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PDA Letter

Volume XLVI • Issue #5

www.pda.org/pdaletter

May 2010

In This Issue:

Mission Excellence: Over 60 Talks at PDA Annual Meeting on Improving Manufacturing

Walter Morris, PDA

The success some firms are having with efforts to modernize manufacturing and control processes was manifest at the *2010 PDA Annual Meeting*. Talks covered the gambit of innovations and solutions from process analytical controls to quality by design programs.

A unifying theme among the more than 60 presentations on the topic was the central role of process control software and modern analytical tools. Whether used for collecting data from online analyzers or tracking and trending quality systems information across sites, speakers repeatedly demonstrated how good information technology can transform old processes, particularly when paired with comprehensive cultural changes.

In the plenary session, attendees were treated to a presentation outside the scope of their daily jobs, but served as a reminder that good science is fundamental to advancements in every field.

NASA scientist **Janice Meck**, PhD, ignited the meeting with a discussion about the development of drugs to reduce or prevent cardiovascular dysfunction in returning astronauts.

Next time you complain about wearing a gown in the clean room for an entire shift, keep in mind that about 20% of astronauts return from spaceflight suffering from orthostatic hypotension (the inability to maintain standing blood pressure). This condition causes those suffering from it to faint while upright. The likelihood of suffering from orthostatic hypotension increases dramatically for those serving on the International Space Station; 83% are affected.

Despite years of research and several trials, NASA's effort to find a solution to the problem, a tangible solution has yet to be found.

Meck described the various starts and stops in NASA's efforts, including exploration of dehydration as a cause of the orthostatic hypotension. However, the solution—a fluid loading protocol—saw no results. Next, they examined the use of Florinef® to restore plasma volume in those tested, but it did not reduce the incidences of fainting.

REPORT FROM THE 2010 PDA ANNUAL MEETING

continued on page 15

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This workshop will focus on the challenging subject of safety syringes reviewed from various angles covered by the following sessions:

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- Regulatory issues (current status: What is a must)
- Technology Design issues (links to supplier, pharma, and user)
- Technology Safety systems, what is available on the market
- Manufacturing: How to integrate safety features to pre-filled syringes
- Manufacturing Processes Case Studies
- Manufacturing Quality/control/secondary packaging

For further details please contact Leon D. Lewis at lewis@pda.org

Workshop Co-sponsors:

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Week [illegible]-29 SOLD OUT!
Week [illegible]uary 22-26

Session 2:
Week [illegible]6 SOLD OUT!
Week [illegible] April 19-23

Session 3:
Week [illegible] SOLD OUT!
Week [illegible] June 14-18

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

Session 5:
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Week 2: November 8-12

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- Learn to incorporate proper documentation practices into your aseptic processing program to facilitate regulatory compliance

LEARNING OBJECTIVES:

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

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

FOR MORE INFORMATION CONTACT:

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

LOCATION:

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Cover art:
Achieving manufacturing excellence involves good personnel, expanded knowledge of the product, and good procedures.

Coming Next Issue:
Good Distribution Practices

Editor's Message

PDA's Annual Meeting: The Glue Holding PDA Together

In this and the next several issues of the *PDA Letter*, we will be running articles from the *2010 PDA Annual Meeting*. It was a noteworthy event in many ways but of import to the Letter are the good presentations that will contribute to good articles. The cover story of this issue provides a glimpse into some of the presentations that enlightened attendees about the benefits of "Manufacturing Excellence." We also have reports on the Honor Awards Banquet, the New Member Breakfast and TRI course demonstrations. Next issue, we will publish a lengthy "Faces and Places" with photos from the sessions, the networking events and the exhibition, along with other reports.

The Annual Meeting is an important event for PDA beyond the talks that often are the topics of *PDA Letter* articles. The meeting brings together a number of Task Forces, Interest Groups and other PDA committees so that they can advance technical reports, plan conferences, share views on specific topics, and further overarching plans for the organization. The Board of Directors also meets at the Annual Meeting, along with PDA's Strategic Planning Committee. The PDA Technical Book Committee convened this year, along with an impromptu meeting of several members of the *PDA Letter* Editorial Committee.

Why tell you about all of the ancillary meetings? Well, if not for the volunteers who meet regularly at the Annual Meeting and other PDA meetings, and sometimes even PDA headquarters, PDA would not be able to offer its membership the various high quality and valuable tools we offer as part of your membership or at membership rates.

So I encourage you to stop reading this and turn to the News and Notes section to see the winners of the 2009 Honor Awards. These people—your colleagues and, in some cases, coworkers—have expended a lot of effort helping shape PDA.

Finally, I encourage you to get involved with PDA, too!

PDA Letter

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

PDA Europe
Adalbertstr. 9
16548 Glienicke/Berlin
Germany
Tel: +49 33056 23 770
Fax: +49 33056 23 7777
Email: petzholdt@pda.org

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

Annual Meeting Banquet Honors PDA's Dedicated Members

At the *2010 Annual Meeting* in Orlando, Fla., PDA recognized dedicated contributors who have shaped the Association in recent years. The Honor Awards were presented at the traditional banquet the night before the meeting commenced.

PDA congratulates each winner and thanks them for their service to the Association.

Look for future coverage on each award winner throughout the year leading up to the 2011 Annual Meeting in San Antonio, Texas.

**Those with an asterisk following their name were not present for the banquet.*

James P. Agalloco Award

This award is presented annually to the PDA TRI faculty member who exemplifies outstanding performance in education. The selection is based on student and faculty evaluations and is named for James P. Agalloco in honor of his work in developing the PDA education program. This year's recipient is:

Barry Friedman, PhD, Consultant


Barry Friedman

President's Award

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

Feng Chen, PDA

Antje Petzholdt, PDA

Honorary Membership

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

Edmund Fry, Lachman Consultants


Edmund Fry

Distinguished Service Award

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

Stephan Rönninger, PhD, F. Hoffmann-La Roche

Peter Rauenbuehler, PhD, Genentech

Jean-Louis Saubion,* PhD, Centre Hospitalier Universitaire de Bordeaux

Amy Scott-Billman,* GlaxoSmithKline


Stephan Rönninger, PhD


Peter Rauenbuehler, PhD

Frederick J. Carleton Award

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

Vincent Anicetti, Genentech

Yoshihito Hashimoto, Chiyoda Corporation


Yoshihito Hashimoto

Frederick D. Simon Award

This award is presented annually for the best paper published in the *PDA Journal of Pharmaceutical Science and Technology* and is named in honor of the late Fred Simon, a previous PDA Director of Scientific Affairs. The winning article is "Distribution of Silicone Oil in Prefilled Glass Syringes Probed with Optical and Spectroscopic Methods, " *PDA Journal of Pharmaceutical Science and Technology*, March/April 2009, pages 149-158. This year's recipients are:

Zai-Qing Wen, PhD, Amgen

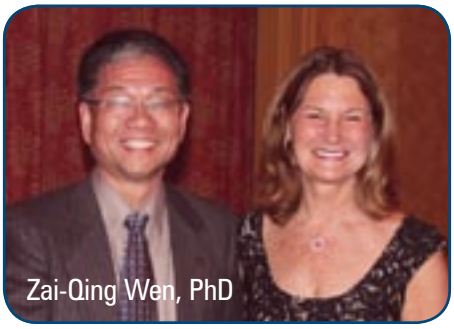
Robert Schulthesis *

Fabian Vega, Instituto Technologico de Morelia

Aylin Vance,* Amgen

Xiaolin Cao,* Amgen

Bruce Eu,* Amgen


Zai-Qing Wen, PhD


Fabian Vega

Service Appreciation Award

This award is given in recognition of special services preformed on behalf of PDA. This year's recipients are:

John Shabushnig, PhD, Pfizer

Louise Johnson, Aptuit

Stefan Köhler, AstraZeneca

Robert Caunce,* Hospira

Robert Buchholz,* Becton-Dickinson


John Shabushnig, PhD


Stefan Köhler

Gordon Personeus Award

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

Susan Schniepp, Antisoma


Susan Schniepp

PDA/DHI Editor/Author Award

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

Jack Lysfjord, Lysfjord Consulting

Theodore Meltzer, PhD, Capitola Consulting

Maik Jornitz, Sartorius Stedim Biotech


Jack Lysfjord


The 2009 Honor Award Winners

Science & Technology Snapshot

Technology *Trend*

Green Packaging = Efficient Packaging

Emily Hough, PDA

You might be surprised to learn that when your firm adopts an environmental-friendly system, it is also implementing an efficient process.

According to **Eric Lindquist**, President, Entropy Solutions, in the next year there will be a huge jump in the number of companies using reusable packaging, not necessarily because the product is good for the environment, but because of enhanced thermal performance. In the past, "if you wanted to do what was right or what was deemed right and go green, there was always a sacrifice … typically higher cost or less performance or a change of process." Today, life science companies look at their internal sustainability initiatives and realize they can implement systems that improve temperature performance, save the company money, and reduce packaging waste, or as Lindquist put it, "the holy trinity," which allows firms to "win on all accounts."

But there are a lot of choices out there to pick from. To make a decision, Lindquist said that life science manufacturers must analyze various aspects of packages, such as what effect, if any, the system has on their current processes and the energy required to implement it. "If you are a pharmaceutical company that wants to utilize a sustainable packaging system, there are programs out there that allow you to do that and recognize a cost savings…"

When analyzing the various "green" or "sustainable" packaging, Lindquist said you must consider the amount of energy and material that are consumed in its production, the effect it has on the environment during its useful life, and the end of life effects. Hard questions have to be asked even for a recyclable system: How easy is it to recycle? How much does it cost? How much energy is consumed at the end of its life scenario?

Testing standards for sustainable packaging requires a different set of factors as well. A temperature-sensitive package that is used multiple times must undergo a rigorous validation process to make sure that the components are in the same working order as they were the first time the package was used.

Consider the ramifications of a product reaching the end of its life cycle. When it is tossed into a landfill, unless it is 100% biodegradable, the product and others like it will probably produce leachables into the ground that will cause that site to eventually become toxic.

It does not make sense not to utilize a "true" sustainable product considering how many incentives there are for implementing it, such as cost and increased performance and what the consequences are for ignoring this growing trend.

Technical Report *Watch*

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

- *Points to Consider for Biotechnology Cleaning Validation* **(BioAB)**
- *Technical Report No. 22: Process Simulation Testing for Aseptically Filled Products* **(BoD)**
- *Recommendations for the Production, Control and Use of Biological Indicators for Sporicidial Gassing of Surfaces with Technical Exposures* **(BoD)**
- *Technical Report No. 3: Validation of Dry Heat Processes Used for Sterilization and Depyrogenation* **(BoD)**

In Publication: TR is approved and ready for publication.

- *Technical Report 48: Moist Heat Sterilizer Systems*

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1 United States Pharmacopeia Convention, Inc. 2009. The United States Pharmacopeia 32/The National Formulary 27. 2009. The United States Pharmacopeial Convention, Rockville, MD.
2 European Pharmacopeia, 6th Edition. European Directorate for the Quality of Medicine, Council of Europe. 226 Avenue de Colmar BP907, F-67029 Strasburg Cedex 1, France.
3 Japanese Pharmacopeia, Fifteenth Edition.
4 Clinical and Laboratory Standards Institute. 2004. Quality control for commercially prepared microbiological culture media; Approved Standard – Third Edition, M22-A3. Clinical and Laboratory Standards Institute, Wayne, PA.

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Recent Sci-Tech Discussions: Filter Validation and Hold Time Studies

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.

Filter Validation

Is filter validation required for an injection product at Phase I clinical stage? If not, what is the minimum activity that needs to be performed before using the filter in the GMP Phase-I clinical supply batch?

Respondent 1: Normally you don't have enough product available to do filter validation for a Phase I supply. Also it is somewhat pointless as the formulation and manufacturing process is inevitably going to change.

When I was working at a clinical manufacture plant (not at Wyeth), we typically only covered filter sterilization validation and integrity test validation prior to Phase I. Even then we typically tried to do a water wet pre-filtration integrity test and a water or water/IPA post-test since there was never usually enough product available even to generate product wet IT parameters.

We never attempted to do full filter validation until the process was scaled up. Usually this was during Phase III. I hope this is helpful.

Respondent 2: Filter integrity testing (non-destructive) to be performed prefiltration depends on your batch plan for biopharmaceuticals, extractables and leachables. Data must be evaluated and documented—given by the vendor.

Respondent 3: It's not a question of *if* it is required or not by someone else (regulatory agencies), but it's your own need to have this data with you to properly develop the product as all components of filter validation (product bubble point, compatibility, leachables, bact. retention) help you only to properly develop the product even before Phase 1. If you look at it from this point of view (your need rather than compulsion by some one else) this question will not arise.

Hold Time Studies

Hold time studies are performed to justify holding intermediate production stages (e.g. granules, or bulk tablets) before a process is completed. Are there any guidelines (U.S. FDA, EMA, QHO, etc.) that require these hold time studies to be performed … for three separate batches of the bulk material? If so, could someone please provide me a lead to these documents?

Respondent 1: I can't think of anything that addresses this specifically. I've seen this type of expectation in audit reports and 483's but never explicitly clarified in any regulatory guidance.

Respondent 2: I have not seen any FDA guidance on this. My experience has been that you do at least one batch in a container/closure system that is identical to the one you would use to hold the material and in the same storage condition.

Respondent 3: I am not aware of a guideline, but it is definitely the expectation of regulatory authorities to perform hold time studies for three separate batches. Moreover, for biotech products they expect you to run hold time studies for API intermediates through the end of stability of the DS [drug substance].

Respondent 4: The requirement for performing hold time studies is in the FDA's Aseptic Processing Guidance. However, it does not provide any details about how to do the studies. If you look earlier in the section, it will tell you what section of the GMP's are referenced as "why" you must do it.

Respondent 2: The requirement for hold time studies is based on 21 CFR 211.111, which states the following: *When appropriate, time limits for the completion of each phase of production shall be established to assure the quality of the drug product. Deviation from established time limits may be acceptable if such deviation does not compromise the quality of the drug product. Such deviation shall be justified and documented.*

The hold time data required for a biologic (i.e., biotech product) could be much more stringent than for a solid dosage form. **[Editor's Note:** Respondent 2 corrected this sentence in a different response. Initially, the respondent accidently said the opposite—that the requirement was less stringent for biologics. The Letter decided to correct this response rather than run the author's correction.**]**

FDA is going away from the "three batch requirement" even for process validation studies. There is no such magic number for hold time studies for solid dosage forms.

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

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

SECTION TITLE

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RELATED IGS AND GROUP LEADERS

Biotechnology
Group Leaders (USA):
Jill A. Myers, PhD
BioPro Consulting
jmyers@bioproconsulting.com

Stephen Notarnicola, PhD
Biogen IDEC
stephen.notarnicola@biogenidec.com

Group Leader (EUR):
Hannelore Willkommen, PhD
Reg. Affairs & Biological Safety Consulting
hannelore.willkommen@gmx.de

Lyophilization
Group Leader (USA):
Edward H. Trappler
Lyophilization Technology
etrappler@lyo-t.com

Group Leader (EUR):
Harald Stahl, PhD
GEA Pharma Systems
harald.stahl@geagroup.com

Vaccines
Group Leader (USA):
Frank S. Kohn, PhD
FSK Associates Inc.
fsk@iowatelecom.net

Microbiology/ Environmental Monitoring
Group Leader (USA):
Jeanne E. Moldenhauer, PhD
Excellent Pharma Consulting
jeannemoldenhauer@yahoo.com

Group Leader (EUR):
Philippe Gomez
Sartorius SA
philippe.gomez@sartorius.com

Pharmaceutical Cold Chain
Group Leader (USA):
Rafik H. Bishara, PhD
rafikbishara2@yahoo.com

Group Leader (EUR):
Erik van Asselt
Merck, Sharp & Dohme
erik_van_Asselt@merck.com

Supply Chain Management
Group Leader (USA):
Lucy Cabral
Genentech, Inc.
cabral.lucy@gene.com

Visual Inspection of Parenterals
Group Leader (USA):
John G. Shabushnig, PhD
Pfizer Inc.
john.g.shabushnig@pfizer.com

Group Leader (EUR):
Markus Lankers, PhD
Rap.ID GmbH
markus.lankers@rap-id.com

Facilities and Engineering
Group Leader (USA):
Christopher J. Smalley, PhD
Pfizer Inc.
chris.smalley@pfizer.com

Group Leader (EUR):
Philippe Gomez
Sartorius SA
philippe.gomez@sartorius.com

Filtration
Group Leader (USA):
Russell E. Madsen
The Williamsburg Group, LLC
madsen@thewilliamsburggroup.com

Group Leader (EUR):
Michael Rook
Global Consepts EURL
glocon@orange.fr

Pharmaceutical Water Systems
Group Leader (USA):
Theodore H. Meltzer, PhD
Capitola Consulting Co.
theodorehmeltzer@hotmail.com

Prefilled Syringes
Group Leader (USA):
Thomas Schoenknecht, PhD
Amgen
tschoenk@amgen.com

Group Leader (EUR):
Brigitte Reutter-Haerle
Vetter Pharma-Fertigung
GmbH & Co. KG
brigitte.reutter-haerle@vetterpharma.com

Sterile Processing
Group Leaders (USA):
Ken Muhvich, PhD
Micro-Reliance, LLC
ken.muhvich10@comcast.net

Edward C. Tidswell
Baxter Healthcare
edward_tidswell@baxter.com

Clinical Trial Materials
Group Leader (USA):
Vince L. Mathews
Eli Lilly & Company
vlm@lilly.com

Combination Products
Group Leader (USA):
Michael A. Gross, PhD
Biologics Consulting Group
michaelgross.chimera@gmail.com

Packaging Science
Group Leader (USA):
Edward J. Smith, PhD
Packaging Science Resources
esmithpkg@msn.com

Quality Risk Management
Group Leaders (USA):
Mike Long
KPM International Associates
mlong@kpmint.com

Jeffrey L. Hartman
Merck & Co., Inc.
jeffrey_hartman@merck.com

Process Validation
Group Leader (USA):
Scott Bozzone
Pfizer, Inc.
scott.bozzone@pfizer.com

Technology Transfer
Group Leader (EUR):
Andrea Morelli
Kedrion
a.morelli@kedrion.com

Inspection Trends
Group Leader (USA):
Robert L. Dana
PDA
dana@pda.org

Regulatory Affairs
Group Leader (USA):
Amy Giertych
Baxter Healthcare Corporation
amy_giertych@baxter.com

Inspection Trends
Group Leader (EUR):
Dr. -Ing. Stephan Rönninger,
F. Hoffmann-La Roche Ltd.
stephan.rönninger@roche.com

Regulatory Affairs
Group Leader (EUR):
Barbara Jentges, PhD
PhACT GmbH
barbara.jentges@phact.ch

Quality Systems
Group Leader (USA):
Anders Vinther, PhD
Genentech
vinther.anders@gene.com

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Lothar Hartmann, PhD
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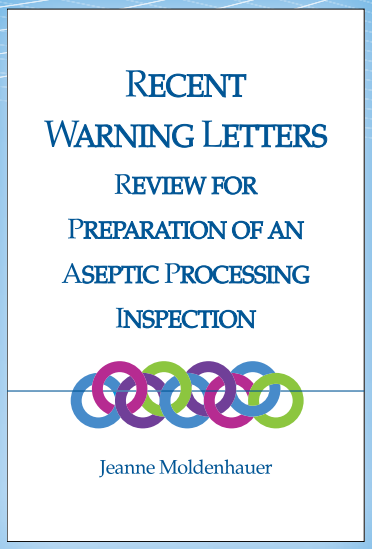
New Release

New Release at the PDA Bookstore



Recent Warning Letters: Review for Preparation of an Aseptic Processing Inspection

By Jeanne Moldenhauer

Recently, the US FDA has increased the number of Warning Letters issued to pharmaceutical companies following aseptic processing inspections. To ensure your facility passes your next FDA inspection, it is instructive to preview these warning observations and proactively prepare your facility. Ordinarily, this process is very time intensive since you have to search for those Warning Letters you believe would be of some help to you.

This novel book focuses on the following observational areas:

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- Equipment Cleaning and Maintenance
- Equipment Design, Size and Location
- General Requirements (Laboratory Controls)
- Responsibilities of the Quality Control Unit
- Stability Testing
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To learn more about this publication or to order your copy please visit: **www.pda.org/warningletters.**

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PDA Member **$265**
Nonmember **$329**

2 Cleaning and Cleaning Validation, Volume 1
By Paul L. Pluta
Item No. 17288
PDA Member **$335**
Nonmember **$419**

3 Environmental Monitoring: A Comprehensive Handbook, Volume I, Volume II, Volume III and Protocol CD
By Jeanne Moldenhauer
Item No. 17286
PDA Member **$875**
Nonmember **$1,049**

4 Risk-Based Software Validation: Ten Easy Steps
By David Nettleton and Janet Gough
Item No. 17256
PDA Member **$225**
Nonmember **$279**

5 Practical Aseptic Processing: Fill and Finish, Volume I and II
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Mission Excellence: Over 60 Talks at PDA Annual Meeting on Improving Manufacturing, continued from cover

Moving on, they launched an effort to create negative pressure around the lower body of the astronauts. While the funny-looking negative pressure pants worked, depressurizing the lower limbs did not prevent internal fluid shifts, thus failed to provide a solution.

Finally, NASA turned to a pharmaceutical solution, choosing midodrine because of various characteristics deemed favorable for the study. One, it acts in place of norepinephrine on blood vessels and does not stimulate the central nervous system nor the heart. In addition, its peak effect is at one hour and is short acting.

The drug was administered for a 14-day head-down tilt test. Positive results led Meck and her team to initiate trials after spaceflight. Even though results were positive, NASA discovered an ominous conflict with the use of midodrine—it interacted with the drug promethazine, commonly used by astronauts to treat motion sickness. Seven of eight subjects showed mild to moderate akathisia, or involuntary movement, anxiety and aggressive behavior, as a result of the combination.

As such, NASA does not allow the concomitant use of the two drugs, and the search for a treatment for post-flight orthostatic hypotension continues.

Industry Moving Forward with Excellence

Decisions, processes and technologies based on sound, scientific analysis are essential in the pharmaceutical industry today. Following tradition, custom, or cultural norms is no longer acceptable. In a sense, the "C" is becoming the most important letter in "CGMP," and if a firm has not embraced the principles of QbD, process analytical technologies, or the culture of "Quality Systems," it won't be long before it can be said that it has not kept up with current best practices. In short, if a firm is not working towards manufacturing excellence, it is falling behind.

From the presentations at the *2010 Annual Meeting*, it is clear that advances are happening at a wide breadth of companies, including large, small, innovator, generic, traditional drug, biotech, finished product and raw material.

There was Biogen Idec sharing its experience developing analytical strategies for QbD of biomolecules. **Andrew Weiskopf**, PhD, explained that where product understanding and process development interface resides the design space and control strategy.

Key to this is the identification of critical quality attributes (CQAs). The firm used a simple two-pronged approach for identifying CQAs: 1) Those attributes which were known or were likely to directly impact efficacy and/or safety; and 2) Attributes whose impact on safety/efficacy was unknown or uncertain would be examined closely.

For the first group, Biogen Idec included process-related impurities, contaminants, product-related impurities, potency and protein concentration, among others. The second group—the unknowns—included glycosylation, charge isoforms, post-translation modifications, oxidation and deamidation.

Weiskopf went into detail on the battery of tests the firm used to determine if any of the unknown attributes were CQAs. Following that, he discussed how the firm developed models for design space and the analytical challenges in doing so.

In conclusion, he advised the treatment of analytical support for design space development like a manufacturing campaign. There should consider holding "readiness meetings" between process development scientists and analytical staff. A "high level of engagement with defined start and end dates" should be maintained between the two groups. Finally, companies need to be "strategic in managing testing workload."

A number of companies providing enabling technologies and services were represented throughout the meeting.

Michael Miller, PhD, Microbiology Consultants and **Dawn McIver**, MicroWorks provided insight into the value and suitability of rapid microbiology methods (RMMs). Miller's presentation outlined an approach to measuring Return on Investment for RMMs. McIver demonstrated the comparability of one RMM system with USP <71> test methodology.

Peter Watler, PhD, Hyde Engineering & Consulting, offered a look at the usefulness of using mechanistic models in creating chromatography design space. **Heino Prinz**, Uhlmann Visiotec, demonstrated the value of utilizing inline tools to measure content uniformity and to identify unlabeled bulks.

There was also Wilco's **Gerhard Schramm**'s presentation on the use of laser absorption for head space studies

Challenges for Analytical Support of Design Space

- **Variations in matrix composition**
  - **Reality check: do your qualified methods tolerate your planned extremes of buffer, pH, etc.? Is dialysis/buffer exchange an option?**
- **QC method throughput and robustness for QbD applications**
  - **Will a method validated for 2-6 samples per day hold up for 50-100 samples in sequence?**
  - **Evaluate method performance to degree consistent with intended purpose**
- **Bridging developmental methods back to QC methods**
  - **Leverage high-throughput assays (Caliper LabChip GXII, intact mass analysis for glycans)**
  - **Need to correlate back to release methods**
- **Handling large testing workload**
  - **Large volume of samples in multiple assays**
  - **Critical path data to keep studies moving forward**

Weiskopf outlined the challenges of supporting QbD with analytical methods

on freeze dried vials.

Case studies from large manufacturers offered the best glimpse into industry's future. Two, in particular, highlighted the benefits of the new manufacturing and control paradigm—Genentech's program for operational excellence and Pfizer's implementation of real time release for an oral solid product.

A tag-team discussion by Genentech's **Robert Lippe**, Site Head of Manufacturing, and **Patricia Lufburrow**, Site Head of Quality, on the firm's continued pursuit of "operational excellence" reviewed the evolution of Genentech's culture over the last decade.

In the early part of the new millennium, the culture "depended on, and rewarded, functional expertise." This incentivized employees to focus "on the performance of their functional silo."

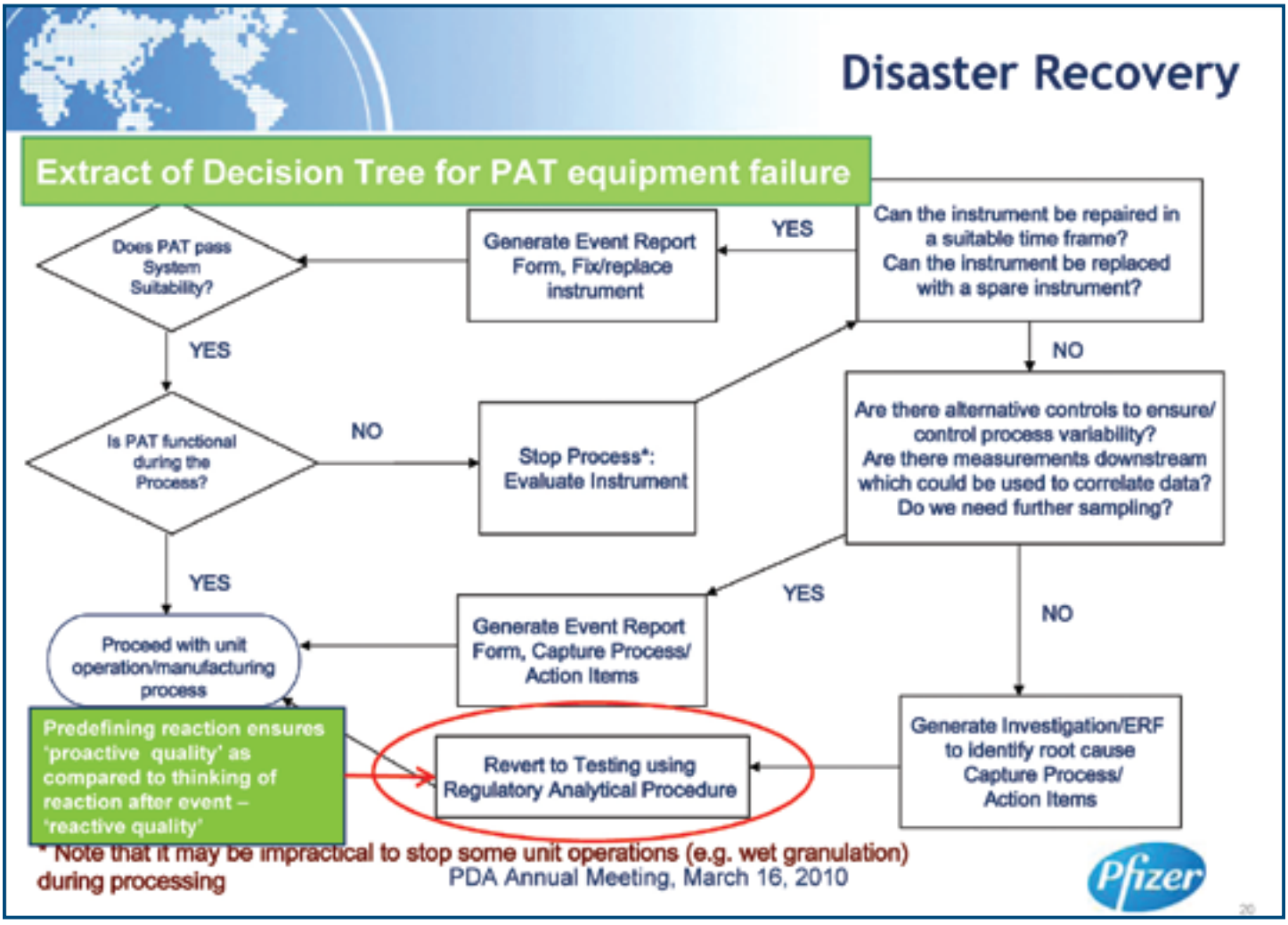
The firm undertook an initiative to transform this culture so it moved beyond technical excellence toward operational excellence. Since then, the firm has placed emphasis on developing highly agile and competitive production sites. The strategic approach involves balancing "right first time with simplification to maximize value."

The program involved changing behaviors, improving processes and upgrading technologies. The results so far, according to Lippe and Lufborrow, have been a reduction in loss rates to "insignificant" levels, the manufacturing site transitioned from one to two plants, volume demand and product mix "increased dramatically," and investigation rates "decreased over 70%."

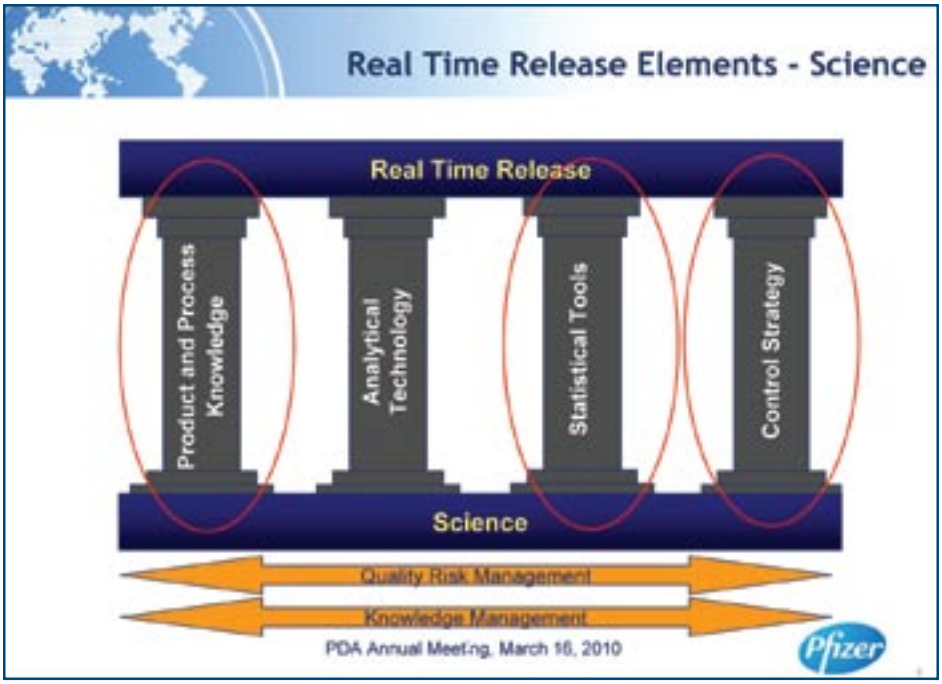
Moving forward, Genentech is looking to apply risk-based methodologies to increase validation efficiency, increase change control velocity, simplify deviation management and the effectiveness of CAPA, and continuously improve regulatory compliance. It also wants to "operationalize" process development and site manufacturing sciences, with the goal of reducing variation, among other goals.

Pfizer's presentation, "Enabling Real Time Release (RTR)," as another example. **T.G. Venkateshwaran**, PhD, Senior Director, New Product Quality and Process Knowledge, discussed the practical challenges and opportunities during RTR implementation for "Product X"—a BCS Class 3 compound, monolithic extended release and high dose tablet.

Venkateshwaran noted that RTR should not be the expressed goal of QbD, yet "it is a possible outcome." Yet, Pfizer has long been out in front of industry efforts to apply the principles of QbD and implement PAT, so it was no surprise that the case study presented dealt with a new product



Venkateshwaran shared a portion of Pfizer's disaster recovery plan for failing PAT equipment



The foundation and pillars of Real Time Release, from Venkateshwaran's slides

that Pfizer recently received approval on and that had gone through the U.S. FDA's CMC pilot program.

Product X was one that lent itself perfectly to a RTR strategy, meeting key requirements of RTR, according to Venkateshwaran. The process understanding developed at pilot-scale "translated well to commercial manufacturing scale" and the firm had a "robust control strategy" for the product. Key knowns about the product included:

1) Tablet surface area to volume ratio and polymer concentration influenced product performance.
2) Small variation of polymer concentration yielded acceptable performance.
3) Variation of polymer viscosity, particle size, moisture levels, and substitution ratio had no impact on dissolution.
4) API particle size distribution, coating, nor manufacturing process impacted dissolution.
5) Level A IVIVC for all dose strengths.

Finally, the firm developed science and risk-based quality systems in alignment with ICH Q10.

Venkateshwaran provided a detailed discussion of the various elements that support RTR. These are depicted in figure above. Knowledge Management (see the February 2010 *PDA Letter* for more on Knowledge Management) and Quality Risk Management comprise the hard-packed earth beneath a foundation of science. On top of that rest the pillars of Product and Process knowledge, analytical technology, statistical tools and control strategy that prop up RTR.

For the control strategy, Pfizer implemented a holistic approach. Venkateshwaran illustrated the strategy by discussing the controls for content uniformity. To take a holistic approach, the company employed process analytical technology at three steps of the process: sensors at the initial and final blend stations to measure real-time blend uniformity, another at the roller compaction stage to monitor granule particle size, and finally at the compression stage to monitor weight, hardness, potency, drug concentration, and identity rate.

This holistic approach was taken for each attribute of the drug product, comprising a control strategy that "increased quality assurance and, therefore, real time release is achievable," said Venkateshwaran.

The statistical tools were used to link the in-process tests to the quality of the material. These tools helped Pfizer determine if the sampling plan was adequate, develop a relationship between the RTR tests and the pharmacopeial methods, and determine the placement of PAT devices on the manufacturing equipment. Venkateshwaran discussed the various statistical models employed, including Monte Carlo simulations to assess risk.

The Quality System was challenged with new considerations as a result of the RTR. For instance, disaster recovery plans had to be developed for possible PAT equipment failure. Venkateshwaran presented a "simplistic" model of a disaster recovery plan and noted that the model included all the possible failures that could be thought of.

The Quality System also had to account for chemometric model maintenance and update, outliers, and batch disposition.

In the end, Venkateshwaran concluded that the benefits derived by Pfizer through RTR include lower manufacturing costs and cycle times, improved yields through less waste and increased assurance of quality.

These case studies exemplify manufacturing excellence. Anyone in attendance at the *2010 PDA Annual Meeting* could see that the concepts of QbD, PAT and RTR are no longer just part of the regulatory alphabet soup. Instead, they are concepts that have are increasingly being applied within the pharmaceutical industry and the results speak for themselves.

Didn't make it to the meeting? Then purchase audio and the slides from every session. Contact PDA's **Leon Lewis** at lewis@pda.org for more details.

Quality & Regulatory Snapshot

Hailey's Comments: The Structure of the KFDA

Hailey (HeeYoung) Park, PDA

Have you worked with the Korea Food and Drug Administration (KFDA) before? I think that in most cases, you may have interacted indirectly with KFDA via your Korean partner. However, it is a fact that regulatory inspections are growing in numbers, and more KFDA inspectors will visit pharmaceutical manufacturing sites outside of Korea as the Korean drug regulations are becoming stricter. I'd like to tell you more about the KFDA, which I work for, to improve your understanding about its role in ensuring drug safety.

The KFDA, established in 1998, is an agency that belongs to the Central Korean Government. It regulates foods and all drugs except veterinarian drugs, cosmetics and medical devices. Before the KFDA, the Ministry of Health and Welfare had regulated those products since the modern Korean Government was established in 1948. Fifty years later, the Kim Dae-Jung Administration, the 8th President of Korea, established KFDA to have a more specialized and independent agency for food and drug safety.

KFDA began with 700 employees in Seoul, the capital city of South Korea. As public interests in food and drug safety increased, the KFDA outgrew its offices. Since it is hard to find another new larger space for offices in the middle of Seoul any more, and currently the KFDA has over 1400 regular employees, KFDA is going to move this coming November to a newly built, bigger facility in Osong, about 80 miles south of Seoul.

KFDA consists of regional offices, the National Institute of Food and Drug Safety Evaluation and headquarters. See the organization chart on page 21 for a more complete picture.

Each regional office is located at six metropolitan cities respectively in Korea. These offices have partially taken charge of the entire headquarters responsibilities and perform regulatory manufacturing site inspections, quality surveillance for marketed products and investigate specific issues. Each office can make an annual work plan; however, usually it is instructed by headquarters or a work plan issued from the headquarters is followed. Some regional offices review and approve more generic drugs with abbreviated applications rather than marketed drug surveillances.

History and Development of the KFDA

The KFDA came about as part of the Government Organization Act; it was amended by the Kim Dae-Jung Administration in 1998 and subsequently the KFDA's Organization Act was issued. This act describes which divisions make up the KFDA and what it is responsible for. Another act, the Pharmaceutical Affairs Act has been a significant regulation which KFDA has applied to the pharmaceutical industry.

The definition of a "drug" in the act includes finished drugs, APIs, narcotics, biopharmaceuticals, in vitro diagnostics, packaged crude herbs for traditional Korean therapies and herbal medicines prepared from crude herbs. Under the law, the quasi-drugs provide for milder treatment than drugs, but contain active pharmaceutical ingredients. Quasi-drugs are items such as gauze, deodorant, toothpaste, hair dye products, contact lens cleaners, etc are required to be approved by KFDA prior to being marketed. However, quasi-drugs can be sold freely by any retailers; whereas, both OTC and prescription drugs are only available at a pharmacy in Korea. See **Table 1** for a timeline of acts which make up the KFDA's responsibilities.

The National Institute of Food and Drug Safety Evaluation, another section of the KFDA, is primarily focused on researching pharmacology and toxicology studies on drugs; however, recently it strengthened its function to support scientific evaluation on safety issues more with headquarters after the Melamine adulterated foods issue. Because of these changes, the biologics product review called the National Lot Release Evaluation came under the auspices of the division.

The National Lot Release Evaluation is a duplicate review on a biologic product for KFDA to ensure the safety and quality before distribution. Under the Pharmaceutical Affairs Act, the KFDA commissioner can designate biologic products which require a National Lot Release Evaluation. These license holders need to submit an application for a National Lot Release Evaluation to release their products on top of the batch review. The National Center for Lot Release examines the submitted quality assurance documents and compares them to to the tests done on the collected samples. If the result is accepted, the center issues certificates which will be exhibited on the label of the released products.

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Regulatory *News*

Ongoing Collaboration Between European Medicines Agency/ U.S. FDA Regarding Orphan Drugs

Barbara Jentges, PhACT

Orphan Drugs: What is a "Rare Disease?"

The definitions of rare diseases and conditions differ regionally and are laid down in the respective regional legislations.

According to the European legislative framework on Orphan Drugs, ***(1,2)*** a severe disease or disorder is defined as "rare," when it affects less than 5 in 10,000 (respectively 1 in 2000) citizens of the European Union.

It is estimated that about 5,000–8,000 rare diseases affect approximately 6-8% (27-36 million) people in the European Union. Eighty percent of rare diseases have been identified as of genetic origin, while others are the result of bacterial or viral infections, allergies, or are due to degenerative and proliferative causes. ***(3)***

In the United States, the criteria for the designation of an orphan drug are laid down in 21 CFR Part 316 (Orphan Drug Regulation), Subpart C. ***(4)*** Here, it needs to be demonstrated that either: The drug effects or is administered to *fewer* than 200,000 people in the United States or the drug effects or is administered to *more* than 200,000 people with an expectation that the costs of research and development can be recovered by sales of the drug in the United States.

On the one hand, medical and scientific knowledge about rare diseases is lacking. On the other hand, the market potential for orphan drugs is small and drug products for rare diseases generally offer little prospect for a fair return on research and development investment.

Regional Governments Encouraging Research into Rare Diseases

With the aim of encouraging research into rare diseases, regional governments have been laying down several incentives for orphan drugs. The U.S. "Orphan Drug Act" in 1983 was followed by similar regulations in Japan and in the European Union.

Within the European Union, the sponsor of a designated orphan drug benefits from a number of incentives, ***(3)*** among them financial incentives (100% fee reductions for protocol assistance/follow up and pre-authorization inspections and 50% fee reductions for application fee and for post-authorization activities) and a 10-years market exclusivity.

The requirements, however, for establishing the quality, safety and efficacy apply equally to designated orphan drugs as for products not designated as such.

EU Procedural Milestone 1: Orphan Drug Designation

[Author Note: In the following the terms "drug" or "drug product" are used in place of the term "medicinal product" that is used in the European pharmaceutical legislation without

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Advisory Board *Watch*

Steve Mendivil Discusses His Involvement With RAQC

[Editor's Note: The *PDA Letter* spoke with **Steve Mendivil**, about his Regulatory Affairs and Quality Committee (RAQC) membership. Steve is an Executive Director of Corporate Quality EHS External Affairs at Amgen. **]**

PDA Letter: You've served on this committee as a member, as well as a co-chair. What motivated you to join and retain your membership with RAQC?

Steve: I got involved in RAQC when **Glenn Wright** nominated me to participate as a biotech member. Glenn was instrumental in getting me to volunteer with PDA. Up until this point, I had just attended various conferences off and on. RAQC was a very interesting group to be a member of. This is the advisory board that identifies new or revised regulations/guidance and drafts and approved PDA comments to be submitted to the Board of Directors for final approval. It is a great group of dedicated PDA members that work hard to contribute their knowledge and experience to help PDA take a position on proposed regulatory documents.

PDA Letter: How have you benefitted professionally and personally from your activity on RAQC?

Steve: I didn't know it at the time, but serving on RAQC became the starting point for more involvement with PDA. This turned out to be an important role as the head of Corporate Quality GMP Compliance to better understand new global expectations. Later on my PDA involvement allowed me to establish an External Affairs function within Amgen to manage and coordinate various external activities from GMP intelligence gathering to coordinating Amgen staff's participation on various committees and conferences. Member based scientific organizations, such as PDA, are critical for our industry and its important within firms to coordinate the volunteer work to be sure it's valuable and pushing in the same direction.

PDA Letter: During your tenure on RAQC, a number of important, game-changing guidances and regulations were issued, both in the U.S. and in Europe and through ICH. How important is it for the PDA community to develop unified responses to these?

Steve: This is extremely important and regulators look to PDA for consensus feedback from our diverse membership based scientific organization. RAQC works hard to create comment drafting committees that have both the subject matter experts on the topic and representation from large and small firms (including consultants) and from various regions. We do our best to draft comments that represent the PDA membership.

PDA Letter: In your opinion, what was the hardest document

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Hailey's Comments: The structure of the KFDA, continued from page 18

Table 1: A Brief Timeline of Korean Drug Related Acts

Act	Enactment Date	Timeline of Amendment				
		1971	1978	1987	1992	1998
Government Organization Act	**7/17/1948**					KFDA was established
Pharmaceutical Affairs Act	**1/28/1954**	The definition of a new drug was established.	GMP guideline was issued.	GCP was established.	GMP was established.	

Act	Enactment Date	Timeline of Amendment				
		2000	2004	2005	2006	2008
Pharmaceutical Affairs Act *(Continued)*	**1/28/1954**	GMP for biologics was separated.	The Articles about medical devices were separated as the Medical Device Act	A Bioequivalence test requirement was expanded to larger drugs.	Child-resistant packaging was required	Pre-approval GMP inspection was required prior to all product approval.
Narcotics Act	**6/23/1957**	The three Acts related illegal combined one as the Narcotics Act				
Cosmetic Act	**7/1/2000**	The Act was issued				
Medical Device Act	**5/30/2004**		The Act was issued	The Act about human tissue was issued at first.		
Act of Safety and Management for Human Tissue	**1/1/2005**			This Act was established		

KFDA's Organizational Structure

The National Center for Lot Release division was created in the National Institute to manage the National Lot Release Evaluation procedure. This center also partners with the World Health Organization (WHO) to perform WHO's Lot Release Test of vaccines.

The Clinical Trials Management division supervises all clinical trials, as well as proposals for clinical trials depending on the study. Within a clinical trial approval process, the Clinical Trials Management division examines the submitted applications and approves them based on scientific review results from the Drug Evaluation department or Biopharmaceuticals and Herbal Medicine Evaluation department.

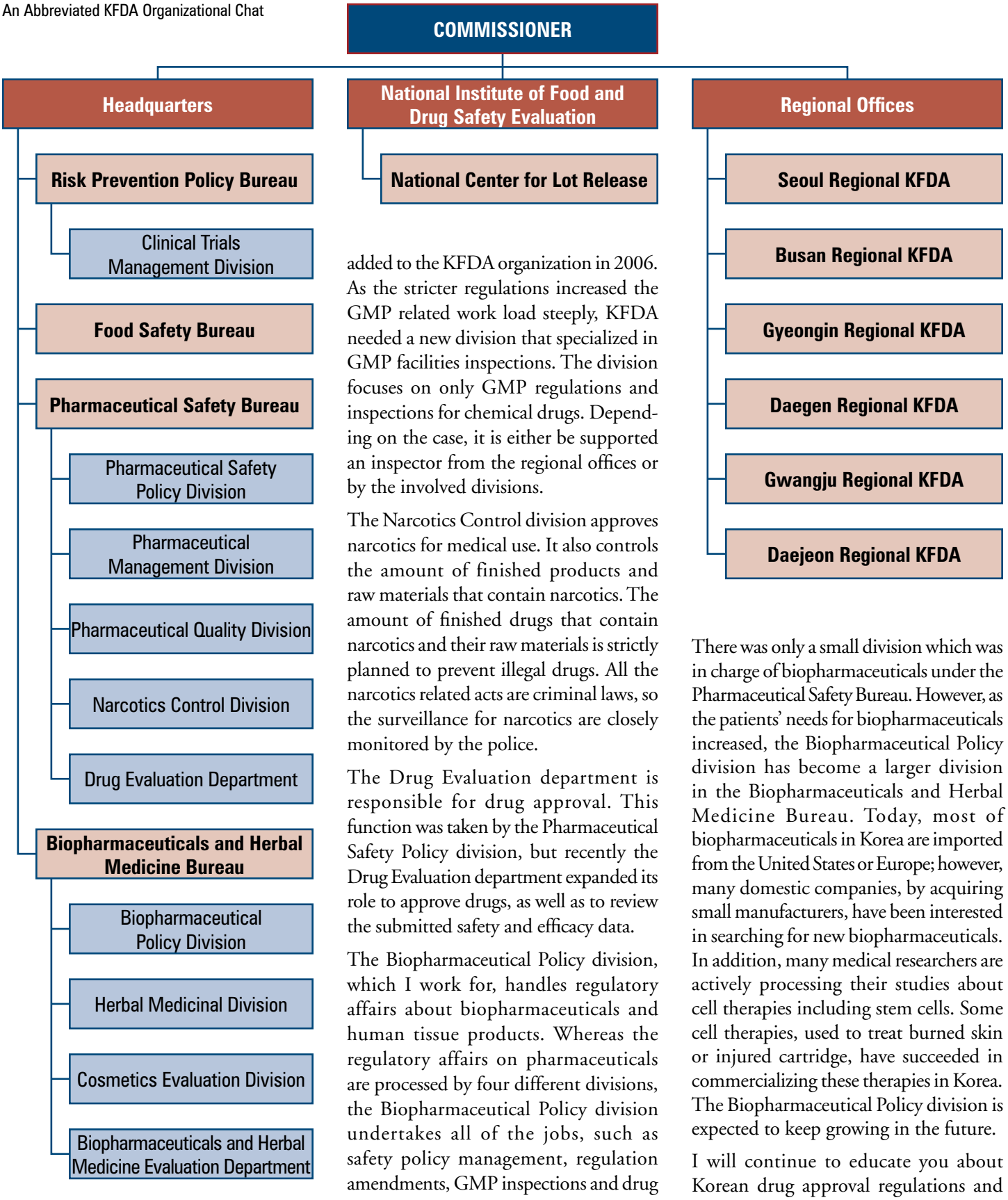
The Pharmaceutical Safety Bureau and the Biopharmaceuticals and Herbal Medicine Bureau are the main bureaus for policy management and regulation enforcement such as drug approvals, GMP inspections and drug surveillance. These two bureaus are responsible for the regulatory affairs on chemical drugs and biopharmaceutical/herbal drugs respectively.

The Pharmaceutical Safety Policy division established drug safety policy related to a drug/quasi-drug approval and it is involved from drug development to its approval. The division is responsible for writing draft amendments of regulations and issues the Korean Pharmacopeia.

The Pharmaceutical Management division takes care of drugs which are approved from KFDA. This division initiates the annual surveillance plan, such as setting up regular inspections; performing quality tests on marketed products; monitoring safety events; watching over drug advertising; and investigating counterfeit or defective drugs. The GMP inspection was also a duty for this division, but it was moved to the Pharmaceutical Quality division.

The Pharmaceutical Quality division was

An Abbreviated KFDA Organizational Chat



added to the KFDA organization in 2006. As the stricter regulations increased the GMP related work load steeply, KFDA needed a new division that specialized in GMP facilities inspections. The division focuses on only GMP regulations and inspections for chemical drugs. Depending on the case, it is either be supported an inspector from the regional offices or by the involved divisions.

The Narcotics Control division approves narcotics for medical use. It also controls the amount of finished products and raw materials that contain narcotics. The amount of finished drugs that contain narcotics and their raw materials is strictly planned to prevent illegal drugs. All the narcotics related acts are criminal laws, so the surveillance for narcotics are closely monitored by the police.

The Drug Evaluation department is responsible for drug approval. This function was taken by the Pharmaceutical Safety Policy division, but recently the Drug Evaluation department expanded its role to approve drugs, as well as to review the submitted safety and efficacy data.

The Biopharmaceutical Policy division, which I work for, handles regulatory affairs about biopharmaceuticals and human tissue products. Whereas the regulatory affairs on pharmaceuticals are processed by four different divisions, the Biopharmaceutical Policy division undertakes all of the jobs, such as safety policy management, regulation amendments, GMP inspections and drug surveillance. The Biopharmaceuticals and Herbal Medicine Evaluation department evaluates the efficacy and safety data of drugs and approves biopharmaceutical drug products.

There was only a small division which was in charge of biopharmaceuticals under the Pharmaceutical Safety Bureau. However, as the patients' needs for biopharmaceuticals increased, the Biopharmaceutical Policy division has become a larger division in the Biopharmaceuticals and Herbal Medicine Bureau. Today, most of biopharmaceuticals in Korea are imported from the United States or Europe; however, many domestic companies, by acquiring small manufacturers, have been interested in searching for new biopharmaceuticals. In addition, many medical researchers are actively processing their studies about cell therapies including stem cells. Some cell therapies, used to treat burned skin or injured cartridge, have succeeded in commercializing these therapies in Korea. The Biopharmaceutical Policy division is expected to keep growing in the future.

I will continue to educate you about Korean drug approval regulations and related division's functions further in future articles.

Ongoing Collaboration Between the European Medicines Agency/U.S. FDA, continued from page 19

any intention to alter its regulatory meaning.]

The orphan drug status needs to be applied by submitting an "application for orphan drug designation"***(5)*** to the European Medicines Agency. As part of the application it needs to be justified that the criteria laid down in the European orphan drug regulation are fulfilled for the drug product affected.

An Orphan Drug Designation (ODD) can be submitted at any stage of development but needs to be submitted **before the application for marketing authorization.**

Once a drug product has been designated as an orphan drug, it will be added to the "Community Register Of Orphan Drugs."***(6)***

Annual updates on the status of the development of the designated orphan drug ("Orphan Drug Designation Annual Report") need to be provided to the European Medicines Agency. In case the criteria for the orphan drug status are no longer met before a marketing authorization has been granted, the drug product concerned will be removed from the Community Register of Orphan Drug Products.***(1)***

Procedural Milestone 2: Protocol Assistance

Once a drug product has received the European Commission decision on the designation of orphan drug status, the sponsor of a designated orphan drug may request "protocol assistance" from the European Medicines Agency prior to a marketing authorization.***(1)***

Protocol assistance (PA) needs to be applied by the sponsor. PA is restricted to scientific issues relating to any questions concerning quality, non-clinical and clinical aspects that might arise during development of the orphan drug. The procedural steps for protocol assistance follow mainly the procedure for "Scientific Advice"–a statutory responsibility of the European Medicines Agency for advising future applicants during the development phase of a drug products. A PA meeting is held between the sponsor and members of the "Scientific Advice Working Party," a standing working party of the Committee for Medicinal Products for Human Use (CHMP) with the task of providing scientific advice and protocol assistance to applicants.

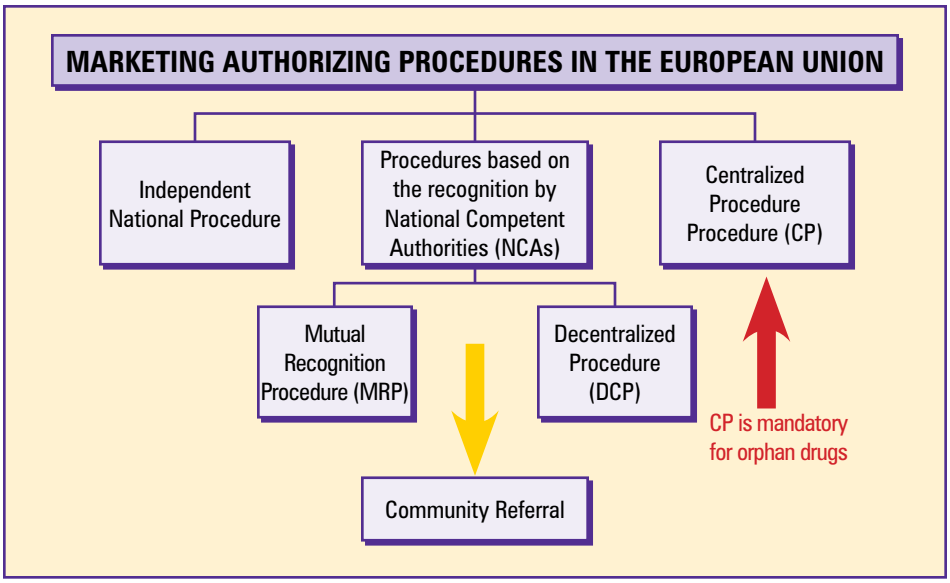


Figure 1: Procedures for Marketing Authorization Application within the EU

Regulatory aspects will be dealt with separately in a "Protocol Assistance Presubmission Meeting," if requested by the sponsor.

Procedural Milestone 3: Marketing Authorization of a Designated Orphan Drug

Regulation 726/2004 ***(7)*** mandates the use of the centralized (Community) procedure for the application designated orphan drug (see **Figure 1**).

10 Year Market Exclusivity for Orphan Drugs on the EU Market

One integral element of the incentives program is that the sponsor benefits from a 10 year market exclusivity once a designated orphan drug has been licensed by the Community. Within this period, the Community may neither accept another application for a marketing authorization, nor grant a marketing authorization or accept an application to extend an existing marketing authorization for the same therapeutic indication, in respect of a similar drug product.***(1)*** However, in the following exempted cases, a market authorization may be granted to a similar medicinal product with the same indication:

- If the holder of the marketing authorization for the original orphan drug has given his consent to the second applicant
- If the holder of the marketing authorization for the original orphan drug is unable to supply sufficient quantities of the drug product
- If the second applicant can establish in the application that the second drug, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior.

The period of market exclusivity may be reduced to six years if, at the end of the fifth year, the criteria for the orphan drug status are no longer met or if it is proved that the product is sufficiently profitable.***(1)***

Within the European Union, the 63rd orphan drug recently received a positive opinion by CHMP.***(8)***

By being granted a marketing authorization, the Community Register of Designated Orphan Medicinal Products will be updated accordingly by providing information about trade names and authorization dates.***(6)*** Additionally, the entries in the Community Register are linked to the European Public Assessment Reports (EPARs) ***(9)*** that are published on the European Medicines Agency website. The product-specific EPARs provide detailed information about the procedural steps taken before and after authorization and the scientific discussion.

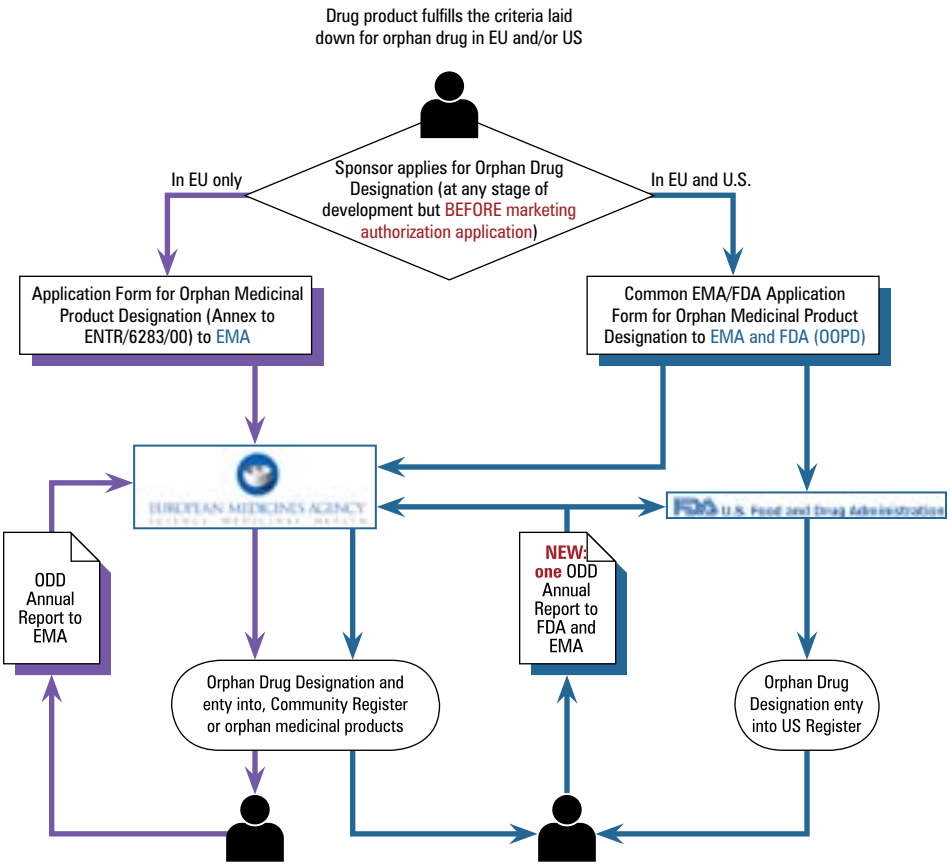


Figure 2: European Medicines Agency/FDA Collaboration on Orphan Drug Designation and Annual Report

At the end of the market exclusivity period, a (designated) orphan drug is removed from the Community Register of Orphan Drugs.

Recent FDA/European Medicines Agency Collaboration on ODDs

In order to further simplify the administrative burden and facilitate a market access of orphan drugs in both regions, the European Medicines Agency and the U.S. Food and Drug Administration have initiated a collaboration on orphan drug designations (see **Figure 2**) comprising:

- The use of a "Common European Medicines Agency/FDA Application Form for an Orphan Drug Designation"(***10***)
- An agreement to accept a single orphan drug designation annual in place since February 28, 2010.***(11)***

Common EMA/FDA Application Form for Orphan Drug Designation

Sponsors, who intend to apply for an orphan drug designation of the same drug product for the same use in both regions, the European Union and in the United States, benefit from reduced regulatory burden by submitting one application form—the "Common EMA/FDA Application Form for Orphan Medicinal Product Designation"—to both regulatory agencies, the European Medicines Agency Central Information Group and to the U.S. FDA Office of Orphan Products Development. The respective regional requirements of both, European Union and United States, are addressed in the specific sections of the form.

Once the application form has been submitted to both agencies, further procedural steps follow separately according to the legislative frameworks for orphan drug designation in the EU and the U.S.

FDA and European Medicines Agency Accept a Single Orphan Drug Designation Annual Report

Both regulatory agencies, FDA and the EMA, require the submission of an annual report for designated orphan drugs. These reports *"provide information on the status of the development of orphan drug products, including a review and status of ongoing clinical studies, a description of the investigation plan for the coming year, any anticipated or current problems in the process, difficulties in testing, and any potential changes that may impact the product's designation as an orphan product."****(11)***

Sponsors, who have obtained an orphan designation status for their product in either the European Union or United States may take advantage of the latest FDA/EMA agreement to accept a single Orphan Drug designation annual report meeting the requirements of both the FDA and the EMA.***(11) Since February 28, 2010, a single ODD annual report may be submitted to each Agency on a voluntary basis.***

Review and assessment of the annual report will be conducted separately by each authority according to the regional legal and scientific requirements. Nevertheless, the initiative to co-ordinate regulatory activites between the two most important pharmaceutical regions–the United States and the European Union–is very much appreciated and will hopefully be continued.

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2. Commission Regulation (EC) No 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a drug (medicinal) product as an orphan drug (medicinal) product and definitions of the concepts "similar drug (medicinal) product" and "clinical superiority" http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:103:0005:0008:EN:PDF
3. Doc.Ref. EMEA/290072/2007 – Orphan drugs and rare diseases at a glance http://www.ema.europa.eu/pdfs/human/comp/29007207en.pdf

4. 21 CFR Part 316 (Orphan Drug Regulation), Subpart C Designation of an Orphan Drug; http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/ucm124562.htm
5. Annex to ENTR/6283/00: Application form for orphan drug (medicinal) product designation (Annex to 'Guideline on the format and content of applications for designation as orphan drug (medicinal) products) http://www.ema.europa.eu/pdfs/human/comp/628300an.doc
6. Community "Register of designated Orphan Drug (medicinal) products (by number)" http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/community-register/html/orphreg.htm
7. Regulation (EC) No 726/2004 of the European Parliament and of the Council of March 31.2004 laying down Community procedures for the authorization and supervision of drug (medicinal) products for human and veterinary use and establishing a European Medicines Agency http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:EN:PDF
8. EMA/CHMP/95106/2010, Press release from February 19, 2010: Meeting highlights from the Committee for Drug (medicinal) products for Human Use (CHMP), February 15-18, 2010. http://www.ema.europa.eu/pdfs/human/press/pr/9510610en.pdf
9. European Public Assessment Reports (EPARs) for authorized drug (medicinal) products for human use, A-Z Listing of EPARs: http://www.ema.europa.eu/htms/human/epar/a.htm
10. Common EMEA/FDA application form for Orphan Medicinal Product Designation (Published November 2007); http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048361.pdf
11. Press release from February 26, 2010 (EMA/121846/2010): FDA and EMA agree to accept a single Orphan Drug Designation Annual Report http://www.ema.europa.eu/pdfs/human/comp/pr/12184610en.pdf

Steve Mendivil Discusses His Involvement With RAQC, continued from page 19

to comment on in terms of getting consensus from the commenting group, the RAQC and then from the PDA Board of Directors?

Steve: Certainly the work on the FDA draft Validation guideline comes to mind. This was lead by **Hal Baseman** and **Scott Bozzone**. There were so many comments it had to be split into three types. Those most critical were referenced in the cover letter, those other major comments were in an attached spread and finally a second spread sheet containing all PDA comments received was also sent to FDA. There was a tremendous amount of work to pull all of this together.

PDA Letter: During your time as RAQC co-chair, the group worked on revising its SOP. What was the focus of this effort and how will the new SOP improve the committee in the future?

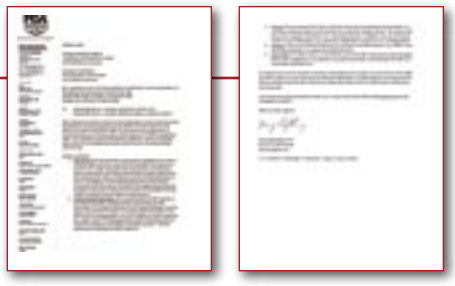
Steve: A number of years ago when **Zena Kaufman** was the Chair of RAQC, she established an annual strategic planning session for RAQC to establish some goals to make RAQC more effective and efficient. One of our early goals was the establishment of a new member handbook and an SOP on the commenting process. We finalized the SOP last year and provide this to commenting committee leaders to help clarify the process and the timing. The handbook not only includes the SOP but also governance of RAQC regarding voting on ballots, roles and accountability, term limits and the process of bringing new members on board. A team works much better and harder when everyone knows what's expected and feels everyone is lifting their share of the weight. My co-chair **Stephan Rönninger** and the rest of the RAQC were instrumental in drafting and working through the details of our governance handbook.

PDA Letter: Finally, what would you say to other PDA members to encourage them to join RAQC?

Steve: The greatest benefit to joining a committee such as RAQC is the people that you meet and the network you develop. We can't possibly keep up on all the new requirements and expectations that are going on globally, so you develop a network of colleagues and friends to help you understand the external environment. RAQC is a dedicated group of PDA members that work hard to stay abreast of new requirements and provide comments that help make process workable for the industry. We have over 100 PDA members that have expressed an interest in joining and we review their experience, skills, type of company and region they work in before a slate of candidates is agreed to by RAQC. I encourage any interested PDA member to send their CV to **Iris Rice** or **Bob Dana** so it can be considered. Terms end in June and we bring on new members at that time, so get those applications in quickly.

PDA to Agency: Exclude Individual Product Related Filing and CMC Info in SMF

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



March 30, 2010

European Medicines Agency
Compliance and Inspection, London
ADM-GMP@ema.europa.eu
European Commission
Pharmaceuticals Unit, Brussels
entr-gmp@ec.europa.eu

Reference: Explanatory notes for pharmaceutical manufacturers on the preparation of a Site Master File and content of a Site Master File;

ENTR/F2/MT/AM/jr D (2009), 10 December 2009

Deadline for comments: 31 March 2010

To: Responsible Person: European Commission, Pharm. Unit

Responsible Person: European Medicines Agency, Inspections Sector

PDA is pleased to provide comments on the *Explanatory notes for pharmaceutical manufacturers on the preparation of a Site Master File and content of a Site Master File*, dated 10 December 2009. Our comments were prepared by an international group of volunteer experts with experience in GMP and regulatory affairs. Our comments consist of five general comments, covered in this letter, and a series of more detailed technical comment found in the attached EMA matrix format.

General comments:

1. New Part III: PDA recommends this document be published as an Annex to the EU GMP, and not as a new Part III of the GMP. The creation of a new Part III is a major step which may have long term consequences poorly understood by the affected stakeholders including inspectorates. We understand all content of EudraLex to be the binding regulations in the EU. The addition of informational guidance documents may be inconsistent with the purpose of EudraLex. We suggest approaching the European Commission to request that creation of a new GMP Part III be subject to broader discussion before implementation.
2. Product Related Information: We recommend that the SMF exclude, to the extent practicable, individual product related filing and CMC information. This includes references to PAT, Quality by Design, real time release, and parametric release. To include product information in the SMF renders it unmanageable in size and complexity as well as repeating the content of the CTD. Excluding product specific information will not reduce the usefulness of the SMF for its primary purpose – efficient planning and undertaking of GMP inspections.
3. Format: We recommend the format of the document be reconsidered and amended. It is currently structured similar to the content of a company's quality manual. This may not the best way to organize information for a manufacturing site. In addition, the current format results in some redundancy, e.g. contractors addressed in sections 4.2, 8, and Appendix 8.
4. Glossary: There are occasional references to acronyms and abbreviations, e.g. DUNS. These should be explained in an Appendix entitled Glossary.
5. Size of SMF: As written, there is a risk that the size of the SMF could easily exceed 30 pages. Many of our suggestions, e.g. deletion of product information, will help keep the SMF to a reasonable and useful size.

As referenced in our first General Comment, PDA believes the creation of a new Part III of the GMP should be subject to more discussion by affected stakeholder, including industry and inspectorates. We are willing to help with the creation of a public discussion forum or other means of achieving that discussion.

If you have any questions please contact me, or James Lyda of the PDA staff (lyda@pda.org) who managed this project.

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

PDA Requests Longer Commenting Time

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

April 12, 2010

Division of Docket Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852
Reference: [Docket No. FDA–2009–N–0247]
Transparency Task Force; Request for Comments
Ref: FR, Vol. 75, No. 48; March 12, 2010

Dear Sir/Madam,

PDA is responding to the referenced FR Notice seeking comments from interested persons on ways in which FDA can increase transparency between FDA and regulated industry. Our comments relate to area No.2 in the FR Scope statement, "The guidance development process," and to products regulated by CDER, CBER, CVM and CDRH.

Problem statement: The time period stipulated by FDA for comments on proposed rules or industry guidance published in the FR is often insufficient, thereby creating difficulties for the development of high quality and useful comments from interested persons.

Discussion: The FDA time frame for commenting varies with the norm being 60 days from the date of publication in the FR. On occasion, as is in the case of this notice, there is only 30 days. Such short timeframes are difficult for membership or constituency-based organizations such as PDA to meet. In order to prepare scientific based and consolidated comments, PDA usually reaches out to our worldwide members to (1) recruit volunteer experts on the subject, (2) organize the volunteers to review the document through a peer-based process, (3) prepare redrafts of our commentary until consensus is achieved, and (4) secure internal institutional review and approval via a formal balloting procedure involving two or more internal bodies including our governing Board of Directors. This process ensures high quality comments that are useful and helpful to FDA.

Recommendation 1: We encourage FDA to adopt a standard notice and comment time frame of 6 months, or 90 days for time sensitive issues, for rules and guidances affecting the regulated industry. This will give FDA the benefit of receiving high quality comments for use in the guidance development process, and in achieving the Agency goal of improving transparency.

Recommendation 2: We also encourage FDA to partner with member-based scientific organizations (such as PDA) to hold discussion workshops on the issues that drive new or revised rules or guidances. Similarly, after rules and guidances are finalized these same organizations can help educate stakeholders on requirements and intentions through training workshops and conferences, or by providing FDA speakers at training venues (such as the PDA Training and Research Institute) to provide more in depth understanding. These actions would increase understanding of and compliance with new requirements through educational programs serving as an adjunct to the inspection and compliance approach.

Please contact me if you have any questions.

Sincerely,
Richard Johnson
President, PDA

Regulatory Briefs

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

North America

U.S. FDA Guidance to Close Gaps in Supply Chain

The U.S. FDA recently released a final guidance on the develop of standards for the identification of and validation of technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded or expired drugs.

The guidance, *Standards for Securing the Drug Supply Chain – Standardized Numerical Identification for Prescription Drug Packages*, is intended to assist with the standards and systems for identification, authentication and tracking and tracing of prescription drugs. The guidance identifies SNI for package-level identification only.

More guidances and regulations are anticipated that will implement the requirements of the U.S. FDA Amendments Act of 2007.

Proposed Rule Gives Directors of CBER and CDER Authority to Approve Exceptions/ Alternatives to Biologics Reg

The U.S. FDA would like to amend the biologics regulations to permit the Directors of CBER and CDER, as appropriate, to approve exceptions or alternatives to the regulation for constituent materials.

FDA is taking this action due to advances in recent biological products licensed under the Public Health Service (PHS) Act and to provide greater "flexibility" for the manufacturers of biologics products. FDA deems some of the some provisions of the PHS Act "too prescriptive and unnecessarily restrictive" as such, regulatory work-arounds are considered appropriate, if initiated by the Directors of the two Centers.

The rule provides manufacturers of licensed biological products with flexibility, as appropriate, to apply advances in science and technology as they become available without diminishing public health protections.

Comments on the proposed rule should be submitted by June 28.

The *Federal Register* announcement also contained an information collection provision on the proposed rule and comments should be submitted by April 29.

PCV 1 Found in Rotavirus Vaccine, Regulators Investigating

The rotavirus vaccine, Rotarix, that is used to guard against severe diarrhea and dehydration in infants, was found to contain components of porcine circovirus (PCV) 1, a virus composed of a single strand of DNA not known to cause disease in animals or humans.

An independent U.S. academic research team discovered the virus in the vaccine when they applied a new technology for detecting viral genetic material to two lots of the Rotarix. When the researchers notified the manufacturer, GlaxoSmithKline, of their findings, the firm initiated extensive experiments to confirm the results and investigate further. The follow-up tests confirmed the presence of copies of DNA from PCV 1 in the two finished lots.

The U.S. FDA and GlaxoSmithKline are currently investigating how DNA from PCV 1 came to be present in the Rotarix. There is no evidence at this time that this finding poses a safety risk, though the FDA is temporarily suspending the use of the vaccine while gathering additional information about the situation.

The European Medicines Agency Committee for Medicinal Products for Human Use (CHMP) currently has determined that no action is necessary and the findings of the PCV 1 do not present a public health threat. However, they do acknowledge that the virus should not be present in the vaccine and that further information is needed from the manufacturer.

Key Regulatory Dates

Comments Due:

April 29
Agency Collection of Information on permit the Directors of CBER and CDER, as appropriate, to approve exceptions or alternatives to the regulation for constituent materials

June 28
Propose rule comments are due on if the Directors of CBER and CDER, as appropriate, should approve exceptions or alternatives to the regulation for constituent materials

The CHMP Vaccine Working Party is holding meetings with the participation of the WHO and international counterparts from Canada and the United States.

Agency Collection of Information Notice on Product Jurisdiction Available

The U.S. FDA is allowing the public to comment on a proposed FDA collection of information notice which is related to product jurisdiction and the determination of organizational components that are assigned primary jurisdiction for premarket review and regulation of products that are comprised of any combination of drug, device or biological product.

A second purpose of the regulation is to enhance the efficiency of Agency management and operations by providing procedures for classifying and determining which Agency component is designated to have primary jurisdiction for any product where such jurisdiction is unclear or in dispute.

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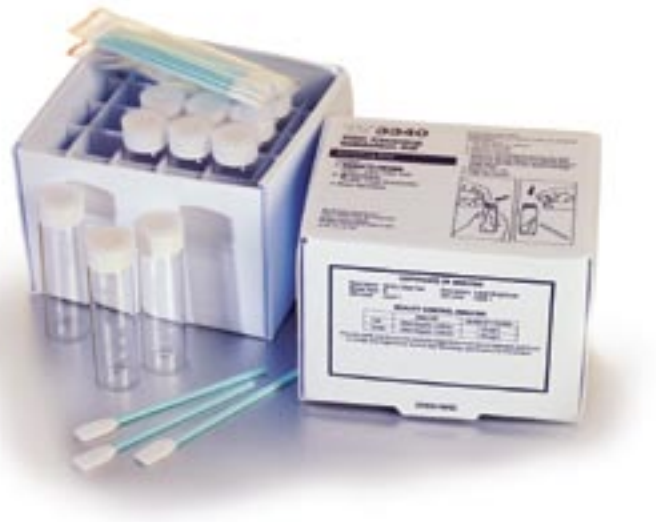

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It's Not Just About Profitability & Survival: Leaders Need to Lead

Pat Heydlauff

Political and economic influences have great implications for today's leaders as they maneuver their way through ever-expanding mine fields. This economy and political climate are forcing leaders to re-think their operating plan. This is a time for action not reaction; a time for decisive leadership to guide the company safely through a quagmire while preparing for the future.

"Maintaining market share, maximizing operational tightness and propagating the long term view for the company are critical during an economic downturn," said the CEO of a major privately held corporation. This thought process isn't just common sense but crucial for economic survivability and mobility once the economy starts to move forward again.

The CEO went on to say, "a company cannot afford to lose any market share nor erode operating capital during a downturn because there will be nothing left for marketing, advertising and hiring when the economy does turnaround. A business gets into real trouble when it loses its market share and depletes its capital; it will not survive—no matter how good the economy might get. Therefore, leadership needs to focus on the long-term view while getting everyone aboard to think survival, expense reduction and increasing income without any negative financial impact on existing capital."

When leadership focuses on short-term business survival, assets are protected, jobs continue to exist and market share and profitability is maintained. Once a carefully laid out short-term plan for survival has been accomplished it is crucial that leaders not get so bogged down with survival that they forget to look at the long term view.

These are the kind of times, circumstances and events that require leaders to make hard decisions and realize there is a way to behave during an economic crisis. Survivability is all about reducing expenses, making profits and maintaining capital. Company leaders who understand how to make money are the survivors and will be the change makers who help turn the economy around and ensure their companies thrive.

The longer the downturn, the more the consumers will dig in and hold onto their hard-earned money. Once the economy does turnaround, they will pay down their accumulated debt before spending. To bridge these turbulent times, leaders need to have a plan that includes a long term view covering everything from being prudent on expenses and increasing employee efficiency to eroding the competitions market share. Here are some easy-to-implement survival principles that focus on the future:

- **Shift everyone's thinking.** Move from a cost-cutting mode to a money-making and increasing-market-share mode while not digging into existing capital. Employees tend to spend capital, so they need to be engaged from the bottom up to look for ways to either save money or increase sales and revenues. When encouraged to participate in the company's survival, they take a piece of ownership in its survival and become part of the solution team instead of an individual trying to survive.
- **Increase employee efficiency.** Eliminate energy drainers and clutter in the workplace and organize it so employees can find anything they need at a moment's notice. Time is money, and employees are a huge investment. Clutter is a distraction that prevents an employee from maximizing their productivity and the company's profitability.
- **Upgrade your organizational chart.** Be an all inclusive organization and share this philosophy with your employees. Eliminate the old 19 century Newtonian pyramid-shaped organizational chart and replace it with one that works from the center out like a spider's web where everyone is connected, productive and within the playing field. Employees do their best work when they feel they are relevant and make a difference in the outcome.
- **Leaders need to lead.** Focus on the long-term view. Once you've devised and implemented a plan for survival, focus all your energy on the big pic-

ture and where you want the company to be when the economy starts moving upward. Let someone else worry about the number of paper clips being used. It takes a leader to move safely through todays economic mine fields. Followers need a leader with a vision to lead them into creating the future.

- **Eliminate stress.** Being a leader is stressful enough during normal times. The stress is greatly magnified during this difficult economic and political environment. Plan some creative time during hectic days to get the right side of the brain working. Stress comes from logical left brain thinking not being balanced by creative right brain thinking. It's the right side of the brain that helps you create new ideas and solve problems such as getting through this economic downturn.

Leaders need to find ways to solve problems improve survivability and increase market share while protecting existing capital. This type of breakthrough thinking comes through creativity. Add some right brain activities to your schedule such as creative writing, painting, listening to classical or new age music, quiet walks in nature or meditation. If you're stuck at your desk, take a few minutes to do some creative visualization. Close your eyes and mentally visit a place you love—remembering to breathe deeply while in that frame of mind. You will feel refreshed and the creative juices will flow, helping you solve the most complex of problems.

It takes a leader with vision and the creative know-how to turn things around and have everyone in the company think as one instead of as a number of individuals. Leaders must realize they cannot use 19 century leadership tools in the 21 century—especially those that are narrow and top down instead of inclusive.

Leadership is all about creating tomorrow's vision while living through today's difficult times. Profitability and maintaining the company's market share while not dipping into capital must be the long term objective which builds a fertile foundation for company growth when the economy turns upward.

About the Author

Pat Heydlauff is president of Energy Design, a company that uses proven Feng Shui design principles to improve the bottom line. As a consultant and speaker, Pat helps organizations and businesses of all sizes remove stress and clutter, while increasing creativity, employee retention and productivity. Her book, *Feng Shui: So Easy a Child Can Do It* outlines the small changes that can lead to a big improvement in one's personal and professional success. For information, visit www.Energy-by-Design.com or call 561-799-3443.

Learning About Drug Product Distribution

Emily Hough, PDA

Being at PDA for a little more than two years has given me multiple opportunities to learn about the challenges in production and delivery of drug products. But, when I was told there was another occasion to discover *even more* about the complexities of drug product transport and storage, I jumped at the chance and signed up for the PDA New England (NEPDA) Chapter event.

The meeting featured a facility tour of Masy Systems, Inc. and a dinner meeting with two speakers on the topic of shipping logistics. Masy provides validation and calibration services and controlled storage for biopharmaceuticals, pharmaceuticals and medical devices,

On March 10, I flew into Logan International Airport, where Chapter President **Jerry Boudreault** very graciously met me and drove me over 46 miles to the Masy plant in Pepperell, Massachusetts. Once there, I, along with other participants, was escorted to areas of the facility designed for the storage of temperature-sensitive product. Guides at the facility explained Masy's calibration techniques and how the firm handles client notification when the system goes out of spec.

Next, visitors heard about Masy's routine monitoring that involves thermocouples that test for temperature and produce a reading every ten minutes. The firm is currently converting to wireless sensors in place of the thermocouples.

A highlight of the tour was Masy's new BioPharma Storage facility. There, participants were exposed to the innovative ways that the firm has improved temperature-controlled storage for biopharmaceuticals. For example, even though the new facility was on the same campus as Masy's older facility, the BioPharma Storage warehouse operates with a different shipping code to ensure that the cold chain will not be broken by mistakenly going to the wrong building. Once a product has been received at the facility, it is unpacked into an environment that identically matches the temperature conditions in which it arrived. The facility is equipped with cryogenic, as well as reach-in and walk-in cGMP storage. Storage temperature is also available at ambient and ICH stability conditions. To reduce the risk of product loss, the warehouse has two independent generators each capable of running the entire facility for 3 days, triple redundant HVAC system and a LN_2 backup. According to Masy, there are only two other facilities like this in the world.

After the tour, it was time to go to the dinner meeting. The meeting opened with Jerry announcing the winner of the Chapter's student scholarships. Four $1,000 scholarships were granted to members of the NEPDA student chapter who attend Middlesex Community College (see box below).

The first speaker, **Anthony Rizzo**, focused his presentation on recently released *PDA Technical Report 46: Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User*, which was developed because of the lack of guidelines from the handoff of a product from the manufacturer to the end user. Anthony noted that the task force was currently working on developing training documents from the technical report.

When in transit, products are dependent on available technology, weather conditions and the method of shipping. For example, when shipping by air, it is necessary to take into account pressure differences that can impact packaging. When moving temperature-sensitive product without protective packaging by truck, shippers need to ensure that the truck is maintained and qualified to be able to control a specified range of temperatures. During his presentation, I discovered that load planning is an extremely important task. When shipping, it is important to ensure that air flow within a refrigerated container can be moved around without any heaters, otherwise, its ability to hold temperatures will be greatly reduced.

The most common challenges, Anthony said, are when shipments are moved to different modes of transportation. For example, when a product is placed into a container with insulation and heating and cooling elements that rely on external power when shipping by sea and moved once the ship is docked to a truck, there is a chance that there would not be an external power source.

"Those handoffs are critical areas that really need to be focused on." Anthony said contingency plans are important to reduce risks that can come up due to major weather events, lack of necessary equipment or malfunctions of equipment.

His talk drove home that the regulations and guidelines for wholesale distribution are incomplete. So even though manufactures are highly regulated, once a product is handed off, it is a "crapshoot," Anthony asserted. For example, a patient orders a product that has gone through a temperature-controlled supply chain, but when it gets delivered from a pharmacy, it sits on the patient's doorstep in the sun for hours.

The next speaker, **Jim DiTolla**, gave his account on how to avoid logistical nightmares pertaining to shipping. He

Four students from the MIddlesex Community College who belong to the NEPDA Student Chapter won a $1000 scholarship at the NEPDA Dinner Meeting:

Thelma Cromwell-Moss

Kamal Patel

Sheba Mubiru

Ayelet Katzelnik

has noticed that at every point of the chain of logistics, compliance issues have occurred.

The most important step, he said, is to properly classify and label the material correctly to avoid negative consequences like fines or rejection of the shipment by customs officials. I learned that understanding all of the relevant regulations and keeping abreast of changes is critical to maintaining the proper paperwork.

There are three categories of regulations:

- **The IATA regulations:** These are the regulations that are handed by a governing body that will allow you to put goods on an aircraft in a safe and proper manner to an airline to ensure safety is maintained. Jim said that if you bring a product to the airport that is not up to IATA code, it can get rejected on the spot and that will hurt your shipping times. He also mentioned that customs sometimes holds up products because of missing paperwork, which might result in a loss of product if cold chain is broken.
- **Import/Export regulations:** This varies by government, material you are shipping and where you are shipping to. For example, you can ship one product to Spain with one specific permit, but a different permit must be used if you are shipping to Italy. This is because every county has their own specific regulations. Jim reminded audience members to check countries regulations often, as they change frequently.
- **Trade compliance issues:** Every item that is imported to a country has a specific code on it that allows a government to determine a percentage of a tax to the importers material so that they can collect money when the shipment has been cleared based upon the commercial value of the product and percentage of the tax that was assigned to the product. Fines can occur if the price of a product has been misreported.

Jim reminded members to do as much front-end work as they could before they ship products to other countries. Use of an experienced customs broker in each specific country can be helpful, he said.

It struck me, at the meeting, that the complexities to drug product transportation are truly numerous, and it is amazing that so few incidents *do* occur. Until the pharma industry solves the problems that arise from transporting product that are in the supply chain, contingency plans are still the best bet on avoiding the loss of a product.

PDA Who's Who

Jerry Boudreault, President, Drug Development Resources and President of the NEPDA Chapter

Jim DiTolla, OPS Manager, Biocair

Anthony Rizzo, Strategic Account Engineer, Cold Chain Technologies

PDA Japan Chapter Holds 16th Annual Meeting in Tokyo

PDA Japan Chapter Board Member Masashi Imamura, Toyama Chemical

Towards Further Advancements in Quality Assurance was the theme of the 16th Annual Meeting that the PDA Japan Chapter held on November 10–11, 2009 at the Tower Hall Funabori in Tokyo. The meeting had a healthy attendance of 388 delegates.

Meeting Chair **Izumi Saitoh**, PhD, Shionogi & Company, gave a few opening remarks at the conference.

The meeting was a lively one thanks to timely presentations by industry representatives and regulators from the Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) on current topics, such as supply chain, quality system and issues of common interest like GMP inspections conducted by the PMDA.

Questions and exchange of opinions among the participants added to the success of the academic assembly.

Members of the audience listen intently at the PDA Japan Chapter's Annual Meeting

The meeting had a healthy attendance of 388 delegates

Katsuhide Terada, PhD, Toho University, gives the opening address at the reception

L-R: Junko Sasaki, Dainippon Sumitomo Pharma; Izumi Saitoh, PhD, Shinogi & Co.; Masashi Imamura, Toyama Chemical; Michihisa Inokuma, PhD, Towa Pharmaceutical; Eiji Wantanabe, Terumo

Toshinobu Aoyama, Rion, makes the closing address at the conference

Yukio Hiyama, National Institute of Health Sciences

L-R: Shigeru Hayashi, PhD, Pfizer; Takamasa Okugawa, Pfizer; Michihisa Inokuma, PhD, Towa Pharmaceutical; Masashi Imamura, Toyama Chemical; Shigeo Kojima, PhD, Pharmaceuticals and Medical Devices Agency

L-R: Daikitiro Murakami, Taikisha; Tsutomu Kamikukita, 3M Health Care; Shinji Sugaya, PhD

New to PDA? Learn More at a PDA New Member Breakfast

Hassana Howe, PDA

PDA hosted the 5th annual New Member Breakfast at the *2010 PDA Annual Meeting* in Orlando, Fla. The Membership Advisory Board, chaired by **Susan Schniepp**, Antisoma, plans these events every year in an effort to familiarize PDA members with their member resources. The success of these events can be attributed to the Membership Advisory Board, speakers and the PDA staff.

For the New Member Breakfast, Chair **Maik Jornitz**, Sartorius Stedim Biotech, and long-time New England Chapter volunteer **Louis Zaczkiewicz**, Genzyme, gave insightful presentations on their PDA membership experiences and informed members how to utilize PDA's membership opportunities.

"It is wonderful to meet new members and share one's own experience on how PDA supports one's career and enhances one's knowledge base," Maik said.

If you are a new PDA member and were unable to attend the breakfast, you can view the PDA Membership Orientation presentation online at www.pda.org/membership. The next PDA New Member Breakfast will be hosted at the 2011 PDA Annual Meeting in San Antonio, Texas. If you would like more information, please contact the Membership department at info@pda.org.

We thank all the PDA volunteers who make these events possible and we look forward to meeting you in San Antonio in April 2011.

PDA is pleased to launch a virtual member orientation in the coming months. Please keep an eye out for the *PDA Connector* that will announce this complimentary web seminar, which will give new and current members a "How-To" about navigating the website and utilizing all member benefits online.

Volunteer Spotlights

Eric L. Berg, Director of Supplier Quality, Amgen

PDA Join Date: 2005

Areas of PDA Volunteerism: PDA/FDA Ingredients conference organizing committee member, speaker and moderator (in Washington D.C. (September 2008), San Diego (December 2008), Munich (March 2009), Shanghai (June 2009)); PDA/FDA Regulatory conference speaker in Washington D.C. (September 2009).

Interesting Fact about Yourself: Last year I met Nobel prize winner Archbishop Desmond Tutu in San Juan, Puerto Rico. I use the photo of the Archbishop and me as the profile photo on my LinkedIn account.

Of your PDA volunteer experiences, which stand out the most? Serving on the committee and speaking at the PDA/FDA/SHFDA Ingredients Conference in Shanghai, China. As part of that trip we visited the SHFDA offices and were given a tour of a museum of traditional Chinese medicines—it was fascinating.

Which PDA event/training course is your favorite? I have appreciated the PDA/FDA Annual Regulatory Conference where I've learned a lot and really expanded my professional network.

How has volunteering with PDA benefited you professionally? Through PDA I have benefited by getting to know and learning from colleagues from numerous companies and regulatory agencies. My PDA friends have really helped me grow as a quality professional by rapidly helping me to expand my understanding of our industry, regulatory considerations and challenges that we all face.

Friedrich Haefele, PhD, VP Biopharma Operations, Boehringer Ingelheim

PDA Join Date: 2002

Areas of PDA volunteerism: Since becoming a member of PDA in 2002, I personally contributed to the following events in discussion, case study presentations or working as a facilitator: Validation on Steam Sterilization in Autoclaves (October 2002); PDA International Congress (February 2004); PDA Scientific Forum on Visual Inspection (October 2004); PDA/EBE Conference Biopharmaceutical Dev. & Manuf. (June 2007); PDA Conference on Cleanrooms/RABS/Isolators (October 2007); PDA/ISPE/ PIC/S Workshop on EU-GMP Annex I and Quality Risk Management (November 2008); PDA Visual Inspection Interest Group Meeting (November 2009); PDA Parenteral Conference (upcoming October 2010)

Interesting fact about yourself: In my spare time, I enjoy outdoor activities like jogging, hiking in the mountains, rafting or canoeing on the rivers and lakes and being together with my family, friends and colleagues. My favorite indoor sport is basketball—a fast and thrilling game.

Why did you join PDA? In the beginning, I joined PDA to learn about aseptic processing and related sciences. I had the opportunity to catch up with technologies and standards required to serve markets in Europe, North America and Japan. My key professional interests are in the latest developments of aseptic technologies in fill & finish of biopharmaceuticals, lyophilization, filling of high concentrated liquids and development of innovative dosage forms, as is prefilled syringes, pens and cartridges. I feel that the application of PAT tools and continuous process improvement in house and at our suppliers of components and raw materials are key elements for business process excellence.

These days I regard PDA as the forum where new ideas in our business can be challenged in open discussions amongst professionals, technologies and procedures can be developed to an achievable level, and harmonization of standards are strived for.

Of your PDA volunteer experiences, which have you enjoyed the most? Serving as a facilitator at the 2008 PIC/S Workshop for Regulators and Industry in Geneva, Switzerland. This workshop, organized by PDA and ISPE, related to EU/PICS revised GMP Annex 1 for sterile products and new and possible uses of Quality Risk Management. Working with international experts from worldwide regulatory bodies and industry was a really exciting experience. My job was to facilitate discussions on current topics in aseptic processing and summarize the sometimes controversial views to achieve a common understanding.

How has volunteering in PDA benefited you professionally? Volunteering at PDA gives me professional benefits through contact with opinion leaders from industry and regulatory bodies. When giving a presentation at a PDA workshop or interest groups meeting, I find it provides a forum to challenge ideas and share opinions not only with international industry colleagues and regulators but also with raw material/component suppliers and machine vendors.

Which PDA conference/training course is your favorite? There is no special one—the favorite one is the one where we have decided to contribute!

What would you say to somebody considering PDA membership? Join in today! PDA is the best way to quickly be part of a global network!

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Chapter Contacts

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

Asia-Pacific

Australia
Contact: Ano Xidias
Email: ano.xidias@pharmout.com.au
www.pdachapters.org/australia

Japan
Contact: Katsuhide Terada, PhD
Email: terada@phar.toho-u.ac.jp
www.j-pda.jp

Korea
Contact: Woo-Hyun Paik, PhD
Email: whpaik@hitel.net

Taiwan
Contact: Frank Wu
Email: Frankwu@mail.ubiasia.com.tw
www.pdatc.org.tw

Europe

France
Contact: Philippe Gomez
Email: philippe.gomez@sartorius.com
www.pdachapters.org/france

Ireland
Contact: Colman Casey, PhD
Email: colman.casey@ucc.ie
www.pdachapters.org/ireland

Israel
Contact: Raphael Bar, PhD
Email: rbar@netvision.net.il
www.pdachapters.org/israel

Italy
Contact: Stefano Maccio, PhD
Email: stefano.maccio@ctpsystem.com
www.pdachapters.org/italy

United Kingdom
Contact: Siegfried Schmitt, PhD
Email: siegfried.schmitt@parexel.com
www.pdachapters.org/unitedkingdom

North America

Canada
Contact: Vagiha Hussain
Email: vagiha_hussain@baxter.com
www.pdachapters.org/canada

Capital Area
Areas Served: DC, MD, VA, WV
Contact: Allen Burgenson
Email: allen.burgenson@lonza.com
www.pdachapters.org/capitalarea

Delaware Valley
Areas Served: DE, NJ, PA
Contact: Art Vellutato, Jr.
Email: artjr@sterile.com
www.pdadv.org

Metro
Areas Served: NJ, NY
Contact: Lara Soltis
Email: lsoltis@texwipe.com
www.pdachapters.org/metro

Midwest
Areas Served: IA, IL, IN, KY, MI, MN, MO, ND, OH, SD, TX, WI
Contact: Peter Noverini
Email: peter_noverini@baxter.com
www.pdachapters.org/midwest

Mountain States
Areas Served: CO, ID, KS, MT, NE, NM, OK, UT, WY
Contact: Patricia Brown
Email: patricia_brown@agilent.com
www.pdachapters.org/mountainstates/

New England
Areas Served: CT, MA, ME, NH, RI, VT
Contact: Jerry Boudreault
Email: boudreault@ddres.com
www.pdachapters.org/newengland

Puerto Rico
Contact: Manuel Melendez
Email: manuelm@amgen.com
www.pdachapters.org/puertorico

Southeast
Areas Served: AL, AR, FL, GA, LA, MS, NC, SC, TN, VA
Contact: Michele Creech
Email: pdase@bluestarservices.net
www.pdachapters.org/southeast

Southern California
Areas Served: AZ, CA, HI
Contact: Saeed Tafreshi
Email: saeedtafreshi@inteliteccorporation.com
www.pdachapters.org/southerncalifornia

West Coast
Areas Served: AK, CA, NV, OR, WA
Contact: Elizabeth Leininger
Email: eleininger@ymail.com
www.pdachapters.org/westcoast

Please Welcome the Following Industry

Monica Adams, Bristol-Myers Squibb

Wayne Adcock, CSL

Yasser Alejo, Steri-Pharma

Francesca Alteni, Alfa Italian Medicines Agency

Christine Arbesser-Rastburg, Baxter

Shapour Asslani, Vital Therapies

Jeffrey Atkinson

Fred Austin, Amgen

Brian Bauer, TCA Engineering Group

Christopher Beganski, Biogen

William Belus, FedEx Supply Chain

Patty Benson, SAFC

Travis Besanger, Centre for Probe Development and Commercialization

Tina Beshears, Medco Health Solution

Panos Boudouvas, The Quality Advisory Board

David Bricker, Eli Lilly

Brad Brickhouse, Ellab Incorporated

Thomas Buckley, Allergan

Patrick Causey, Centre for Probe Development and Commercialization

Jennifer Clark, Morphotek

Robert Clayborough, Sagentia

Jasmeet Dhanju, Shire

Wanda Eng, Actavis

Annika Envall, AstraZeneca

Craig Fairchild, Cubist Pharmaceuticals

Joseph Famulare, Genentech

Chris Fong, Amgen

Eric Forrand, Shire Pharmaceuticals

Bruce Frazier, Laureate Pharma

Maarten Frijlink, CynergiQ

Nicole Gaines, Morphotek

Kiee Garland, OPK Biotech

Debra Garvin, Morphotek

Jeffrey Garvin, Kelly Services

Karen Gertz, ISTA Pharmaceuticals

Cedric Geyer, Millipore

Michael Gills, West Pharmaceuticlas

Anne Goodbody, Centre for Probe Development and Commercialization

Eric Gottlieb, Particle Measuring Systems

Adam Green, Cold Chain Technologies

William Grice, Talecris Biotherapeutics

Michael Guss, Otsuka America Pharmaceuticals

Jeff Gutkind, Temptime

Paul Hartigan, Partilce Measuring Systems

Robert Harting, Zimmer

Jason Hartman, Genzyme

Garrick Heidt, Cephalon

Michelle Heine, Catalent Pharma Solutions

Jeffrey Hessekiel, Gilead Sciences

Marjorie Hiestand, APP Pharmaceuticals

Joseph Homan, Opex

Matthew Hurst, GlaxoSmithKline

Shinji Inamura, Asahi Food and Healthcare

Cynthia Ipach, Compliance Insight

Nouri Istanbooly

Alicia Jeanveau, Centre for Probe Development and Commercialization

Allan Jensen, Biogen Idec

Sung Phil Jin, Hanmi Pharmaceutical

William Jones, Broad Creek Consulting

Steven Junker, Bristol-Myers Squibb

Brigitte Kiecken, Biolyse Pharma

Segawa Koki, Toaeiyo

Vivian Lai, Genzyme

Guy Lattelais, Alpha

Ron Lawson, Seidenader Vision

Richard Lee, Centre for Probe Development and Commercialization

Chris Leon, Centre for Probe Development and Commercialization

Drorit Lew, Kamada

Paul Lockner, Emergent BioSolutions

Samuel Lopez, Amgen

Scott Mackie, IDEO

Angela Majeski, Eli Lilly

Kenneth Manning, CIMA Labs

Emilio Marasigan, SNC Lavalin

Teresa Marks, Cephalon

Ramon Martinez, Prisma Consulting

Bob Mawanda

Martin Mayer, Fresenius Kabi

John McAnally, Merck

Jill McWilliams, Catalent Pharma Solutions

Kirsy Melo

Wayne Miller, Millpore

Nabalende Mills

JoAnne Minardi, Mallinckrodt Baker

Seiji Mochizuki, Japan

Kristopher Moffatt, Hospira

Sheba Mubiru

Hope Mueller, Catalent Pharma Solutions

Danielle Nanez

Alice Nantege

Andrew Nordby, HealthFirst

Michel Nouyrigat, Galderma

Robert Pinder, Roche Diagnostics

Mark Piosko, Genzym

Cheryl Poole

Jamie Pope, Genzyme

Iann Rance, Cytheris

Nathalie Renaud, GlaxoSmithKline

Brita Rippner Blomqvist, Octapharma

Michael Rogers, Hospira, Inc.

Bruno Rossi, Millipore

Kimberly Rymer, Baxter

Beatriz Sanchez De Carrillo

Rainer Schmidt, F.Hoffmann-La Roche

Michael Schmitz, Medtronic

Jim Searles, Aktiv-Dry

Megan Sedlacek, Catalent Pharma Solutions

Robert Seevers, Eli Lilly

Chhorn Serieyreath

Angela Serra, Lilly Del Caribe

Kathleen Shadley, Commissioning Agent

Abhinav Shukla, Bristol-Myers Squibb

Kwah Siew Min, F. Hoffmann - La Roche

Anne Simmons, GlaxoSmithKline

Jennifer Singh, EMD Chemicals

Emily Skuza, GlobeImmune

Elaine Smith

Lorna Smith, MedImmune

Mark Spinelli, Covidien

Lee Taing, OPK Biotech

Sam Tan, Merck

Masahiro Teramoto, Sepa-Sigma, Inc.

Vanly Thipphavong, OPK Biotech

Linhdi Tran

Leaders to the PDA Community

Clarence Wang, Cangene

Eileen Wilson, GlaxoSmithKline

David Wilson, Genzyme

Robert Worsham, Hyaluron Contract Manufacturing

Melissa Zafirelis, OPK Biotech

Hanne Lindvig Ziegler, Novo Nordisk

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

Navigate through Quality and Compliance Issues in the Aftermath of a Merger

2010 PDA/FDA Joint Regulatory Conference • Washington, D.C. • September 13-15 • www.pda.org/pdafda2010

Sue Schniepp, Antisoma

The *2010 PDA/FDA Joint Regulatory Conference* is just around the corner. This year's conference title is *The New Paradigm: Quality and Compliance in Merging and Emerging Cultures*. The meeting will take place September 13-15 in Washington, D.C. and promises to be one of the best conferences to date. The theme was inspired by recent announcements and events in the industry regarding the merger of some major pharmaceutical companies. In today's environment, companies are combining work forces and streamlining processes in order to be able to compete in a multinational global marketplace while trying to implement and incorporate emerging global regulatory requirements and complicated product strategies into company cultures and philosophies by strategically managing change. This conference will discuss some of the challenges facing the industry today as it tries to navigate compliance, achieve worldwide quality improvement and maintain control of their quality systems and regulatory compliance through merging and emerging cultures.

The committee is busy planning the details of each session that make up the backbone of the conference. There will be three learning tracks for conference attendees to choose from:

- Foundations
- Quality Today
- Merging and Emerging Issues

The **Foundations** track is focused on getting back to quality basics in times of change. Individual sessions discussing CAPA, inspection management, recalls and quality unit responsibilities are all planned, in addition to a session entitled FDA 101.

The **Quality Today** track is discussing many of the challenges facing today's quality professional including supply chain management, knowledge management and biologics.

The **Merging and Emerging Issues** track will focus on new worldwide regulations, merging quality systems, regulatory communication and foreign inspection practices.

Attendees will leave this conference understanding and being able to discuss:

- Practical approaches to compliance and implementation as best practices
- Emerging risk-based approaches, including first cycle approval, harmonization and critical path initiatives and illustrate case studies in adopting these concepts without delaying or disrupting product approvals while increasing supplemental filings
- Bringing quality into the global business platform
- Leveraging results to drive continuous improvement
- Interpreting supply chain and good distribution practices for incoming materials, as well as the final product for commercialization
- Defining quality systems as it relates to contract manufacturing
- Managing product knowledge through product transfer activities
- Anticipating emerging regulations
- Summarizing foreign inspections practices and expectations from foreign regulators
- Describing basic principles of the new ICH paradigm
- Responsibilities of the quality unit

In the coming months you will learn more details about the conference as the committee continues to finalize what is promising to be a dynamic and unique conference.

Advancing Microbial Control, Quality at the Micro Conference

Washington, D.C. • October 25-28 • www.pda.org/microbiology2010

Program Co-Chairs Ed Balkovic, PhD, Genzyme and Lynne Ensor, PhD, U.S. FDA

The program planning committee would like to invite you to attend *PDA's 5th Annual Global Conference on Pharmaceutical Microbiology*, October 25–28 in Washington, D.C. The theme of this year's meeting is *Advances in Microbial Control and Product Quality*. This conference offers an excellent opportunity to meet and interact with your fellow microbiologists, regulatory representatives, key product vendors and other global leaders in pharmaceutical microbiology.

Again this year, the conference will feature two keynote addresses. **Duane Pierson**, PhD, Chief Microbiologist, NASA has been invited to speak on microbes in the controlled environment of spacecraft. This talk should be of special interest to all of us who monitor the microbes in own controlled environments. Our second speaker is **Thomas Arista**, Investigator, National Expert, Pharmaceutical/Biotechnology, Division of Field Inves-

tigations, FDA, who has been invited to speak on practical regulatory guidance on risk assessment of microbial issues.

Other planned sessions include discussions on objectionable microorganisms, investigations of microbial data deviations, manufacturing and product attributes impacting sterility assurance, bioburden contamination control and new technologies. The Urban Myths and Expert Panel Discussion sessions will return this year. Additional podium presentations and posters will be selected from submitted abstracts. Abstracts are still being accepted until April 30, 2010.

The third day of the conference will be a full-day joint program in partnership with the U. S. Pharmacopeia. These sessions will be targeted to topics related to Rapid Microbial Methods.

The PDA Training and Research Institute will also host four courses on October 28 to complement topics presented at this conference. Courses include:

- "Auditing for Microbiological Aspects of Pharmaceutical and Biopharmaceutical Manufacturing"
- "Rapid Microbiological Methods: Overview of Technologies, Validation Strategies, Regulatory Opportunities and Return on Investment"
- "Validation of Microbiological Test Methods"
- "Investigating Microbiological Failures"

For meeting and abstract information, to submit an abstract and to register, visit www.pda.org/microbiology2010.

Participate at the 2010 PDA Biennial Training Conference

Baltimore, MD • October 11-15 • www.pda.org/biennial2010

Elaine Lehecka Pratt, Lehecka Pratt Associates and Stevens Institute of Technology Graduate Programs in Pharmaceutical Manufacturing and Management

GMP and regulatory compliance trainers from around the world will be gathering this October 11-15 in Baltimore, Md. for the *2010 PDA Biennial Training Conference*. The theme of the conference is *Compliance Training and Performance in a Changing Environment*, and the speakers and topics will focus on how to maintain training excellence in the face of changing conditions.

The general sessions will include confirmed U.S. FDA speaker, **Rebeca Rodriguez**, National Expert Investigator, who will provide agency perspective on current training issues. The keynote speaker will be **Allison Rossett**, PhD, Professor of Educational Technology, San Diego State University, well known as a dynamic speaker in the field of training and education, who will speak about job aid and performance support.

The concurrent sessions will feature a wide variety of speakers from the industry. This year, the program planning committee has required that all concurrent sessions feature interactivity and audience participation. You will definitely take a lot of great new ideas back to the job. Additionally, we are introducing a new mini-track featuring facilitated attendee brainstorming/Q&A around timely training topics. We expect these sessions to be extremely popular, as they will combine fast-paced information sharing with networking opportunities.

The conference will also feature a vendor exposition where you can see the latest and greatest in commercially available training programs and services.

On October 14-15, right after the conference, the PDA Training and Research Institute is offering a series of one and two day courses on training-related topics:

- "Designing and Presenting Effective GXP Training Programs to Meet New FDA Training Requirements" (1 day)
- "Introduction to Competency-Based Training" (2 days)
- "Developing and Using Virtual Learning Opportunities" (1 day)
- "FDA Inspection Readiness for a Training Systems Audit" (1 day)

Plan now to join other industry training and quality professionals at the Sheraton Baltimore City Center Hotel, in the beautiful Baltimore Inner Harbor area, to learn and share the most current information about compliance training in our industry! For more details on the conference and to register, please visit www.pda.org/biennial2010.

Keep your eyes open at PDA's Biennial Meeting—you don't know what you'll see. This photo of James Vesper, LearningPlus, was taken from the 2006 Biennial meeting.

Missed the TRI Courses at Annual? Sign up for In-house Training

Stephanie Ko, PDA

This year at the Annual Meeting, the Training and Research Institute was at it again with crowd-pleasing activities at the booth and in-depth training opportunities following the conference.

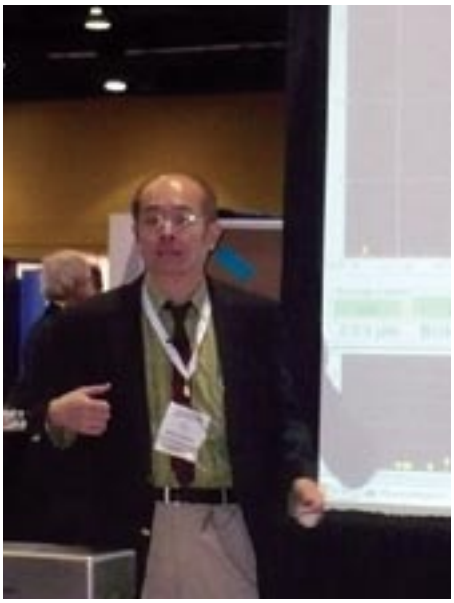
During the conference, TRI gave four 15-minute demonstrations on gowning, particle identification, rapid microbial detection and anti-microbial effectiveness testing. We'd like to thank **Art Vellutato, Jr.**, V.P. Technical Support Operations, Technical Services, Veltek, Inc; **Oliver Valet**, CEO, Rap-ID, Inc; and **J.P. Jiang**, Chief Technology Officer, R&D, BioVigilant, for dedicating their time in sharing their expertise with conference attendees.

We couldn't help but give our booth another twist of excitement. **Dave Matsuhiro**, President, Cleanroom Compliance, sponsored a fun and exciting Wii golf challenge for a chance to win a new 40 inch LCD TV. Conference attendees gave their hardest swing to drive the ball as close to the pin as possible. After two days of competition, the winner was **Richard O'Keeffe** who made it exactly 3 feet from the pin in one swing.

Of course, we couldn't possibly have held the Wii challenge just for fun! We made use of the opportunity by asking all participants to complete a brief survey that would help us give you more focused and accessible training in the future. We always strive for ways to improve our strategies and give our constituents the best opportunities to advance their career potential. If you didn't have the chance to provide your thoughts during the meeting, please contact us at info@pda.org. It will take less than 5 minutes to complete the survey and your input will help us in the future.

Immediately following the Annual Meeting, we offered nine in-depth training courses. The courses this year were selected based upon the theme of the PDA Annual Meeting, *Manufacturing Excellence*. Well, it worked—we beat last year's attendance!

What might interest you are the top three courses with the highest number of attendees, which indicates a few of the hot industry topics. The winner was **"Role of the Quality Professional in the 21st Century,"** taught by **Robert Kieffer**, President, RGK Consulting. This is actually the second time the course scored within the top three attendance level of a course series. There seems to be no doubt that there is a need for quality professionals to perform at a higher, more proactive level in improving quality, ➤



J.P. Jiang gave the second demonstration on particle identification

Art Vellutato explains the correct gowning method

We'd like to thank our other very dedicated instructors who contributed their time and efforts to our success with the following courses:

"Applying Lean to Aseptic Processes"
Mike Long, PhD, Director, Pharmaceutical and Medical Device Consulting, KPM International Associates

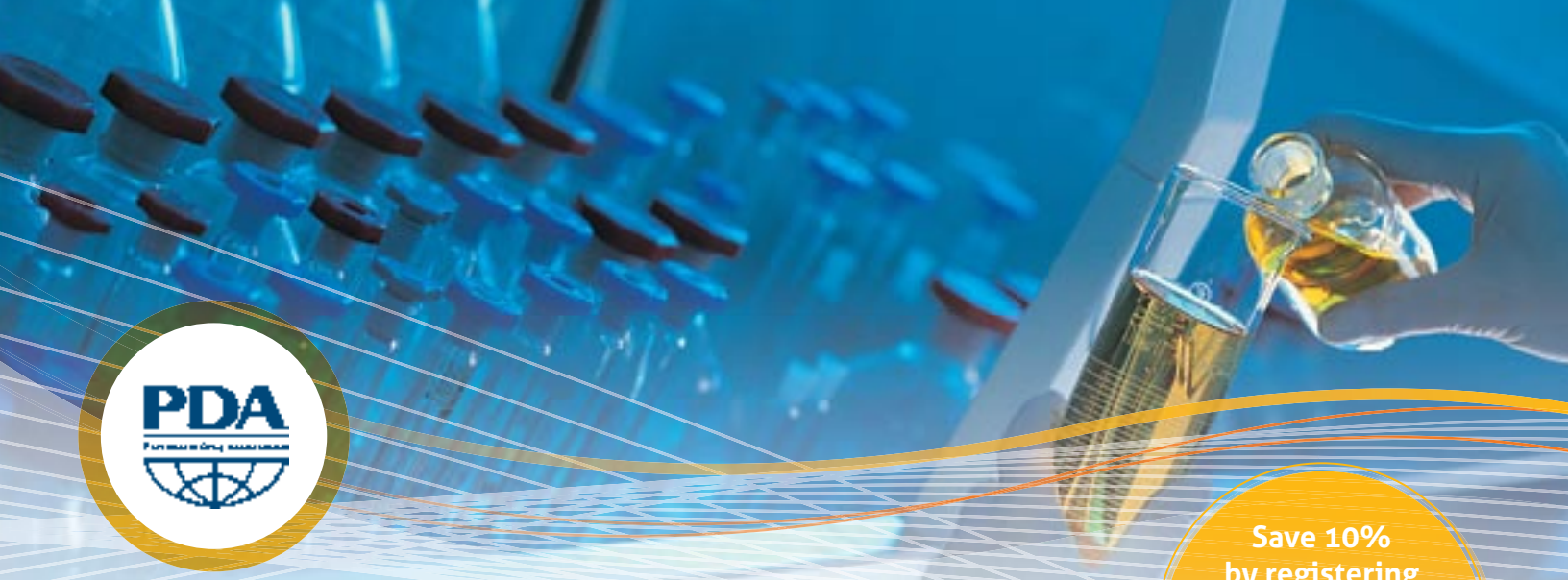
"Isolators: From Concept through Qualification"
Eddie Ballance, Senior Manager, Parenteral Pilot Plant, Eisai

"Risk Mitigation Solutions: The Response to Risk Assessment"
Anne Marie Dixon, President, Cleanroom Management Associates
J. Scott Kemp, Principal, JSK Consulting Services

"Fundamentals of Lyophilization"
Edward H. Trappler, President, Lyophilization Technology

"Change Control: A Practical Workshop"
Peter Smith, Vice President, Pharmaceutical Compliance, Parexel Consulting

"Use of HACCP for Microbiological Control in Pharmaceutical Manufacturing"
J. Kirby Farrington, Consultant, JKF Microbiology Consultants



PARENTERAL DRUG ASSOCIATION TRAINING AND RESEARCH INSTITUTE (PDA TRI)

Upcoming 2010 Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

Save 10% by registering early! Visit the course listing page for more information*

May 2010

19-20: PDA Vaccines Conference Courses
Bethesda, Maryland
www.pda.org/vaccines2010courses

Courses Include:
- Vaccines 101
- Uses of Bioassay for Vaccine Development and Product Control: Practical and Statistical Considerations
- Principles of Microbiological Containment

24-26: Boston Course Series
Boston, Massachusetts
www.pdatraining.org/Boston

Courses Include:
- Sterile Pharmaceutical Dosage Forms: Basic Principles
- Risk-Based Analytical Method Validation – New Course
- What Every Biotech Startup Needs to Know about CMC Compliance
- Virus Clearance – New Course

June 2010

2-4: Developing a Moist Heat Sterilization Program within FDA Requirements
Bethesda, Maryland
www.pdatraining.org/DMHS

3-4: Elements of Risk Management
Bethesda, Maryland
www.pdatraining.org/elements

23-25: Fermentation/Cell Culture Technologies Training Workshop
Bethesda, Maryland
www.pdatraining.org/fermentation

July 2010

20-23: Downstream Processing: Separations, Purifications and Virus Removal
Bethesda, Maryland
www.pdatraining.org/downstream

26-30: Basic Microbiology for Aseptic Processes
Bethesda, Maryland
www.pdatraining.org/basicmicro

August 2010

2-6: Rapid Microbiological Methods
Bethesda, Maryland
www.pdatraining.org/rapidmicro

10: Writing Standard Operating Procedures
Bethesda, Maryland
www.pdatraining.org/writingSOP

11: Six Sigma in Process Validation
Bethesda, Maryland
www.pdatraining.org/sixsigma

16-20: Aseptic Processing Training Program - Session 4
(Week 2: September 20-24)
Bethesda, Maryland
www.pdatraining.org/aseptic
ALMOST SOLD OUT

24-26: Developing an Environmental Monitoring Program
Bethesda, Maryland
www.pdatraining.org/DEMP

26-27: Application of Disposables in Biopharmaceutics
Bethesda, Maryland
www.pdatraining.org/disposables

30-September 1: Pharmaceutical Water System Microbiology
Bethesda, Maryland
www.pdatraining.org/watermicro

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

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

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

compliance and customer service while reducing costs.

The second highest attended course was **"Clean Room Design, Contamination Control, and Environmental Monitoring for Controlled Environments,"** taught by **Bob Ferer**, President, The Ferer Group. Participants identified opportunities for improvement within their companies with case studies and practice failure investigations, which were used to demonstrate common errors to avoid as well as best practices to implement.

Oliver Valet illustrates how to detect rapid microbial contamination

And the third most popular course was **"Bioprocess Validation,"** taught by **Trevor Deeks**, Senior Consultant, CMC and Manufacturing Development, Emergent Biosolutions. This course provided both a basic understanding of current expectations and industry norms, as well as practical advice on how to manage a bioprocess validation project. Participants learned about the planning and risk assessment tools available and how to apply them in practical situations of relevance to their jobs.

These courses are offered only once a year. If you missed your chance, there's no need to wait another year. In fact, a more cost-effective way of taking the course is by having it come directly to you as in-house training. Please go to www.pdatraining.org for more details.

Art Vellutato explains how to preform anti-microbial effectiveness testing

lyoseal™ one step class A freeze drying & capping

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- ▲ Eliminates sticking rejects
- ▲ Optimizes operations

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USA - Philippe LeGall - 212 Carnegie Center, Suite 206 - Princeton, NJ 08540
Tel (609) 524 2561 - email : plegall@biocorp.fr

EUROPE - Alain Fontaine - ZI Lavaur la Béchade, BP 88 - F-63503 Issoire Cedex
Tel + 33 473 55 70 61 - email : afontaine@biocorp.fr

Pros & Cons of Isolators, RABS & Clean Rooms Discussed

2010 PDA Conference on Isolator, RABS, Clean Rooms • Basel, Switzerland • June 8 – 9 • www.pda.org/europe

Volker Eck, PhD, PDA

The choice of whether to go for a clean room, an isolator or a restricted access barrier system (RABS) is difficult and will depend on several variables. One of them certainly being the direct investments needed to create and run such a facility. Recently, **Kevin Schreier, Jorge Ferreira,** and **Beth Holden** were interviewed in the January 2010 issue of *Pharma Manufacturing* about their study on the comparison of capital and operating costs for aseptic manufacturing facilities using conventional clean room technology, restricted access barriers (RABS) and isolator technology. Their opinions are based on a hypothetical facility for aseptic manufacturing that fills vials and syringes, as well as producing lyopilized products. In essence, they found that for manufacturing the same amount and type of product, the clean room would require the most space, RABS almost the same and a solution built on isolators would require approximately 24% less.

In classified areas, RABS would require approximately a third more Grade B area. With isolators the Grade C area would need to double in regards to the amount of room needed for clean room technology. Also, facility costs for the RABS and isolator systems would require more upfront investments (14% for RABS and 24% for isolator lay-out, respectively) than clean rooms. For initial validation costs, clean rooms and RABS don't differ, whereas isolators will require more than double the investment for this activity. The authors see the advantages of isolator technology clearly in the annual operating costs that could be reduced by half with regards to clean rooms or RABS, which are both essentially identical in this respect. This leads to the conclusion that from a cost perspective over ten years of operation, clean room and RABS technology are not significantly different. If evaluated over this period, isolator technology because of its presumed lower annual operating costs shows a distinct advantage and ends up in a 15% savings when compared.

The scenario might change if flexibility towards process design and accessibility is required. Here a clean room would accommodate most of these demands. Also, when it comes to change-overs, the time required to perform disinfection, change-over and a test run can easily require close to 16 hours when employing hydrogen peroxide gassing for an isolator. A clean room would require three to four hours, according to a published study by **Corinna Schneider**.

So in conclusion, it can be stated, that the solution chosen very much depends on the manufacturing environment these technologies are embedded. Under certain circumstances, it may still be the best compromise to run clean room technologies rather than using isolators.

To learn more about this, come to the PDA event in Basel, Switzerland on June 8–9. You will be able to attend the conference and workshop on *2010 PDA Conference on Isolator, RABS, Clean Rooms*. For more information, please visit www.pda.org/europe.

PDA's Who's Who

Jorge Ferreira, Technical Manager, Jacobs Engineering

Beth Holden, Architect, Jacobs Engineering

Corinna Schneider, QA Specialist GMP Compliance, Baxter Healthcare Corporation

Kevin Schreier, Manager, Process Engineering, Jacobs Engineering

Don't Waste a Trip, Stay in Basel and Attend PDA's Aseptic Technologies Conference on June 10-11

Learn about safety and contamination control, compliance with regulatory requirements and industry best practices and how it relates to innovative aseptic technologies. For more information, visit www.pda.org/europe

PDA Parenteral Drug Association

Connecting People, Science and Regulation®

2010 PDA Europe Conference on

Isolators, RABS, Clean Rooms

Join speakers from organisations like: Swissmedic | Bioquell | Bosch | Novartis | Patheon | Pharmatec | PMT AG | Skan | Veltek | and others

8-9 June 2010
Basel, Switzerland

Conference, Exhibition

For more information go to
www.pda.org/cleanrooms

Register by 11 May 2010 and SAVE!

Attending this conference will be essential for who is involved in, or responsible for running ,monitoring or maintaining a manufacturing area designed as a Clean Room, especially when equipped with Isolator or RABS technology. Attending will allow to:
• Identify critical steps in qualification, validation and maintenance of Isolators • Assess the appropriateness of Isolators, RABS and Clean Rooms for specific products and processes • Identify critical aspects and involved risks in Environmental Monitoring programmes and practices • Define crucial elements in design of processes run in Isolators, RABS or Clean Rooms • Examine the critical aspects of continual particle counting • Challenge practices and techniques in aseptic production areas and benchmark to latest concepts and solutions • Understand and interpret regulatory requirements, as defined e.g. by Annex 1 to the EU and PIC/S GMP Guide, respectively

Integrating Process, Technology and Regulation at the Parenteral 2010 Conference

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

Georg Roessling, PhD, PDA, Volker Eck, PhD, PDA and Jim Lyda, PDA

Parenterals products are, by some measures, still a critical and growing class of medicinal dosage form for pharmaceuticals. In 2009 it was forecasted by *Evaluate Pharma* that by 2014, seven out of ten blockbuster products will be parenterals, compared to only two out of ten today.

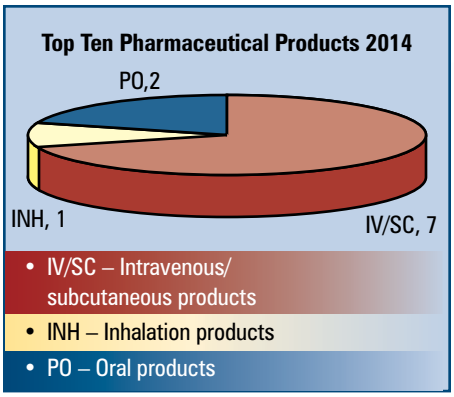
There are a large number of challenges to meet the technical and regulatory challenges of producing parenterals. To help with those challenges, PDA presents *Parenterals 2010* this October in Berlin. This conference will bring together all stakeholders involved in developing and manufacturing parenterals, such as experts from the pharmaceutical and biopharmaceutical industry, technology providers and regulators from the health authorities. The conference will allow an overview of current trends of parenteral manufacturing in the industry, innovations in equipment and process technology, and the practical impact of new regulatory guidances, especially ICH Q8, Q9 and Q10.

The goal of the conference is to focus on practical implementation: What is the current state of the art in technology? What is the current best practice? What impact does regulatory guidance have in a manufacturing environment and how can it be implemented?

As we work in a global market, manufacturers have to consider and comply with international standards. This conference will enable a broad and detailed view on the specific regional requirements of key markets like Europe, the United States and Japan. The drivers are to stay in regulatory compliance but always have the economic and operational costs understood and under control.

Highlights of the conference will cover:

- Production environments and their control
- Components and costs of quality including packaging, serialization, tolerance for defects, glass breakage, ready-to-use and ready-to-sterilize
- Manufacturing including total process control, high speed automation, in-line testing, knowledge management, continual improvement, single-use systems



Gerrit Hauck presented this graph at PDA's conference on IMPs.

- Innovative manufacturing facilities including production planning (push/pull, flexibility), dedicated, single and multipurpose facilities
- Isolators and RABS and current industry trends
- Impact of recent regulatory guidances
- Cost reduction and efficient management

Abstracts for the poster sessions can be submitted at any time until September 30 to **Ailyn Kandora** at kandora@pda.org. The subject line of your email should read "Poster Session Parenterals 2010" and follow the same content guidelines as full abstracts. Visit www.pda.org/europe for additional information.

Well known international experts within the PDA community have accepted to serve on the scientific planning committee. They are dedicated to make this conference what it should be—the place to get a 360° overview of development and production of parenterals and how to prepare for challenges from regulations, technologies and other requirements to come.

The place to be this October is in Berlin at the *Parenterals 2010* conference.

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PDA Europe Conference
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26-28 October 2010
Berlin, Germany
Conference, Exhibition

For more information see:
www.pda.org/Parenteral2010

Register by 28 Sept 2010 and SAVE!

This conference will bring together all stakeholders involved in developing and manufacturing parenterals: Experts from the pharmaceutical and biopharmaceutical industry, technology providers and regulators from the health authorities. The conference will allow an overview of current trends of parenteral manufacturing in the industry, innovations in equipment and process technology, as well as the practical impact of new regulatory guidances, especially ICH Q8, Q9 and Q10. Highlights of the conference will cover:
• Production environments and their control • Components and costs of quality including packaging, serialization, tolerance for defects, glass breakage, ready-to-use and ready-to-sterilize • Manufacturing including total process control, high speed automation, in-line testing, knowledge management, continual improvement, single-use systems • Innovative manufacturing facilities including production planning (push/pull, flexibility), dedicated, single and multipurpose facilities • Isolators and RABS, and current industry trends • Impact of recent regulatory guidances, especially ICH Q8, Q9 & Q10, variations, FDA guidances; PIC/S Annex 1 interpretation; EU GMP Annex 1; dedicated facilities; Inspection trends • Cost reduction and efficient management

The Parenteral Drug Association presents the

2010 PDA/FDA Joint Regulatory Conference

The New Paradigm: Quality and Compliance in Merging and Emerging Cultures

September 13-16, 2010 | Renaissance Hotel | Washington, D.C.

www.pda.org/pdafda2010

The *2010 PDA/FDA Joint Regulatory Conference* offers the unique opportunity for you to join FDA representatives and industry experts in face-to-face dialogues. Each year, FDA speakers provide updates on the current state of efforts impacting the development of global regulatory strategies; while industry professionals from some of today's leading pharmaceutical companies present case studies on how they employ global strategies in their daily processes.

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Take part in three dynamic learning tracks:

TRACK 1

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TRACK 2

Quality Today: Talk about the challenges facing today's quality professional including supply chain management, knowledge management and biologics.

TRACK 3

Merging and Emerging Issues: Focus on global regulations, merging quality systems, regulatory communication and foreign inspection practices.

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Register before June 21 and save up to **$400**!