaging line where all parts could be easily accessed and inspected. At the time, I had also spoken with a company that published an article on cleaning validation for solid dosage packaging lines using "visually clean" only. They had been inspected by FDA and did not receive any 483s or comments on this approach. So, yes, it has been done. And it should be done more. The articles by Richard Forsyth should clearly have opened everyone's eyes by now. Hope this helps.

Respondent 3: It is not unusual for a cleaning validation to fail on visual evaluation after passing other acceptance criteria. Visual evaluation is extremely sensitive, except for people like me with poor eyesight, but it is not a quantitative test. Most companies use a combination of visual evaluation and another verification test, such as TOC [total organic carbon] or conductivity, for cleaning validation, to compensate for the variability in visual evaluation. This does not mean, however, that visual evaluation cannot be used as the sole method for evaluating cleanliness for validation or for ongoing verification of effectiveness. To do this, however, you should have data to determine the visual limit of detection for the contaminant of interest on the surfaces you will be cleaning. You should be able to show that you can consistently detect the contaminant of interest at levels equal to or below the level of concern for the contaminant. Typically, you would treat the visual evaluation as a limits assay and perform a validation study showing that multiple operators can detect the contaminant of concern at the required levels. ICH Q2B gives further information on qualifying a limits assay.

Respondent 4: I think you will find that virtually no one uses visual inspection exclusively to assess effectiveness of cleaning in CV [cleaning validation] studies. Although visual inspection has been shown to be very sensitive at times (see LeBlanc, Destin), the questions about light, angle of viewing and consistency of viewing have always come up. I would think that a correlation with an accepted chemical test (e.g., HPLC, TOC, Enzyme-Linked Immunosorbent Assay), and even the various direct measurement spectrometric methods (via fiber optics) would

be necessary for visual to be acceptable as a sole technique to demonstrate an acceptable level of cleaning. For certain "simple" equipment, hopefully this may change in the future.

Respondent 5: In my humble opinion, "visually clean," although one of several endpoint criteria in some cleaning validation guidelines, is not sufficiently quantifiable to qualify as a "quality acceptance criteria." The only time I think it has a place is as a supervisory check out, when campaigning the same material between the several batches, or if equipment has been sitting in a "cleaned and then wrapped" condition.

Respondent 6: "Visually clean" is used by some companies, but only after they have quantified it experimentally. It works better when the product is solvent cleaned, and when the product is the only component in the equipment.

Respondent 7: At a previous company, I worked at an OTC manufacturer that manufactured about $200,000,000 in product in two plants. Cleaning validation was done using the visually clean criteria. Cleaning validations were performed in the same manner as if HPLC was used as the analysis technique. Our cleaning validation master plan and protocols could have said "HPLC analysis" instead of "visual analysis," and there would have been very few changes to the program. FDA has inspected our sites twice since then, and, although the cleaning validation program did not come under close scrutiny, our description of the program was found to be acceptable. The cleaning validation program was successful, because operations took cleaning and cleaning validation very seriously, as much as product manufacturing. From an operations perspective, it helped that cleaning validation using visual analysis is an economical and robust choice that keeps all of the responsibility for cleaning, and most of the responsibility for cleaning validation, with Operations. Also, since the manufacturing equipment is visually evaluated after every cleaning and before the start of any new batch, this is an excellent way to monitor the validation status of the equipment over time. The pilot studies that were run on this—for the most difficult-to-clean products-showed undetectable (by HPLC) levels of active in visually clean equipment. In two cases, small parts that were washed in a tub were found to have some detergent residue (although below acceptance limits) left on them, so this information was used to improve our rinsing procedures for the hand-washed items.

Another way to evaluate cleaning procedures is through microbial testing. Since the microbes are plated, microbial growth is a very sensitive technique for evaluating cleaning endpoints. Although microbial testing was kept separate from product residue testing in my last company, operations personnel are very sensitive to any discussions showing that microbes are present, more so than product residue. It would be worthwhile to formally consolidate product residue testing (by using a validated visual analysis technique along the lines of Destin LeBlanc's papers) and microbial testing in a cleaning validation master plan in some manufacturing sites.

Is it necessary to do a microbiological count test of the disinfectant solution that will be used in the disinfection process of aseptic areas, and what regulations support that? I would appreciate any collaboration.

Respondent 1: I think there is no requirement for microbiological counting in the EC guide to GMP, since I understand the word monitoring means a qualitative rather than quantitative. The following is quoted from the EC guide to GMP: Revision to Annex 1 of the EC guide to GMP states that *disinfectant and detergent should be monitored for microbial contamination and should be sterile prior to use in grades A and B areas.* Also, it is recommended that microbial contamination in grade A is less than 1 cfu/m^3.

Respondent 2: Everything that you bring into a class A environment, including disinfectant solutions, must be sterile.

Respondent 3: Does it mean that the disinfectant used in aseptic areas *must* be sterile and that the microbial test on it show < 1 cfu/ml? I'm also wondering: would it be wise to sterilize (by filtration) the disinfectant in house, rather than buying the certified sterilized (or filtered) disinfectant? These grades are very expensive. Does anyone out there have any experience of sterilizing your own disinfectants to be used in aseptic areas?

Respondent 5: Sanitizers and disinfectants do not kill all organisms and can harbor resistant spores in the solution, and they must be sterile prior to use. As for the second question: sterilization of disinfectants or sanitizers that are going to be used in grade A and B areas may be achieved through aseptic filtration or use of a product-compatible terminal sterilization method, or by other means such as irradiation.

Respondent 6: In our injectables unit, we use sterile disinfectants. As you said, buying it already sterile is quite expensive, so we do sterilizing filtration into the sterile core. We use an in-line 0.20 micron sterile filter, and each disinfectant is filtrated into a sterile container. As our disinfectants are used [and] diluted, we did microbiological validation for our maximum practical expiry date. This way we filtrate it pure and when needed (within the validated expiry date). We dilute it with sterile Water for Injection filtrated at the time.

PDA Calendar of Events for North America

Please visit www.pda.org for the most up-to-date event, lodging and registration information.

Conferences

September 11-15, 2006
2006 PDA/FDA Joint Regulatory Conference
(Conference, Courses and Exhibition)
Washington, D.C.

September 13, 2006
Meeting Aseptic Processing cGMPs in the US and EU
Washington, D.C.

October 10-11, 2006
PQRI Workshop on Excipient Testing and Control Strategies
Bethesda, Maryland

October 23-25, 2006
The Universe of Pre-Filled Syringes & Injection Devices
(Conference and Exhibition)
Bethesda, Maryland

October 30-November 1, 2006
PDA's 1st Annual Global Conference on Pharmaceutical Microbiology
(Conference and Exhibition)
Bethesda, Maryland

December 6-7, 2006
2006 ISPE/PDA Joint Workshop: Challenges of Implementing ICH Q8 and Q9 — Practical Applications
(Conference and Exhibition)
Washington, D.C.

January 29-31, 2007
PDA Emerging Manufacturing and Quality Control Technologies Conference
(Conference and Exhibition)
San Diego, California

March 19-23, 2007
2007 PDA Annual Meeting
(Conference, Courses and Exhibition)
Las Vegas, Nevada

Training

Lab and Lecture events are held at PDA TRI Baltimore, Maryland unless otherwise indicated.

Laboratory Courses

October 5-6, 2006
Developing and Validating Cleaning and Disinfection Programs for Controlled Environments

October 24-25, 2006
Validating a Steam Sterilizer

October 26-27, 2006
Fundamentals of D, F and z Value Analysis

October 30-31, 2006
Environmental Mycology Identification Workshop

November 14-15, 2006
DoE Basics for PAT Applications

November 15-17,2006
Cleaning Validation

December 5-7, 2006
Practical Aspects of Aseptic Processing

Lecture Courses

September 20-21, 2006
Computer Products Supplier Auditing Model:Auditor Training

October 23-25, 2006
Advanced Pharmaceutical Filtrations and Filters

Course Series

September 14-15, 2006
2006 PDA/FDA Joint Regulatory Conference Course Series
Washington, D.C.

October 16-18, 2006
Boston Course Series
Boston, Massachusetts

Chapters

September 19, 2006
PDA Delaware Valley Chapter
Dinner meeting: Aseptic Processing
Malvern, Pennsylvania

September 20, 2006
PDA New England Chapter
Dinner meeting: Common Technical Document
Cambridge, Massachusetts

September 25, 2006
PDA Metro Chapter
Dinner meeting: Cleaning Validation
Clark, New Jersey

October 10, 2006
PDA Southeast Chapter
PDA Southeast Chapter Fall Meeting and Vendor Show
Chapel Hill, North Carolina

October 25, 2006
PDA Capital Area Chapter
Dinnermeeting: Evaluating Risk in Aseptic Processing: The Akers-Agalloco Method
Gaithersburg, Maryland

November 3, 2006
PDA Southeast Chapter
Social Networking Event
Chapel Hill, North Carolina

Europe/Asia-Pacific/Web Seminars

Please visit www.pda.org for the most up-to-date event, lodging and registration information.

Europe

September 26-27, 2006
2006 Visual Inspection Forum
(Conference and Exhibition)
Berlin, Germany

October 5-6, 2006
PDA European Pharmaceutical Cold Chain Management Conference: A Global Approach to Harmonization
(Conference and Exhibition)
Berlin, Germany

October 10-13, 2006
2006 PDA/EMEA Joint Conference
(Conference, Courses and Exhibition)
London, England

November 9, 2006
PDA Italy Chapter
Review of the PDA/EMEA Joint Conference 2006
Milan, Italy

November 10, 2006
PDA Italy Chapter
Periodic Quality Review
Milan, Italy

November 23, 2006
PDA Italy Chapter
Review of the PDA/EMEA Joint Conference 2006
Rome, Italy

November 25, 2006
PDA Italy Chapter
Periodic Quality Review
Rome, Italy

Asia-Pacific

November 13-17, 2006
2006 PDA Asia-Pacific Congress
(Congress, Courses and Exhibition)
Tokyo, Japan

Web Seminars

September 19, 2006
Managing the Microbiological Quality of Pharmaceutical Excipients

September 21, 2006
Replication Competency: How Market Leaders Stay Ahead by Rapidly Identifying and Spreading Best Practices

October 4, 2006
Design Space: DoE Basics for PAT and ICH Q8

Times are Changing: The Role of the Qualified Person in the 21st Century, continued from cover

process, more reliance will be placed on process understanding, critical parameters and in-process controls. The QP has to find a new way to assure him/herself of the quality of the product, instead of relying on final-product testing. The QP must be assured that quality is indeed built into the process during development and must also have a thorough understanding of the critical parameters, the design space parameters and the controls required.

It has been said that in spite of these new concepts, most process understanding will be gained after product launch. Process understanding is the key to:

- product quality
- process robustness
- change management decisions
- quality risk management decisions
- decisions on deviations
- decisions on process improvement

All of these require a strong involvement of the QP. Therefore, the QP must be satisfied that the level of process understanding is sufficient for him/her to certify the product for release to the market, even on the first day after launch, and he/she should be part of the team that decides how much process understanding is required to launch the product onto the market. The QP also must ensure that there is a system in place to ensure that changes are made either within the design space and the marketing authorisation or that, where necessary, changes are submitted for marketing authorisation approval by the competent authorities.

The design space concept, as developed in ICH Q8, together with process analytical technology, also allows us to move away from traditional specifications to a control strategy based on in-line and at-line process controls. As a consequence, routine end-product testing may not be necessary, and batches may be certified based on process control measurements that assure product quality. A "process signature" may be used that will look very different from what we see in current release specifications. Decisions then have to be made based on risk assessment and on:

- the frequency of the controls
- the sample size
- the alert and alarm limits

The QP should approve the control strategy in the same way that he/she approves traditional specifications and should be assured that the control strategy guarantees the quality of the product.

Traditional Validation and Continuous Verification

Continuous verification has the advantage of: (1) always being representative of routine production under all conditions, (2) consistently ensuring that the process is under control and (3) making real-time or parametric release possible. In addition, it provides more data which contributes to process understanding, it enables measurement of process capability, and it establishes a framework for continuous improvement. However, carrying out continuous verification by (almost) continuous monitoring of the process does have a drawback—it may well produce more deviations, i.e., values that are outside their limits. In other words the larger the sample size and the more frequent the sampling, the more likely, by normal distribution statistics, a value will be found which is outside the limits, whereas the same batch would have been well within specifications if tested by traditional end-point testing. This presents a dilemma for the QP as to whether the batch can be released or not. In fact, it adds an additional dimension to the control strategy mentioned earlier. The control strategy on which batch release can be based needs to include not only the critical parameters to be tested, the sample size and frequency and the upper and lower limits but also the permitted sigma deviations based on a risk assessment. Furthermore, the QP must ensure that systems are in place to:

- identify causes of values found at the extremes of the Gaussian distribution and to take corrective action
- monitor and review trends and take preventive action
- ensure continual improvement of the process

The process should still be considered to be operating in a state of control, when, as a result of the increased sampling level, values are found within preset action limits and within the predicted normal distribution range.

Batch Certification

Traditionally, batch certification took place based on the results of end-product testing, on GMP compliance and on compliance with the marketing authorisation. However, if there is no end-point testing done, how does the QP certify the batch? In such cases, the QP has to have assurance that the control strategy is appropriate and was followed, and that systems are in place for the review of the batch record and the in-process control results. However, there is a dilemma, as a traditional certificate of analysis cannot be issued giving the actual results of end-point testing compared to final product specifications. Probably QPs are going to have to run hybrid systems for those countries or customers still insisting on a certificate of analysis, and some persuasion may be needed before a certificate of conformance or compliance—which the QP certifies that the batch has the required quality, was manufactured under GMP, and was manufactured according to the marketing authorization—is universally accepted.

The Case for Quality and Reliability

The release of individual batches based on end-product testing begs the ➤

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question of what the QP should do when batches are failing with too high a frequency. Should the QP certify the passing batches while rejecting the failing batches? If the sample size is small, then the chances are that some batches are being passed that should be failed, and vice versa. The robustness of the process is surely a far better indicator of product quality than individual batch results. As Moheb Nasr, PhD, Director, Office of New Drug Quality Assessment, FDA, CDER, has said: "A robust process is capable of handling changes in process inputs without negative impact on end-product quality," and "Reproducible means consistently and predictably delivering the same quality material." A process with a high reject rate probably has a high chance of unreliability of supply, and the patient is surely far better served by relying on process reliability than on a concept of individual batch quality.

International Multi-site Supply Chains

The world is becoming smaller and more complex. Today it is not unusual for APIs to be manufactured in China or India, excipients to be bought from several countries around the world, for part of the processing to be done in one country and other steps in another country, with final packaging and release taking place in several different countries. Under current requirements, the QP is expected to review all noncompliances with GMPs at the various manufacturing sites, review all critical deviations and investigations in the supply chain, review and approve all changes, ensure work is carried out within the terms of the contract, certify suppliers of APIs, qualify suppliers of excipients, and take personal responsibility for all manufacturing stages. The job has become impossible and certainly requires a super-human to perform it. Surely the role and responsibility of the QP should be to ensure that there are systems in place which:

- evaluate and approve the quality systems used by all players in the supply chain
- ensure that:
  - GMPs are appropriate at each manufacturing site
  - deviations are reviewed and investigated correctly
  - changes are reviewed and approved correctly
  - supplies of APIs are appropriately certified
  - suppliers of excipients are qualified

Some tasks may also be delegated to other QPs or to other suitably qualified competent experts.

Looking at the distribution network, we again see supply to multiple international markets, and the QP has to certify that the batch has been manufactured and checked in accordance with each of the relevant marketing authorisations, with EU GMP requirements and with the local GMP requirements, along with any other legal requirements of the country in which the product is to be marketed. Again, this is a very difficult task, which could be better fulfilled by making the QP responsible for ensuring that there is a system in place which:

- monitors global marketing authorisation applications, approvals and changes
- monitors local GMPs and legal requirements
- ensures that each batch *is* manufactured in accordance with its marketing authorisations and local legal requirements.

Conclusion

The qualified person should ensure that the quality system is fit for purpose and is operating effectively.

Probably anybody who has been a QP or has seen QPs at work has seen the burden of administrative paperwork focusing on individual batch release. Yet there is a better way to protect the patient than by individual batch release. The role of the QP should be to ensure that quality systems are in place, and that these quality systems are fit for purpose and operating effectively, so as to:

- provide assurance that the system can be relied upon to support batch certification
- ensure that issues are raised, if necessary, at an appropriate level prior to batch certification

The QP should also be able to delegate and rely on the decisions of other competent professionals within a proven quality system.

Finally, if this view of the role and responsibility of the Qualified Person is accepted, then one of the consequences is that management also has to take its responsibility for ensuring that a robust quality system is in place, is appropriately resourced, and is enforced. Only when this concept is fully recognized will a company be able to claim that quality systems are fit for purpose.

About the Author

Joyce Ramsbotham recently retired after working for 37 years in the pharmaceutical industry. Her most recent position was Vice President Global Quality Assurance for Solvay Pharmaceuticals, where she was responsible for coordinating all quality issues within the company. For 14 years, Joyce represented EFPIA and has been the chairperson of the EFPIA Manufacturing-GMP working group and a member of the Quality group. She was also the EFPIA topic leader for ICH Q7A. During the past three years she has been very closely involved in the ICH Quality topics, particularly in promoting ICH Q10 on quality systems and the need for continuous improvement within pharmaceutical manufacturing. Joyce also was a strong supporter of and contributor to PDA, speaking an numerous conferences. Joyce has worked in The Netherlands for the past 34 years and will be retiring in the Netherlands where she can be contacted at joyce.ramsbotham@wxs.nl.

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EMEA "Questions and Answers"

The following is a sampling of GMP "Questions and Answers" a currently posted on the EMEA Inspections Sector website. The answers are the official opinion of the EMEA Inspections Sector and can be considered the GMP interpretation in the EU. For additional Q & A, go to www.emea.eu.int/Inspections/GMPQaA.html.

Question: *Is it possible to use multiple batch numbers in packaging of medicinal products?*

Answer: GMP inspectors recently discussed the desirability of more than one batch number appearing on the packaging of medicinal products.

It is normal practice for companies to use a bulk batch number that is different from the finished product batch when the bulk is packaged as several sub-batches. There is normally an element in the numbering format common to the bulk batch and finished product batches that clearly ties these together, and the difference normally takes the form of a suffix, prefix or both.

A matter of concern for the inspectors is when the bulk and finished product batch numbers are completely different, and there is no obvious connection between the two. Even though the manufacturer has a system of traceability, the inspectors agreed that this is an undesirable practice and should be avoided. The main reasons for this are:

- Patients and health care professionals may mistakenly believe that there has been a packaging error
- Hospitals often remove products from the outer packaging, and traceability may therefore be lost
- Confusion may occur in the case of recall rendering such action potentially ineffective.

It is accepted that there may be exceptional cases where multiple batch numbers are displayed on a pack, such as in combination product packages. In addition, products that require relabelling following parallel distribution are expected to display the original manufacturer's batch number. Manufacturers are recommended to discuss individual cases with the relevant Supervisory Authority. In all cases traceability must be maintained.

Question: *When a new application is submitted in the European Economic Area (EEA) and a GMP inspection is deemed necessary, which competent authority carries out the inspection?*

If the site is located in the EEA, it is the competent authority of the member state where the site is located that carries out the inspection.

For sites located in countries outside the EEA, the responsible authority for inspection ("Supervisory Authority") is the authority in whose territory the importing site is located. In case the supervisory authority for any reason is not able to carry out the inspection, this can be delegated to another EEA competent authority.

If there is a Mutual Recognition Agreement (MRA) in place between the countries where the site is located and the European Community, the results of GMP inspections carried out by the MRA partner authority are normally recognized by the EU authorities.

Question: *What is a certificate of Good Manufacturing Practice (GMP certificate), and what is the difference between GMP certificates, certificates of medicinal product (also called certificates of pharmaceutical products, CMP or CPP) and certificates of suitability to the monographs of the European Pharmacopoeia (CEP)?*

Answer: A GMP certificate is a certificate issued, following a GMP inspection, by the competent authority responsible for carrying out the inspection, to confirm the GMP compliance status of the inspected site. GMP certificates are site specific but can be restricted to particular activities, depending on the scope of the inspection (e.g., manufacturing activities related to a specific product). Directives 2001/82/EC and 2001/83/EC, as amended, state that after every GMP inspection and within 90 days of the inspection, a GMP certificate shall be issued to a manufacturer if the outcome of the inspection shows that the manufacturer complies with GMP.

CMPs are product specific certificates, issued by the competent authority that granted the marketing authorization (EMEA issues CMPs on behalf of the European Commission for centrally authorized products), in the context of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce, to confirm the marketing authorization status of the products. These certificates also confirm the GMP compliance status of the manufacturing site(s). CMPs are mainly used by companies to support applications to export their pharmaceutical products to countries with less-developed regulatory systems.

CEPs are certificates issued by the EDQM (European Directorate for the Quality of Medicines), to confirm that a certain active substance is produced according to the requirements of the relevant monograph of the European Pharmacopoeia or of the monograph on TSE. CEPs can be used by companies when submitting an application for marketing authorization, and replace much of the documentation required for the active substance in the marketing authorization dossier. GMP inspections of active substance manufacturers can be requested by EDQM in the context of the CEP certification scheme.

Question: *How can GMP compliance for active substance manufacturers be demonstrated?*

Answer: Directive 2001/83/EC as amended (Directive 2001/82/EC for veterinary medicinal products) states that manufacturing authorization holders are obliged to use as starting materials only active substances that have been manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials. Thus, the legislation puts the responsibility on the manufacturing authorization holders using the active substance and does not [specify] mandatory routine inspections of active substance manufacturers.

To provide guidance on how GMP compliance of active substance manufacturers should be established, two documents have been published on the EMEA website. The first document is the *Guidance on the Occasions When it is Appropriate for Competent Authorities to Conduct Inspections at the Premises of Manufacturers of Active Substances Used as Starting Materials*. This document is published as part of the Compilation of Community Procedures on Inspections and Exchange of Information (see www.emea.eu.int/Inspections/GMPCompproc.html) and states that it is expected that manufacturing authorization holders will normally gain assurance that the active substances it uses are manufactured in accordance with GMP through an audit of the active substance suppliers. A second document, *Questions & Answers on Audits of Active Substances Manufacturers* (see www.emea.eu.int/Inspections/GMPfaqAS.html), provides further guidance.

Q&A on Pharmacopeial Issues

The following Q&A is pulled from the EMEA Quality Working Party (QWP) website relating to pharmacopeial issues. Additional Q&A on these topics is available at www.emea.eu.int/Inspections/QWPfaq.html.

Question: *How should industry apply the harmonized general chapter of Ph.Eur. "Uniformity of dosage units" to new and existing marketing authorisations?*

Answer: According to Directives 2001/83/EC and 2001/82/EC the monographs of the European Pharmacopoeia (Ph.Eur.) and the general chapters referred to in the monographs are the official standards of appropriate quality in the Marketing Authorisation procedures. In the pharmacopoeia it is also stated that a preparation must comply with the monograph throughout its period of validity.

The general chapter "Uniformity of Dosage Units" *(2.9.40)* is resulting from pharmacopeial harmonization. It is intended to facilitate achieving a single specification applicable in EU, Japan and USA for a given finished product.

The "Uniformity of Dosage Units" is referred to in relevant monographs of dosage forms in addition to "Uniformity of Mass" *(2.9.5)* and "Uniformity of Content" *(2.9.6)*.

Clarification: The decision by the regulatory authorities of EU is that the "Uniformity of dosage units" chapter is to be applied to all new applications for Marketing Authorisations at time of release.

The alternative to apply "uniformity of content" and/or "uniformity of mass" given in the test section of the monographs of relevant dosage forms is only applicable for already authorized products and submissions of Variations/extensions to those products. The intention is that the harmonized method "Uniformity of dosage units" ultimately will replace the individual methods "Uniformity of content" and "Uniformity of mass".

Question: *How can the text be interpreted in light of the compliance objection made by the FDA to the USP on the 2% RSD clause?*

Answer: The harmonized text is included in the European Pharmacopoeia and the 2% clause will thus be valid in the EU. This will not be dependent on the final outcome of the discussion between the FDA and the USP.

Question: *What is the regulatory consequence of implementing an alternative method for rapid control of microbiological quality of WFI and Purified water?*

Answer: According to EU legislation, pharmaceutical manufacturers are required to use European Pharmacopoeial standard water in the manufacture of medicinal products.

The EP has recently introduced a chapter making reference to the acceptability of rapid microbial methods to replace the standard pharmacopeial methods provided appropriate validation has been performed.

Following discussions at QWP and the ad hoc GMP inspector's group, it is suggested that the introduction of such methods might require specific review to ensure that the appropriate validation steps have been followed and that the water continues to meet the Ph. Eur specifications. Since, in the case of water, the validation will not be product specific, it is suggested that a company could request the Supervisory Authority to carry out a specific site inspection. The performance of such an inspection would be at the discretion of the Supervisory Authority and could involve a pharmaceutical assessor where necessary.

Since it is expected that the water will continue to meet Ph. Eur specification, if tested, no change to dossier requirements* (variations) would be involved and therefore no regulatory impact on individual products would normally be anticipated.

**This will depend on the level of detail in the original dossiers concerned.*

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/regulatory/RegNewsArchive-2006.html. PDA wishes to thank Hiltrud Horn, Horn Pharmaceutical Consulting (Germany), for contributing to the European briefs.

Europe

Dossier Structure and Content for Influenza Vaccines Derived from Strains with a Pandemic Potential

EMEA posted the guideline related to the above influenza topic with a consultation period ending Sept. 15 (EMEA/CHMP/VWP/263499/2006, 24 July 2006).

ICH Q4B, Regulatory Acceptance of Analytical Procedures

EMEA released *Note for Guidance on Regulatory Acceptance of Analytical Procedures and/or Acceptance Criteria*, along with an associated annex (EMEA/CHMP/ICH/222007/2006, June 2006). Comments are due by Sept. 30.

Nanotechnology-Based Medicinal Products

EMEA's *Reflection Paper on Nanotechnology-Based Medicinal Products for Human Use* (EMEA/CHMP/79769/2006, 29 June 2006) was released. The document reflects current thinking and the initiatives taken by EMEA in view of recent developments pertaining to nanotechnology-based medicinal products for human use. Applicants developing nanomedicinal products are encouraged to interact with EMEA from the early stages of development through the EMEA Innovation Task Force and/or the Scientific Advice Procedure. Comments can be submitted at any time to the Innovation Task Force.

Commercially Confidential Information

The draft EMEA document *Principles to be Applied for the Deletion of Commercially Confidential Information for the Disclosure of EMEA Documents* was released, and comments can be submitted to the Medical Information Sector by Sept. 30 (EMEA/45422/2006, 11 July 2006).

EMEA Status Report

EMEA released its July 2006 "Status Report," which gives summary data since 1995 on Medicine for Human Use applications (529), Mutual Recognition procedures completed for human medicines (4,096), Medicines for Veterinary Use applications (85) and Medicines for Rare Diseases (590 since April 2000).

Reexamination of CHMP Opinions

EMEA posted the final *Guideline on Procedures for Re-examination of CHMP Opinions.* An overview of comments received on the draft guideline for re-examination of CHMP opinions was published at the same time. (EMEA/CHMP/50745/2005, 26 June 2006)

Viral Safety for Biotech Investigational Medicinal Products

EMEA's draft *Guideline on Virus Safety Evaluation of Biotechnological Investigational Medicinal Products* was posted. The eight-page guideline is open for comment until Dec. 31, 2006.

Use of NIR in Pharma Manufacturing

In early June, EMEA posted the updated concept paper for the planned guidance on NIR, entitled, *Concept Paper on Revision of the Note for Guidance on the Use of Near Infrared Spectroscopy by the Pharmaceutical Industry and the Data Requirements for New Submissions and Variations* (EMEA/CHMP/CVMP/QWP/173698/2006, 27 June 2006). The concept paper updates the older guidance paper due to the increased experience with NIR, the impact of ICH Q8 and the ongoing discussions on PAT. Comments on the concept paper are being accepted until Sept. 30.

International Harmonization

ICH Posts ICH Q9 Briefing Pack To Website

To support the implementation of Quality Risk Management (ICH Q9) into daily operations for regulators and industry, some members of the ICH Q9 Expert Working Group have prepared a briefing pack (a set of slides) which are intended to be used for information purposes by industry, regulators and other facilitators.

North America

Upcoming FDA Workshops

FDA clinical trial regulatory requirements: The workshop will be held November 15 - 16, 2006 in Indianapolis, Ind. The workshop is for sponsors, monitors, clinical investigators, and those who interact with them. The workshop is cosponsored with the Society of Clinical Research Associates.

FDA-regulated products containing nanotechnology materials: The purpose of this workshop is to help FDA develop a better understanding of developments in nanotechnology materials that pertain to the products FDA regulates. The meeting will be held October 10, 2006 at the NIH in Bethesda, Md. Comments may be submitted until November 10, 2006.

FDA Seeks Comment on UDI System

In the August 8 *Federal Register,* FDA published a notice requesting comments on how the use of a unique device identification (UDI) system can help improve patient safety (e.g., by reducing medical errors, facilitating device recalls and improving medical device adverse event reporting). FDA would also like to receive comments on issues associated with the use of various

continued on bottom of page 29

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PDA's First Cold Chain Management Workshop in Europe

Rafik Bishara, PhD, Chair, PDA Pharmaceutical Cold Chain Discussion Group and Georg Roessling, PhD, PDA

In recent years, global regulatory agencies have increased oversight to ensure the integrity of pharmaceutical products in distribution channels. Pharmaceutical and biopharmaceutical manufacturers around the world and their partners, such as distributors, carriers, wholesalers and device providers are developing good cold chain management systems to ensure that the patient is receiving safe and efficacious medicines. The challenges of handling, storing and worldwide shipping of temperature-sensitive pharmaceuticals require the implementation of new technologies and quality systems to protect the product as it travels through multiple climatic zones and countries with different standards.

Presentations, case studies and panel discussions at the first **PDA European Conference on Pharmaceutical Cold Chain Management: A Global Approach to Harmonisation** will offer an in-depth look at the factors affecting the cold chain management of medicines and provide guidance on how to effectively implement technologies and quality systems to meet regulatory requirements, compendial standards and industry best practices.

Conference participants will also learn how PDA's Technical Report No. 39: *Cold Chain Guidance for Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products Through the Transportation Environment* provides a framework for development, validation and qualification processes to store and ship cold chain products with an adequate assurance of quality.

An update on the cooperation between the Cold Chain Committee, Pharma Logistics Forum and the Pharmaceutical Cold Chain Discussion Group, their harmonization efforts and the formation of the Temperature-Controlled Pharmaceuticals Group will be reviewed.

The agenda for the program is designed to help the participants develop robust and reliable systems to assure the proper handling, storage and shipping of temperature-controlled pharmaceuticals. The sessions of the conference will focus on:

- Global Regulatory Requirements
- Stability
- Packaging
- Validation/Qualification
- Storage, Distribution and Transportation
- Quality Standards
- Partners in the Supply Chain

On behalf of the Program Committee, we look forward to your participation and interaction with the speakers from regulatory agencies, pharmaceutical manufacturers, academia and the partners that provide and supply cold chain solutions. These formal and informal engagements will offer opportunities to discuss ideas that will lead to the development and/or enhancement of good cold chain management practices for your implementation.

Regulatory Briefs, continued from page 26

automatic identification technologies such as bar codes and RFID. Comments are requested by November 9, 2006.

FDA Publishes ICH Q4B and Q4B Annex 1

In August, FDA published ICH Q4B: *Regulatory Acceptance of Analytical Procedures and/or Acceptance Criteria* and a ICH Q4B: *Annex 1: Residue on Ignition/Sulphated Ash General.* The draft guidance describes a procedure to facilitate acceptance by regulatory authorities of pharmacopeial test methods and their interchangeability with test methods in the local regional pharmacopeias. The Annex provides the outcome of ICH's evaluation of the ROI/Sulphated Ash General Chapter harmonized text from the U.S. Pharmacopeia, the European Pharmacopoeia and the Japanese Pharmacopeia. Comments may be submitted until October 10, 2006.

FDA Names First Medical Director for Threat Preparedness

FDA announced the appointment of **Mark Goldberger,** MD, as Medical Director for Emerging and Pandemic Threat Preparedness in FDA's Center for Biologics Evaluation and Research (CBER) on July 20, 2006. Dr. Goldberger was selected after a national search of eligible candidates. In this newly created position, Dr. Goldberger will serve as a Senior Advisor for CBER's pandemic flu program and will plan, coordinate and implement activities related to the development and evaluation of products for emerging and pandemic threats.

CBER's Lot Release Protocols Published

In July, CBER published *Guidance for Industry: Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format -- Lot Release Protocols.* The guidance is intended to provide manufacturers of biological products that are regulated by CBER with recommendations for submitting lot release protocols in electronic format to CBER's Product Release branch. The new guidance finalizes a May 1998 draft document entitled, *Guidance for Industry: Instructions for Submitting Electronic Lot Release Protocols to the Center for Biologics Evaluation and Research*. While comments on the FDA guidance may be submitted at any time, this is a final guidance.

Final Plans in Place for Premier PDA/EMEA Joint Conference

PDA/EMEA Joint Conference • London • Oct. 10-13, 2006

The Program Planning Committee for the premier PDA/EMEA Joint Conference is putting the finishing touches on the program agenda. They have strategically scheduled opening talks that will set the tone for the entire two days of dialogue between European regulators and the industry.

The meeting opens with a two-part plenary session on **Understanding the EU Regulatory Framework.** The first part features **Martin Terberger,** European Commission, Belgium, **Emer Cooke,** EMEA, UK, and **David Cockburn,** EMEA, UK. These expert regulators will explain how law-making occurs; the role of Europe's various ➤

Program Planning Committee

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Emer Cooke, EMEA, UK
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PDA TRI Courses Add Value to PDA/EMEA Experience

In conjunction with the 2006 PDA/EMEA Joint Conference, the PDA Training and Research Institute (PDA TRI) is offering four training opportunities aimed at keeping your facility in full compliance and abreast of the latest guidelines in both the United States and Europe. You will be learning from leading subject matter experts in the pharmaceutical and biopharmaceutical industries.

Quality System Strategies for Investigational Drugs
October 10-11
PDA #149
Karen Ginsbury, *Pharmaceutical Consulting Israel Ltd.*

Risk Estimation in Aseptic Processing
October 10
PDA #402
Klaus Haberer, Compliance Advice and Services in Microbiology, *GmbH*

Risk-Based Approach and Risk Management in Pharmaceutical Manufacturing
10-11 October
PDA #133
Trevor Deeks, *Skanska Pharmaceutical Group*

Manufacturing Requirements for E.U.and U.S. Markets
11 October
PDA #166
Colman Casey, *University of Cork*

Visit www.pda.org/pdaemea2006/courses for full course details.

Final Plans in Place for Premier PDA/EMEA Joint Conference, continued from page 30

review and oversight organizations; and the role of EMEA as it interacts with national bodies, the EU Commission and the EDQM. They will also address the role of EMEA and the national inspectorates in carrying out GMP inspections, both domestically and overseas.

The second part features **Gerald Heddell,** MHRA, UK, **Milan Smíd,** formerly with the State Institute for Drug Control, Czech Republic, and **Stuart Heir,** Novartis, Switzerland. These experts will further address how EU regulation is implemented in the member states and how industry can assist in shaping the future of GMPs. Speakers will also discuss the role of The 1968 Medicines Act in conjunction with EU regulations and directives; the activities related to transportation and implementation of the EU GMP system in the Czech Republic; and new technologies to aid regulatory change.

Concurrent sessions focusing on Contractor Management, Dedicated Facilities, The Role of the Qualified Person, Investigational Medicinal Products (IMPs), Counterfeiting and Veterinary GMPs will follow the opening plenary sessions.

Visit www.pda.org/2006 PDAEMEA for details on additional plenary and concurrent sessions.

PDA wants to thank and congratulate the internationally diverse program planning committee for working through all of the logistical challenges and planning a stellar premier PDA/EMEA Joint Regulatory Conference!

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USP, Regulators and PDA Plan Global Conference on Pharma Microbiology

First Annual PDA Global Conference on Pharmaceutical Microbiology • October 30-November 1, 2006 • Bethesda, Md.

Planning Committee Co-Chairs Michael Miller, PhD, Eli Lilly and Company and Richard Levy, PhD, PDA

PDA has it roots firmly grounded in microbiological science. As members, we look to PDA to help us bridge the gap between environmental microbiology and sterilization and drug manufacturing sciences, and the Association, in turn, always finds sound scientific solutions to most of our challenges.

Over the last two decades, PDA has established 18 Interest Groups, 15 active technical report task forces and 10 Meeting Planning Committees focused either directly or indirectly on pharmaceutical microbiology. In addition, PDA has sponsored several specialized meetings and training courses that involve the science of microbiology, covering topics like aseptic processing, environmental microbiology, mycology, rapid microbiological methods and viral safety.

For the first time, we are hosting a conference on the common thread that binds these various topics together: Microbiology. PDA's first **Annual Global Conference on Pharmaceutical Microbiology** will be held Oct. 30–Nov. 1 in Bethesda, Md.

The Planning Committee is creating a scientific program that will draw upon the knowledge of pharmaceutical/biopharmaceutical microbiology experts from around the world who will discuss the underlying science of the field and address the challenges that face our industry on a daily basis. The agenda, developed by an international program planning committee comprised of regulatory, pharmacopeial and industry professionals, is designed to foster maximum discussion and networking and provide you with the information you can apply immediately upon returning to the workplace. Topics on the agenda include:

- The theory behind critical microbiological practices to better troubleshoot and solve contamination problems
- Sources of contamination to facilitate GMP compliance in pharmaceutical and biopharmaceutical manufacturing
- Basics of environmental monitoring and facility design to identify and control contamination in product manufacturing
- Use of risk assessment and mitigation in aseptic processes and microbial control
- Use of appropriate microbial testing methods to ensure acceptable sterility assurance levels of components and final product
- Airflow principles to reduce the risk of viable contamination of product in your facility
- New and innovative technologies which will change the way we manage our microbiological control strategies

Pleased to be working with the U.S. Pharmacopeia, the program committee is planning to devote an entire day of the conference to pharmacopeial topics, including:

- Disinfectants and antiseptics
- Application of water activity determination to nonsterile pharmaceutical products
- Microbiological evaluation of clean rooms and other controlled environments
- Microbiological best laboratory practices ➤

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Terry Munson
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Bryan Riley, PhD
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Radhakrishna Tirumalai, PhD
U.S. Pharmacopeia

Brenda W. Uratani, PhD
U.S. FDA

Report from the May 2006 PDA Biennial Training Conference

Joanne Cochran, JWC Training Associates and 2006 Program Chair, and Lina V. Divitt, Chiron Corporation and 2006 Program Committee Member

What happens when you get 200+ regulatory trainers, training managers, quality personnel together in one place? A dynamic, fast paced, positive learning experience.

Starting with the energetic "GMP Idol" plenary session and ending with the Keynote Workshop, "Enhancing Training Effectiveness and Performance Results," attendees were treated to 35 concurrent interactive sessions given by their peers and colleagues. Heard often was, "I don't know which one to go to, there are too many choices." Each attendee had the opportunity to attend 6 different concurrent sessions over the course of the conference. Topics ranged from operator training to best practices to training effectiveness. Attendees also had the opportunity to vote for their favorite "Trainer's Choice Award," an award given to their peers by their peers for development of a internal training program.

The conference was capped by an interactive workshop, "Enhancing Training Effectiveness and Performance Results," led by **Stephen Smith,** Senior Vice President and Managing Executive, Rummler-Brache. During the workshop, attendees learned to look at training and on-the-job performance in a different way and to expand their role to performance consultant.

The key theme of the workshop focused on business performance and what we as trainers and performance consultants can do to influence this through our training process and system. According to Rummler and Brache, there are three critical indicators of successful business performance. Companies should be effective and efficient and continually learning how to improve. Performance occurs at three levels: the organization level, the process level and the job/performer level. The training, and ultimately the performance of the individual must align with the critical business needs of the organization if both training and performance will be effective. For the business to perform well, it is critically important that all three levels are aligned. To achieve this, the organization must focus on real issues, prioritize its impact on business goals and align these priorities with those of clients. Since the individual is the fundamental unit of performance, the individual must be part of the process and cannot remain isolated from the organization level and process level.

In the workshop, attendees were shown how to evaluate the business drivers of an organization and link them to human performance. They were also given a simple and repeatable approach for measuring the performance of their training system using some "human performance technology" tools.

Attendees went home tired but with many tools that they can use on their job.

"Dame Edna," played by James Vesper, President, LearningPlus, helped attendees decide what sessions to attend during a funny skit mocking American Idol during the Opening Plenary Session

To keep on improving our businesses through training, mark your calendar now for the 2008 conference in New Orleans, May 19–23, 2008.

We'll be looking for you!

USP, Regulators and PDA Plan Global Conference on Pharma Microbiology, continued from page 32

- Validation of alternative microbiological methods and sterilization
- Sterility assurance of compendial articles

Bring your most challenging questions, because we are also planning an "Ask the Experts Panel" to ensure that all participants take home the answers they need.

In addition, breakfast roundtables, on-site luncheons and evening receptions will provide you with many opportunities to meet and greet old friends and to meet colleagues with mutual interests. Concurrently, exhibitors will be presenting their latest products to help you do your job effectively and efficiently.

Vice President's Message

Gail Sherman

New Facility Countdown: Volunteer Design Team Named

While it is a bit early to officially start a "countdown" to the day TRI moves, we recently hit a milestone that will help us get the clock started! In August, we contracted with Vectech Pharmaceutical Consultants, Inc. to help us with the design of our new facility. **Bob Ferer,** VP, Automated Systems, and **Bill Bennett,** Architectural Designer, will be working with TRI staff to ensure that our new cleanroom mimics a manufacturing site so students can learn in an environment similar to where they work. We want our laboratory space to "flow" (if any of you have ever been to TRI's current location, you will understand what I mean) so that the students can move from labs to classrooms and back to labs easily—without walking down multiple hallways and through the kitchen. (We love you Baltimore, but it is time to move on!)

Our classrooms will be set up, allowing us to host one large lecture or multiple smaller lectures. They will also have state-of-the-art equipment, and will be networked for future IT training. We might have to live with the old furniture for a while, but that's okay, the environment will be oh, so much more pleasant!

PDA's initial estimate for moving TRI was December or January, but after compiling all the factors involved, we have pushed the date back to June 2007. We are anxious to get this right, and in doing so, feel that we need some additional time for the design and construction. In addition, we need time to teardown equipment, reassemble and test and validate. And, most importantly, we want to give our instructors time to get accustomed to the new facility in Bethesda.

We are planning for the design plans to be approved in early September and the build-out to begin shortly after, pending the approval of all the appropriate permits, so by the time you read this, we should have plans in place for the HVAC, water, electricity and big equipment. Because our goal is to run two lab courses at the same time without conflict, equipment placement is critical to our future success as an education provider. We are touring existing laboratory facilities and talking with potential builders on our construction, and I am considering buying a hard hat, though I'm not sure the builders will want me running around telling them where to put things!

In the meantime, it will be business as usual in Baltimore. We have scheduled our laboratory courses to run in Baltimore from January thru May. You will be able to see our entire 2007 schedule in our course catalog, which will be released at the upcoming PDA/FDA Joint Regulatory Conference. We have scheduled several new courses along with our trademark Aseptic Processing Training Program.

The move will coincide with the tenth anniversary of TRI on May 1. Besides the new facility and the new courses, TRI is working on developing a 10-year anniversary retrospective, with articles and photos published in the May 2007 issue of the *PDA Letter.* If you have anything (commentary and/or photos) you would like to contribute to TRI's tenth anniversary retrospective, please contact me as soon as possible.

Look to my column for future announcements regarding the move, the tenth anniversary plans and TRI course developments over the next few months. Oh yeah, anybody got a hammer and a hard hat?

[**Editor's Note:** We asked Gail if members can expect more updates on the big move—which is no longer a big deal for Headquarters' staff since we moved August 1. She stated: "We hope readers don't grow tired of these updates on the move of TRI from Baltimore to Bethesda. For us, this is rather exciting, and while we don't plan to make the journey until after the winter snows, we are moving forward with our planning, as well as the design and build-out of the new lab and office space. Over the next few months, there will be plenty of PDA member volunteers to acknowledge, so I will definitely be getting the word out in the *PDA Letter* and on a website that is currently in development to track the move via narrative and photos."

PDA would like to acknowledge the volunteer efforts of Vectech Pharmaceutical Consultants. Besides contributing key expert advice to the facility design, they have been an ardent supporter of TRI and PDA over the years. In addition, Vectech's Jeanne Moldenhauer is a prolific author for PDA/DHI and contributor to the PDA Journal and participates on many PDA committees. Scott Sutton also contributes to PDA as a TRI instructor, and with his pen and currently sits on the *PDA Letter* Editorial Committee.]

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www.pda.org/calendar/courses

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VISIT US AT THE 2006 PDA/EMEA JOINT CONFERENCE IN LONDON, OCT. 12-13, TABLE #4.