Science • Technology • Quality • Regulatory • Community

PDA Letter

Volume XLVI • Issue #3

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March 2010

In This Issue:

PDA®
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Industry Repairing Links in the Supply Chain

Emily Hough, PDA

Following recent, jarring examples of criminal activity inside the pharmaceutical supply chain, the industry is now mobilized and tightening control over its ingredient supplies. A session at the *2009 PDA/FDA Joint Regulatory Conference* offered four speakers who discussed the human cost of the problem and offered solutions to combating counterfeiting and adulteration in the supply chain.

One of the speakers, **Eric Berg**, Director of Supplier Quality, Amgen, told audience members that industry was responsible for ensuring patient safety and must maintain vigilant scrutiny of its supply chain to ensure the integrity of its products. If not, the consequence could be death to the consumer.

To emphasize this point, Berg showed a video clip on the contamination of cough syrup with DEG in Panama from the National Geographic documentary *Illicit – The Dark Trade*. The clip provided a captivating case study of how a contaminated product can wend its way through the supply chain undetected because of the failure of each successive purchaser to conduct quality testing.

The source of the contamination was eventually traced to the Chinese Taixing Glycerine Factory which was not certified to sell any medical grade glycerin. The Taixing Factory sold its product with a falsified Certificate of Analysis (CoA) to CNSC Fortune Way in Beijing. Fortune Way then removed the manufacturers name from the CoA and put its name on the product instead. The tainted cough syrup next made its way to Barcelona where Rasfer International put its name on the CoA and removed Fortune Way's name. Medicom Business Group in Panama, the next purchaser of the medicine, merely changed the expiration data on the label. The cough syrup finally made its way to Panama's Social Security Administration where it was distributed. In three countries and four different sites, no testing was done on the cough syrup **(See Figure 1)**.

Following the clip, Berg stated, "In a supply chain, it is crucial that information that is passed through be real, that data is checked and that the supply chain has integrity.

"We saw in the video how there is a lack of responsibility being taken by different players in the supply chain, the buck stops with us. I advocate for supplier quality programs, and I know that in our industry

REPORT FROM THE 2009 PDA/FDA JOINT REGULATORY CONFERENCE

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USA - Philippe LeGall - 212 Carnegie Center, Suite 206 - Princeton, NJ 08540
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EUROPE - Alain Fontaine - ZI Lavaur la Béchade, BP 88 - F-63503 Issoire Cedex
Tel + 33 473 55 70 61 - email : afontaine@biocorp.fr

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Cover art:
Industry is taking a proactive role in solving the problems occurring recently in the supply chain.

Coming Next Issue:
Impact and Use of ATSM Standards in the Pharmaceutical Industry

Editor's Message

A Welcome and Thank You

This issue, I'd like to welcome the new members of the *PDA Letter* Editorial Committee (PLEC) and thank those who are cycling off for the time being. First, the introductions. Joining us for the next two years is a mix of members that aligns the PLEC better with the PDA community's areas of interest. We are pleased to welcome two committee members from outside the United States, **Sandra Zoghbi-Gay** and **Karen Ginsbury**. **Georgiann Keyport** brings to the community a consultant's perspective. **Kamaal Anas** joins the committee and represents not a pharmaceutical company or supplier, but rather an international organization supporting the development of an AIDS vaccine. The committee's biotech representation grows further with the addition of **Miriam Estrano**. Finally, we welcome a representative from large pharma, **Matt Schmidt**. You can see all of their affiliations in the masthead on this page.

Now the thank you's. We are grateful to the hard work and input we've received since the PLEC was hatched in 2005 from **Scott Sutton**, **Vinod Gupta** and **Elizabeth Martinez**. These three are charter members of the committee and their greatest contribution is helping us launch this new membership volunteer opportunity. Of course, their careful consideration of articles submitted for publication, has helped us publish a better *PDA Letter* than in years past. We hope that each of them remain active in PDA and consider serving on the PLEC again in the future.

One of the most important tasks the PLEC performs for us each year is the identification of themes for the issues. This month's theme is a winner, for sure. While we've dedicated several issues over the last two years to supply chain, I have trouble thinking of a topic more relevant at this time. The editorial staff took the theme in our own hands and have prepared reports from the fantastic sessions on supply chain at the *2009 PDA/FDA Joint Regulatory Conference* last September. For the many members unable to attend these sessions in person, you will see how industry is moving beyond the problem and coming out with sound solutions. We also include a bonus article on supply chain by **Helena Champion**, Drug Quality Assurance, which originally was published in the October 2009 newsletter of the PDA New England Chapter. We thank them for letting us present the article to the larger PDA audience.

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 77 0
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

Prepare Appropriate Virus Spikes for Virus Clearance Studies

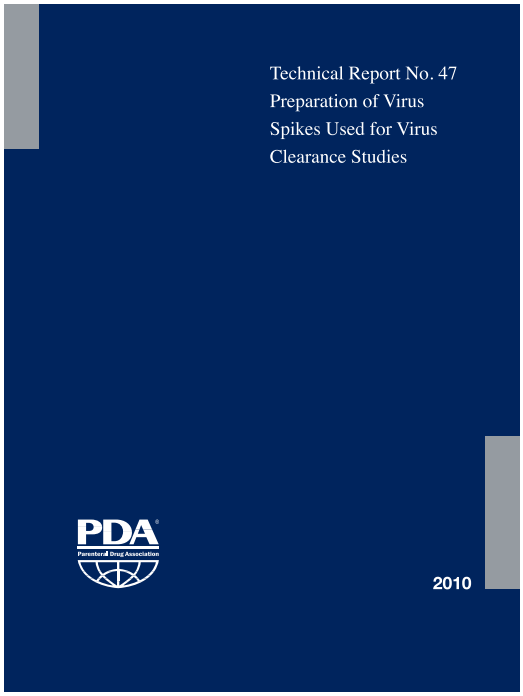
PDA Technical Report No. 47, Preparation of Virus Spikes Used for Virus Clearance Studies Now Available at www.pda.org/bookstore

The Virus Spike Preparation Task Force presents the quality attributes that may be applied to virus and bacteriophage spike preparations, as well as to cell lines used for virus propagation and sample testing in its latest technical report. *PDA Technical Report No. 47, Preparation of Virus Spikes Used for Virus Clearance Studies* complements *PDA Technical Report No. 42, Process Validation of Protein Manufacturing*, which the Task Force completed in 2005.

The virus spike technical report provides guiding principles that can be used to select and define appropriate quality attributes for a virus, with an emphasis on minimizing the impact of the virus spike on the scale down model of the unit operation under validation and virus clearance observed.

PDA members can access this technical report for free until March 31

Just go to the PDA bookstore and use your PDA ID and password when prompted. **Note: PDA passwords are case-sensitive at the PDA bookstore website, so be sure to capitalize the first letter of your password if it is your last name, as issued by PDA.**



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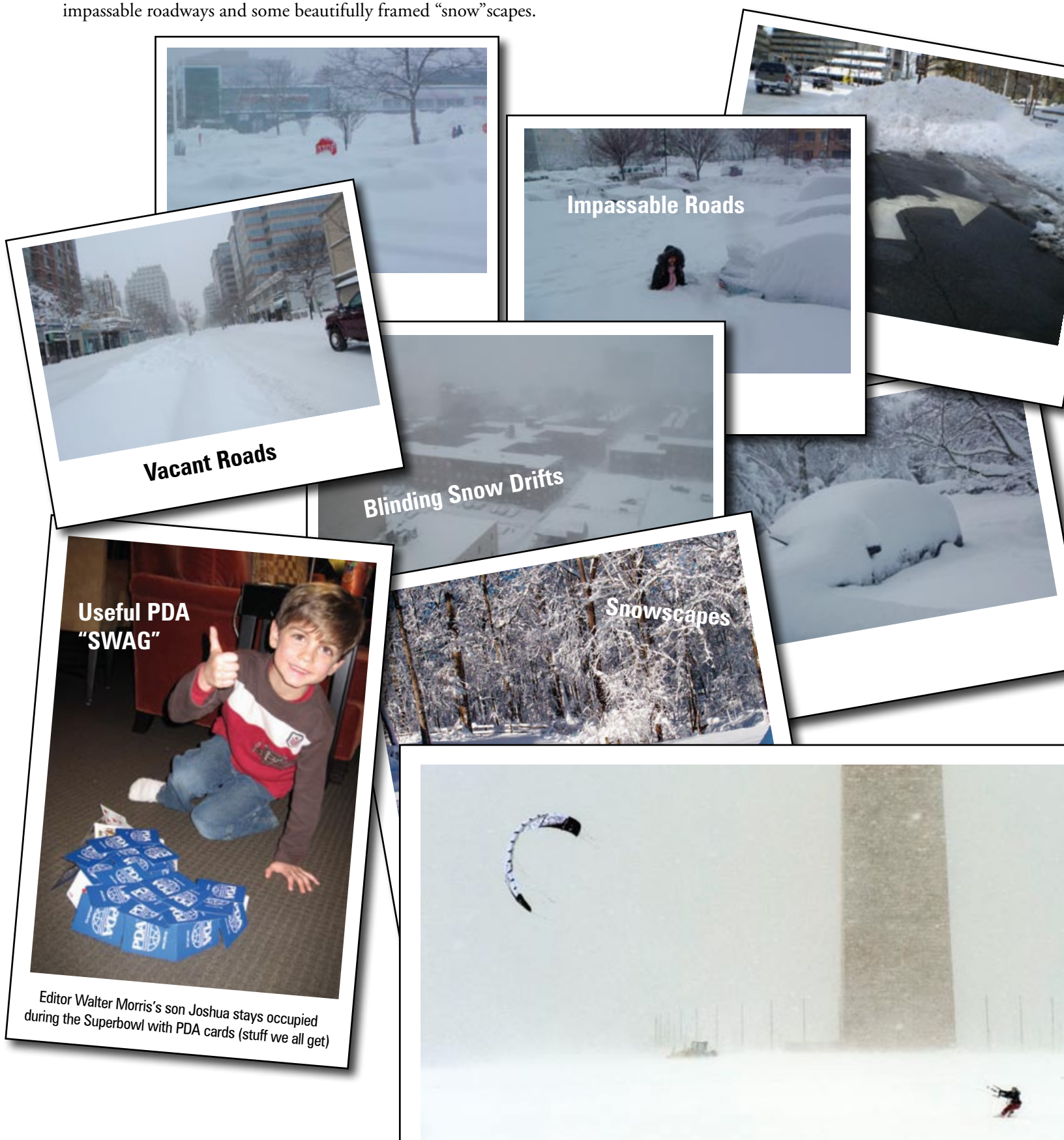
CONFERENCE September 13-15 | **WORKSHOP** September 15-16 | **COURSES** September 16

February Blizzard Blankets PDA HQ

While Bethesda, Md. was inundated with snow, PDA's headquarters closed due to the unplowed and often unsafe roads. Some of the heaviest snow fell in Bethesda, Md., but employees were able to get work done via telecommuting. Staff took the time between work and shoveling to take pictures of the enormous amounts of snow that literally stopped traffic and slowed life down for a few days in the normally bustling metropolitan area. Please enjoy these photos that show vacant roads, blinding snow drifts, impassable roadways and some beautifully framed "snow"scapes.



Editor Walter Morris's son Joshua stays occupied during the Superbowl with PDA cards (stuff we all get)

Science & Technology *Snapshot*

The Challenges of Success – Looking Forward to 2010 PDA SciTech Activities

Rich Levy, PhD, PDA

Each successive year, I have had the pleasure to report to you that PDA's SciTech program has been on an upward trend, as measured by the number of approved Task Forces and participants. In 2010, I expect more teams than ever before in my tenure to complete their goals and publish their deliverables. At the end of February, we will have already published two technical reports, *Last Mile: Gidance for Good Distribtution Practices for Pharmaceutical Products to the End User* (TR-46) and *Preparation of Virus Spikes Used for Virus Clearance Studies* (TR 47).

Because many teams closed their drafting activities toward the end of 2009, the number of technical reports undergoing the required balloting process has increased to the point where the approval process—reviewing and balloting TR content by the relevant Advisory Boards—has placed an added burden on those AB members (see the "Technical Report Watch" below). The same challenge then extends to our Board of Directors, which ultimately approves the TRs for publication and to our Publications Department which transforms the draft documents into the blue covered, easy-to-read documents we have come to expect. This has created bottlenecks in the TR publication process—something that we always hope to avoid.

In terms of deliverables, 2010 looks to be no different than 2009 with Task forces completing their document drafting and global directed subject matter expert reviews toward the middle and end of the year. When we add in the 17 new projects under PCMO (see www.pda.org/pcmo) which are expected to start this year, the PDA pipeline of value-added projects is impressive, as well as daunting. So one of the important goals of 2010 is "timeliness" and ensuring that teams complete their milestones in a reasonable period of time.

To assist our Task Forces and Advisory Boards in this goal, I will be overseeing several initiatives this year.

First, we will be evaluating software-based tools for collaboration and balloting—with the expectation of going beyond WebEx meetings as the main tool we provide for Task force members. We will continue to support teams

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Technical Report *Watch*

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

- *Technical Report No. 3: Validation of Dry Heat Processes Used for Sterilization and Depyrogenation* **(SAB)**
- *Technical Report No. 22: Process Simulation Testing for Aseptically Filled Products* **(SAB)**
- *Moist Heat Sterilizer Systems* **(SAB)**
- *Steam in Place* **(SAB)**
- *Investigating Microbial Microbiological Data Deviations* **(SAB)**
- *The Manufacture of Sterile Pharmaceuticals and Liquid Medical Devices Using Blow/Fill/Seal Technology* **(SAB)**
- *Technical Report No. 30: Parametric Release of Pharmaceutical Products and Medical Devices Terminally Sterilized by Moist Heat* **(SAB)**
- *Alternative Methods for Mycoplasma Testing* **(BioAB)**
- *Recommendations for the Production, Control and Use of Biological Indicators for Sporicidial Gassing of Surfaces with Technical Exposures* **(BoD)**

In Publication: TR is approved and ready for publication.

- *Technical Report No. 47: Preparation of Virus Spikes Used for Virus Clearance Studies*

In *Print*

QbD for Cleaning Validation

The following is excerpted from the chapter, "Quality by Design Approach to Cleaning Characterization," by ***Rizwan Sharnez****, Amgen, and* ***Martin VanTrieste****, Amgen. The chapter appears in the PDA/DHI book,* Cleaning and Cleaning Validation, *Volume 1, edited by Paul Pluta. References have been removed for this excerpt but can be found in the book.*

We have all heard dreadful stories about delays to submissions, new product introductions and product releases because of failed cleaning validation. These types of costly delays can be prevented if we enter into validation after we are confident that the cleaning cycle is robust and validatable. However, far more than we would like to admit, we have witnessed or heard of events that demonstrate that this has not been the mindset or culture. Many firms have adopted an overkill approach, where they have developed extreme cycles to assure success. These cycles consume excess energy, cleaning agents, and water; increase equipment turnaround times; and produce more waste.

If we all thought about cleaning in a holistic manner and not just from the perspective of validating the cleaning process, we would be better off in the long run. The industry has made significant progress in this respect; however, there is still much room for improvement. To that end, Quality by Design (QbD) provides a framework for implementing a systematic approach to process design, development and monitoring (FDA, 2006; Frohlich, 2007; Borman et al., 2007). With the QbD approach, we design and develop a process to ensure predefined quality at the end of the process. This requires that we understand the impact of process parameters on product quality, and that the process be continually monitored and modified, as needed, to assure consistent quality over the lifecycle of the process.

QbD can also be used to reduce the risk associated with periodic monitoring. With the traditional validation approach, we validate a cleaning cycle with three consecutive runs and then we periodically verify that the cycle is still operating as intended. For example, once we validate a cycle, its effectiveness could be verified on an annual basis. During that 12month period, many batches of product would have been produced and released to the market. So what would be the consequences if the periodic monitoring fails?

- First, a major investigation would have to be initiated consuming valuable company resources that could be used elsewhere.
- It is likely that product that has not yet been released would have to be placed on hold until the investigation is complete, potentially leading to issues with the supply of critical products to patients.
- It is possible that regulatory body notification of the failure would be required, such as a biological products

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In *Print*

Defining Quality

From Validation by Design: The Statistical Handbook for Pharmaceutical Process Validation *by* ***Lynn Torbeck****, Torbeck and Associates*

The definition of quality has changed over time and industries. In his second edition of the classic Quality Control Handbook, Juran (1962) gives thirteen meanings to the word "quality". His first definition of quality reads:

"The degree to which a specific product satisfies the wants of a specific consumer"

and the third reads

"The degree to which a specific product conforms to a design or specification."

In the third edition, (Juran, 1974), the definition became

" ... the extent to which the product successfully serves the purposes of the user,

during usage, is called its 'fitness for use.'"

But he then goes on to say

"As yet there is no standard, agreed-upon term to designate the concept of fitness for the user."

In the fourth and fifth editions, (Juran, 1988, 1999), the definition changed yet again:

"1. Quality consists of those product features which meet the needs of customers and thereby provide product satisfaction. 2. Quality consists of freedom from deficiencies."

These general definitions fail to address the specific needs of the pharmaceutical industry.

Defining Quality For The Pharmaceutical Industry

Any definition of quality in the pharmaceutical industry must account for the particular nature of our industry. If we wish to satisfy the customer, we must first decide who is the customer? Is it the patient, the doctor, the pharmacist, or the FDA? The patient, the doctor, and the pharmacist can not always determine if the drug is satisfactory, is meeting its specifications or is essentially free of deficiencies. Given the placebo effect, patient improvement is not always the result of the medicine. How do we define and measure quality when satisfaction or fitness for use cannot be directly determined?

As we cannot control the placebo effect or other variables, the industry must put in place and follow procedures and guidelines that will at least in principle assure quality. We find this quote in the CGMPs: "The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product." 21CFR 211.22(c). This has been dubbed "SSQuIP" for Safety, Strength, Quality, Identity

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Quality by Design, continued from page 9

deviation report.

- In a worst case scenario, a product recall would be necessary.

These consequences can be obviated through better process understanding, and realtime monitoring of critical process parameters and quality attributes, such as conductivity and total organic carbon (TOC). With realtime monitoring one would know of a failure prior to manufacturing the next batch. Procedures could be put in place to ensure that the equipment is recleaned before being released, thereby preventing product contamination, and reducing the risk assumed with the traditional periodic monitoring approach. Combining QbD with realtime performance verification could provide the following additional benefits:

- reduced development times
- reduced development costs
- more efficient, effective and consistent cleaning cycles
- higher cleaning assurance levels.

Realtime performance verification could also eventually eliminate the need for traditional three run validation.

In this chapter, we describe a QbD approach to process development for cleaning. This approach leverages soilant characterization at small scale to enhance process understanding and predict cleaning performance at full scale. We also describe how data obtained at small scale can be used to develop efficient, effective and consistent cleaning cycles. You will see how these approaches have been successfully applied through case studies and examples. The true value of gaining this understanding in the laboratory versus in manufacturing is that many more experiments can be run in a shorter timeframe at small scale than at full scale in manufacturing, allowing the edges of failure to be found more easily. Once we understand well the robustness of the cleaning cycle, we can transfer this knowledge to the fullscale cleaning process, thereby greatly enhancing the likelihood of success at full scale, and reducing the overall time to develop and validate a cleaning cycle. The monitory value of time during product development is substantial and just as important are the savings gained by reducing downtime in manufacturing.

Quality By Design Approach To Cleaning Characterization

The objective of QbD is to develop robust processes through a better understanding of the relationship between operating conditions (inputs) and performance requirements (outputs). Operating conditions are defined in terms of critical process parameters (CPP) and their respective operating ranges. Performance requirements are defined in terms of critical quality attributes (CQA) and their respective acceptable limits. Most processes have multiple CPPs and CQAs. Each CPP or CQA can vary over a specified range defined by its lower and upper acceptable limits (LAL and UAL) as shown on Figure 6.1. The dotted and discontinuous lines represent the set point and worstcase operating point, respectively. An approach for identifying CPPs and CQAs, and their respective acceptable limits has been described previously. An experimental strategy for identifying the worstcase operating conditions and leveraging them to develop a robust cleaning cycle is described later in this chapter.

The QbD approach to process development for cleaning is demonstrated in the following case study. Consider a cleaning cycle that consists of a wash followed by a rinse. The traditional and QbD approaches to cleaning characterization are compared in Figure 6.2, which shows the input–output relationship for the rinse step. With the traditional approach, the rinse step is characterized with the concentration of cleaning solution (CPP) at the set point (1%). With the QbD approach, however, the effect of the concentration on the conductivity of the rinsate (CQA) is used to identify the worstcase operating point (1.25%; represented in Figure 6.2 as the UAL). This is the concentration at which the system is least likely to meet the performance requirements for the conductivity of the rinsate. This worstcase operating point (which is the UAL in this case) is used to challenge the system during character-

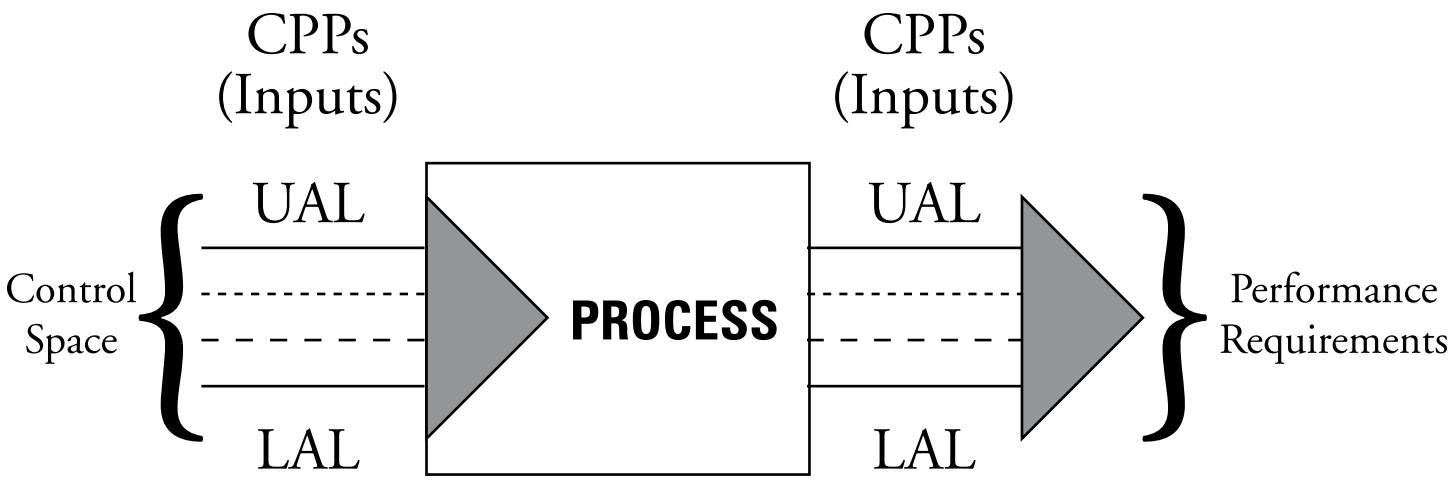

Figure 6.1: Each CPP or CQA can vary over a specified range defined by its lower and upper acceptable limits (LAL and UAL).The dotted and discontinuous lines represent the set point and worst case operating point, respectively.

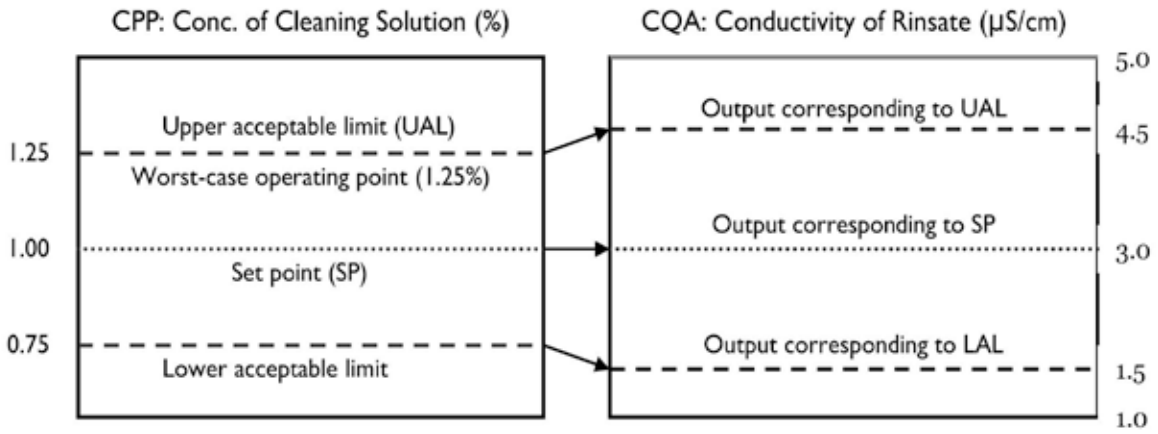

Figure 6.2: With the traditional approach the process is characterized with the CPPs at their respective set points. With the QbD approach the process is characterized with the CPPs at their respective worstcase operating points (shown here to be the upper acceptable limit).

ization. The wider the operating margin between the output corresponding to the worstcase operating point (4.5 µS/cm) and the failure limit (5.0 µS/cm), the more robust the process. An important element of QbD is to strike a balance between the cost of designing a process with wider operating margins (tighter process control), and the higher robustness that results from the tighter control (lower possibility of failure).

Defining Quality, continued from page 9

and Purity.

By default then, quality becomes

"The degree to which a specific product conforms to a design or specification."

That is, does it meet SSQuIP? This is the basis of the GMPs and the basis of pharmaceutical quality assurance and control. And maybe this is why statistics sometimes play a lesser role in quality and manufacturing. If it meets its specifications, it is by definition a quality product and thus acceptable to customer.

How then can quality be redefined but in the context of the GMPs? One overriding concept inherent in the philosophy of the GMPs is consistency. Write what you are going to do in the Standard Operating Procedure (SOP), and then do it that way every time all the time. Zero deviations from each activity is the goal. Deviations and lack of consistency are evidence of unwanted variability.

While variety is the spice of life in many aspects of human endeavor, variation under the regulations is the source of many 483 citations. (That is an investigator's observations on the FDA's Form 483.) Minimizing and eliminating variation in manufacturing and testing are key to improving product quality. How many of the daily crises in the Quality Assurance department would evaporate if there were little or no variation in production, sampling, testing and inspection? Minimizing and eliminating variation must be a goal of every Quality professional.

The Challenges of Success, continued from page 8

by working directly with one of our own PDA staff members, usually **Iris Rice**, to facilitate meetings, document commenting, revision and storage and with AB and BoD balloting.

Second, I want to expand our volunteer Project Manager Program. Currently, four individuals are filling this important role on four of our task forces. These volunteers, all with some PM experience, are assisting the task force leaders and teams to deliver their reports in a "timely" manner. We are looking for additional PMs, so if you or someone you know would like to be involved, we have many new projects in need of assistance. Contact rice@pda.org should you wish to volunteer.

Third, we continue our focus on maintaining the currency and quality of our documents, which is paramount to the PDA mission and brand. This is no small task when you are balancing multiple teams creating consensus documents, while each team copes with the pace of technology and regulatory changes. This is true for most teams since the average task force takes over two- and one-half years to complete their technical report. We will, as necessary, continue our directed reviews (outside of the TF) to ensure that the consensus is broad, the subject matter is current and that the documents do not contradict regulatory guidance or standard-setting consensus documents, such as those from ICH and ISO. Further, we now use professional copy editors to review the document prior to publication.

Finally, in 2010, PDA has undertaken to initiate a portfolio management process. This process will facilitate the review and approval of Technical Report topics brought forth by our membership. We will be talking more about this as we roll out improvement in these efforts during the year.

We Want You – Project Manager Volunteers

PDA is looking for qualified candidates to join our Project Manager Program to assist PDA Task Forces. You will gain valuable experience working with subject-matter experts in the development, drafting and publishing of consensus documents or another deliverable like a course or meeting that benefit the entire PDA community and the industry at large. In turn, you will contribute your project management skills to help organize the Task Force and keep them on schedule.

PDA is looking for help, in particular, for the following projects under the Paradigm Change in Manufacturing Operations (PCMO) initiative, which is aimed at helping industry implement the ICH Q8, 9 and 10 guidelines. The projects are organized by theme:

Lifecycle Approach

Quality Systems

Process Management

Quality Risk Management

To volunteer, email PDA's Iris Rice at rice@pda.org. For more information on PCMO, go to www.pda.org/pcmo and download our dossier.

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March 2010

March 9, 1:00 p.m. – 2:30 p.m.:
Environmental Monitoring in Isolators
James Akers, PhD, President, *Akers Kennedy & Associates, Inc.*

March 11, 1:00 p.m. – 2:30 p.m.:
Fundamentals of Lyophilization in Syringes
Shawn Kinney, PhD, President and CEO, *Hyaluron Contract Manufacturing (HCM)*

March 31, 1:00 p.m. – 2:30 p.m.:
Intrinsic Foreign Particulate Matter Identification and Application of ISO 16232 Cleanliness Testing Procedures and Qualified Equipment to Control and Minimize Foreign Particulate Matter in Parenterals Down to 1 µm
Oliver K. Valet, PhD, Co-Founder, *rap.ID Particle Systems GmbH*

April 2010

April 8, 1:00 p.m. – 2:30 p.m.:
Knowledge Management: Application of Project Management and Program Management Best Practices to Lean Manufacturing and Lean Laboratory Projects
Barbara Berglund, PhD, Quality Control Manager, *Hollister-Stier Laboratories*

April 8, 3:30 p.m. – 5:00 p.m.:
Software Implementation in One Third of the Time and Cost
David Nettleton, FDA Compliance Specialist, *Computer System Validation*

April 21, 1:00 p.m. – 2:30 p.m.:
Adopting ICH Q10 to Achieve Competitive Compliance
Siegfried Schmitt, PhD, Principal Consultant, *PAREXEL Consulting*

May 2010

May 13, 1:00 p.m. – 2:30 p.m.:
Automated Validation Lifecycle Management – A Working Model
Jim McElroy, Manager, Compliance Engineering, *Novartis*
Nagesh Nama, President, *ValiMation, Inc*

PDA Web Seminars are hosted in real time and attendees are encouraged to engaged in group discussions and ask their specific questions.

For more information on PDA web seminars please visit www.pda.org/webseminars

PDA Interest Groups & Leaders

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

SECTION TITLE

Biopharmaceutical Sciences	Laboratory and Microbiological Sciences	Manufacturing Sciences	Pharmaceutical Development	Quality Systems and Regulatory Affairs

SECTION LEADER

Frank S. Kohn, PhD *FSK Associates*	David Hussong, PhD *U.S. FDA*	Don E. Elinski *Lachman Consultants*	Sandeep Nema, PhD *Pfizer Inc.*	Robert L. Dana *PDA*

RELATED IGS AND GROUP LEADERS

Biotechnology
Group Leader (USA):
Jill A. Myers, PhD
BioPro Consulting
jmyers@bioproconsulting.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
Email: rafikbishara2@yahoo.com
Group Leader (EUR):
Erik van Asselt
Merck, Sharp & Dohme
Email: 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.
smallec2@wyeth.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
Chimera Consulting
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
Group Leader (EUR):
Lothar Hartmann, PhD
F. Hoffmann-La Roche Ltd.
lothar.hartmann@roche.oom

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Industry Repairing Links in the Supply Chain, continued from cover

we are all advancing those programs very rapidly." Such programs should build relationships with supplier, establish requirements and ensure that they are met, and sustain the relationship as changes occur, he explained.

Responsibility for the integrity of the supply chain belongs to everyone involved in purchasing, Berg said. "It is important that cross-functional engagement happens....The very best way to negotiate is to be in the critical path of the money. I've personally seen that every time we've negotiated a quality agreement, if the quality agreement is being negotiated before we've bought anything and if my business person has linked arms with me, that quality agreement really works for us. If I'm trying to put one in place after the fact, it is way more of a struggle."

The U.S. FDA understands this. Berg reported that last year CDER Director Janet Woodcock, MD, took the message straight to the business side of the industry when she appeared at the annual dinner meeting of the Drug, Chemical & Associated Technologies Association, the premier business development organization for pharmaceutical manufacturers and suppliers.

FDA's **Edwin Rivera-Martinez**, Chief, International Compliance Branch, Division of Manufacturing and Product Quality, CDER Office of Compliance, said companies that don't have a relationship with their distant manufacturing sites can put the supply chain at risk. In such cases, suppliers usually go unaudited by the firm or, if audits do occur, they can be superficial, often taking the form of questionnaires sent to suppliers. The FDA official reminded audience members of the old adage "paper will basically hold anything." In other words, "Companies can respond to the questions in a very dishonest way and you have no actual way of verifying that information unless you do an on-site audit."

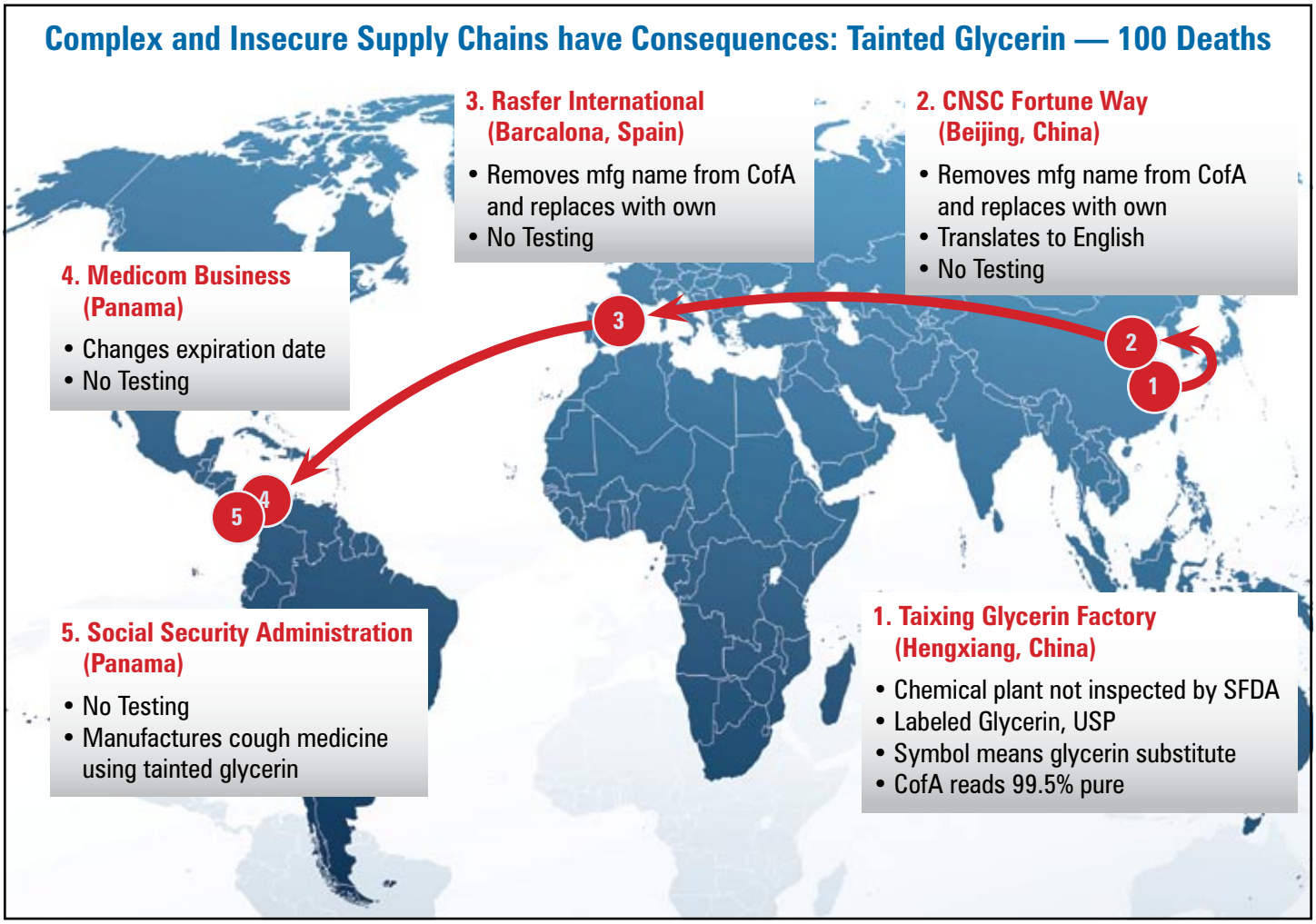
Taking Action

Berg believes the industry should work together to ensure safety and not worry about proprietary information. He pointed to the example the automaker Volvo set when it invented and then gave away the rights to the seatbelt. Safety, according to Berg, is not proprietary.

Indeed, the industry is taking action and advancing solutions.

Berg reminded the audience of the creation of the industry consortium RX-360, which aims to become a clearance house for industry audits. The International Pharmaceutical Excipients Council (IPEC) released a guidance for

Figure 1



A slide from Eric Berg's presentation conveying that complex supply chains can become insecure when unscrupulous businesses take advantage.

industry on the qualification of excipients for use in pharmaceuticals. Meanwhile, industry has worked at gaining a deeper knowledge of its material supply chains.

"I know with discussion with colleagues in other companies, I know by experience at Amgen, that we are drilling into our supply chains to really understand where things are made, what the control points are and to ensure safety of material and authenticity of material comes through," Berg said.

Amgen has found opportunities to advance technologies such as applying Nuclear Magnetic Resonance (NMR) Spectroscopy in the QC areas. "I think many companies are looking at bringing technologies and advanced technologies for detection and prevention."

Amgen also has developed new solutions to see if a product has been counterfeited, such as developing a photo library for incoming supplies. Berg explained, "The warehouse receiver pulls up from their computer in the dock a photographic image that points to key things. We are asking people to look for pattern recognition and to raise the flag if something looks strange. In conversation with FDA and others, we recognized that in the glycerin case, had that been done, it likely would have prevented it."

Berg sees photo libraries and pattern recognition as "a simple solution that can be rapidly advanced."

The Counterfeiter

Katherine Eban, an investigative reporter and author of the book *Dangerous Doses,* a case study on counterfeiting, described the various weapons in the counterfeiters' arsenal: substitution, uplabeling, dilution and repackaging of drug products.

"You have this porous supply chain full of these wholesalers and all kinds of cut-rate drugs moving from them, and into that porous supply chain stem counterfeits."

Eban spent three years researching how a 16-year-old boy and recovering liver transplant patient received counterfeit *Epogen* from a legitimate pharmacy. It all started, she said, when a professional body builder named Jose Grillo in Florida realized he could make a lot of money by uplabeling *Epogen.* He managed to obtain a large quantity of 2,000 U/mL vials--nearly 100,000--and uplabel them to 40,000 U/mL. His scheme was worth about US $43 million.

Further undermining the integrity of the product, Eban explained, the biologic *Epogen* is a very delicate drug that needs to be held in perfect condition—it can't be shaken or heated--and needs to be maintained in a carefully controlled supply chain.

Grillo carelessly kept the vials of Epogen soaked in water overnight under a black tarp. With the help of an accomplice, he skillfully removed the original labels and glued on the high dose labels, which another accomplice made. According to Eban, "these labels were so exact that Amgen packaging specialists could not tell the difference for quite a bit of time."

Grillo next found a urologist, who bought the counterfeit Epogen and stored it a beer cooler in a back room of a gentleman's club. The urologist then found a legitimate wholesaler who had an out-of-state license from the state of Georgia and had a rap sheet. "His goal, and everybody's goal in this corrupt chain, is to sell up. To sell to someone who is more legitimate then they are—they make more money that way," Eban explained.

The uplabeled *Epogen* was eventually sold to a regional wholesaler who in turn called Amerisource, which bought the vials. In an ironic twist of fate, Amerisource was the original source of the legitimately labeled 2,000 U/mL units prior to them falling into Grillo's hands. From there, the product made its way onto store shelves and eventually the boy in New York.

Eban was quick to point that the book could have taken place anywhere since this problem is widespread.

Berg stated, "I think in the *Dangerous Doses* story it's really clear that looking for a lower price point item, is an entry point for danger. We are in a soft economy, everybody is looking for a good deal…. We have to have appreciation in our businesses for total cost of ownership and recognize that a smaller price point might be an indicator of something and that we have to look at the entire cost of ownership."

High Tech not always High Security

Describing current trends, **Marc Payne**, VP, Corporate Security, Novartis, offered a glimpse into his firm's program to combat counterfeits in his talk, *Enhancing the Security of the Supply Chain*.

Novartis, like Amgen, has been a target in recent years. Payne echoed the widely known fact that the source of counterfeits originate outside the United States and Europe.

Payne warned against developing a false sense of security when using high-tech tracking systems—these do not ensure that product is highly secure. For one, counterfeits often travel in alternative, non-legitimate distribution channels. When the tracking systems do work, they are really tracking the packaging, not the product. With repackaging often outsourced, counterfeiters have access to genuine packaging anyway.

Payne discussed two cases that demonstrated how far ahead of pharmaceutical companies the counterfeiters are. In one case, counterfeiters had a false product on the market prior to its official launch by Novartis. In another example, the firm found holograms--favored by firms because they are easy to recognize and hard to produce--on packages of counterfeit products, even though Novartis has not made a decision to use them yet. The hologram was so convincing, Payne explained, it even read *protected against counterfeits.*

As such, Payne expressed concern that industry would be forced to adopt a high tech solution that was ineffective, and in turn, the regulatory officials would "declare victory and go home."

Instead, the battle against counterfeiters needs to be comprehensive that includes stronger laws and enforcement, media cooperation, intelligence and education and training—all elements of the Novartis

anti-counterfeiting program that Payne presented **(see box below)**.

Payne advised other companies to adopt a strong anti-counterfeiting program like Novartis's, because the regulatory and enforcement systems aren't capable, yet, of stopping the problem and the fallout almost always will almost always impact the pharmaceutical companies the heaviest.

"Pharmaceutical counterfeiting will be a serious and growing problem for the foreseeable future. It is an attractive criminal enterprise which even legitimate distributors sometimes dabble in, and enforcement is usually lax. The vast majority of cases resulting in judicial action are the result efforts by the industry, with authorities arriving on the scene just before the news media.

"Despite claims to the contrary, there is no 'solution' on the horizon, and although we give up control of our products early in the distribution chain, any problems (counterfeit, expired, adulterated products) will always be our problem, never McKesson's, Phoenix's, or Walmart's. Regulatory pressure will continue to build as political concerns grow, and we can anticipate possibly being forced to make investments in technologies that are not in the industry's best interest."

Novartis's Anti-Counterfeiting Program

- **Internal and External Education and Training**
- **Intelligence Collection/Early Warning System**
- **Investigations and Judicial Support**
- **Tracking of product**
- **Improved transportation security**
- **Lobbying for stricter/more effective laws and additional enforcement resources**
- **Media interaction to improve understanding of their issue**
- **Technology assessments**

Quality Systems are a Weak Link

Rivera-Martinez pointed out that some of the challenges of securing the supply chain include vulnerability in quality systems, such as a lack of traceability, complexity due to increased trade activity, ingredient repackaging or multiple relabeling. Many companies don't know how drug products came to their front door or what has occurred to the drug before it arrives, and then the testing is not adequate and not specific.

To emphasize the concern, he asked the audience members to raise their hands if they would use a toothbrush found randomly without first ascertaining that it was clean and unused. Nobody raised their hand. When he asked who would use it if tests done revealed it had no microbial contamination or other contaminants, only a few people raised their hands.

"Even though the laboratory showed the toothbrush was clean and had no contaminants, people would still have some reservations about using it," Rivera-Martinez remarked, adding rhetorically, then "why do so many pharmaceutical companies insist on buying pharmaceutical ingredients on the open market without knowing where they are manufactured, whose handled those pharmaceutical ingredients and how they got to your front door? And yet, you rely on limited testing and verification by your laboratory to approve the use of these pharmaceutical ingredients for forming your new drug products. Aren't you taking the same type of risk?"

At the Agency, Rivera-Martinez said, there is a feeling that manufacturers rely too heavily on certificates of analysis (CoAs). One problem with this, the original manufacturer's CoA is not always obtained, and even when it is, it is often altered in a way as to remove the true identity of the manufacturer. "Often times we see reported test results are either unreliable or actually falsified."

Some companies also depend on the regulators to serve as an extension of their QC programs. Rivera-Martinez has seen cases where companies list every possible vendor that they might do business with in their application, from contract drug and API manufacturers and their alternates to testing laboratories and their altrenates. "We will often times see 10-12 establishments listed in an application. Then when we go out to do an inspection, it turns out that none of these sights have been audited by the sponsor."

Other "vulnerabilities" include supplier qualification programs, quality agreements and life cycle monitoring are often times found to be deficient. **[Editor's Note:** For a discussion on the role quality agreements can play in supply chain security from the *2009 PDA/FDA Joint Regulatory Conference*, see related article on page 19.**]**

Regulations Catching Up

Governments recognize they have a problem and that current law and regulation is not capable of addressing the problems. Rivera-Martinez spent a portion of his talk reviewing new initiatives already in place and coming down the pike to improve the legal basis for countering the criminals in the United States. He reminded the audience that, though not specific to APIs, the GMPs to apply to pharmaceutical "components." In 2007, FDA published the guidance, *Testing of Glycerin for Diethylene Glycol* to counter that persistent problem.

The draft Dingell, Pallone and Stupack Bill of 2008, if passed, "will provide for significant changes in current systems and FDA resources," Rivera-Martinez noted, including funding for increased inspections, mandatory country of origin labeling for APIs, and the creation of strong new enforcement tools.

Supply pedigrees need to be stronger and should document each sale or transaction

Supply Chain Transparency is Necessary for Ensuring Safety

- **A chain is as strong as the weakest link**
- **Each link in the chain must add value**
- **Verification and positive checks are required**
- **Information must be true**
- **Data results must be real**

Complex supply chains can become insecure when unscrupulous businesses take advantage

A slide from Edwin Rivera-Martinez's presentation

of the product: *Who* had the product, *when* they had the product, *how long* they had the product, *who* they bought it from, *who* they sold it to and any other pertinent information. Ideally, these pedigrees would be electronic.

Rivera-Martinez said that he hoped industry members in the years and months ahead, would be "motivated" to help ensure the integrity of the pharmaceutical supply chain. "With your participation and assistance, together, we can create the catalyst to change the world."

Collaborate with PDA and FDA on Supply Chain Solutions

PDA/FDA Pharmaceutical Supply Chain Workshop • Bethesda, Md. • April 26-28 • www.pda.org/supplychain2010

Co-chairs Edwin Rivera-Martinez, U.S. FDA and Barbara Allen, Eli Lilly

A reliable supply of high quality, safe and effective drug products depends on having appropriate control over the sourcing of pharmaceutical ingredients, manufacturing operations and the distribution of medicines to patients. To assure drug quality and safety, manufacturers should aim to acquire as much knowledge as possible about the manufacturing and distribution practices in their supply chains. Recent experiences in the market indicate the need for improvements in supply chain practices, prompting a surge in activity toward enhanced globally harmonized supply chain controls.

Regulators and members of industry need to act in concert to identify and implement improved practices that will ultimately secure the drug supply chain and assure patients receive safe and high quality medicines. Legislators are also considering bills containing measures to address counterfeiting and diversion.

On behalf of the Program Planning Committee, we would like to invite you to attend the *2010 PDA/FDA Pharmaceutical Supply Chain Workshop*, to be held April 26-28 in North Bethesda, Md. Through a series of plenary sessions and working group breakout sessions, the program will provide participants the opportunity to:

- Hear from senior FDA personnel on current regulatory environment/ situation
- Share improvements in programs and technology
- Identify any barriers and associated actions to enable implementation of effective solutions

The workshop will focus on solutions to mitigate risk to product quality in the pharmaceutical supply chain. Personnel from quality, supply chain and technical functions with experience in this area will find this level of direct information exchange with members of industry and regulatory agencies useful in improving their specific programs and addressing general supply chain problems. Members of the supply chain, including those that can provide technical solutions will also benefit from attending the workshop.

Barbara and I sincerely hope that you will join us for this historic supply chain workshop. This topic has been widely discussed in several forums in the last two years and many organizations are individually trying to address the problems. It's time for academia, industry and regulators to come together to find and implement solutions—to answer the collective call for urgent action to ensure the safety and integrity of pharmaceutical ingredients and drug products that was echoed at the September 2008 PDA/ FDA Supply Chain Conference in Washington, D.C.

Strong Quality Agreements: Another Tool for Securing Supplies

A session at the *2009 PDA/FDA Joint Regulatory Conference* addressed the central role quality agreements can play in firming up the reliability of drug product supplies. Session speaker **Barbara Zink**, President, Zink Consulting, provided a review of this session in the November/December 2009 *PDA Letter*. Below is a transcript of the dialogue that took place following the three session presentations. Joining Zink in the discussion were speakers **John Eltermann**, Director, Division of Manufacturing and Product Quality, CBER, FDA; **Jamie Shirey**, Director/Team Leader of Contract Operations Quality Assurance, Pfizer; and session Moderator **Martyn Becker**, Managing Director, Martyn Becker Associates. The questioners are unidentified, save for **David Schoneker**, Director of Global Regulatory Affairs, Colorcon, who also represents IPEC-Americas.

Question: In my experience, I found that these are agreements that senior or top level production or quality folks are aware of, but sometimes the rank and file staff are not fully cognizant of actions they may need or not need to take if a situation develops.

Zink: The ideal situation is to inform them about the quality agreement, go through it, let them know, but then take any aspect that are not currently in the SOP and then put them in the SOP. I kind of liken it to the GMPs: We train all our employees on the GMPs but I don't expect the employees who are working down at the bench to have the GMPs open in front of them. They need to have their SOPs in front of them. They are aware of the GMPs, and then the GMPs need to be put into the SOP. Same with the quality agreement—to be aware of the quality agreement, and then any of the aspects from the quality agreement should then be put into the SOPs, because if they are compliant with the SOP then they would be compliant with the quality agreement.

Shirey: I agree with what you are saying. I think the reality of it is, most companies aren't willing to put into procedure a lot of things that are in the quality agreement, because they are concerned that they might not comply with it all of the time. So I think pragmatically, the way that I look at it, that is the reality. [It starts with] the highest level management in the company, that is true. One thing that is important to do, we actually do a quality review meeting before we start… It usually involves the lower management level people who are actually doing the work—somebody who is managing complaints and the QA manager—so we actually have that discussion of expectations… You just need to establish the relationships to ensure that it happens, and hopefully they are aligned with the procedures.

Question: What frequency is recommended for on-site oversight at contract manufacturers? Every batch? Every x-number of batches? Every quarter?

Eltermann: That is an interesting question. I don't really have a frequency in mind, but I think like everything else, as you are starting a relationship, you would probably start more frequently and as you have a level of comfort, perhaps back off. I think the thing is true the other way. I mentioned a couple of examples where it wasn't until the applicant QA actually found problems by the contractor, and in situations like that, we want you to ramp it up and be a little more frequent.

So I don't have a real recommendation, but I think it is based on not only your level of comfort, but I think from the feedback you get early on really will dictate how frequently you need to monitor. But it also depends on what you are doing with it. If you are talking about your critical step, you are talking about viral inactivation or if you are talking about aseptic processing, that may take precedent. You might want to look at it more frequently than something else. Just a general comment there, but there aren't any specified timeframes.

Question: While realizing quality agreement with contract manufacturers is not only a regulatory requirement, it makes a lot of business sense. So we started to apply this requirement to other suppliers, but then we ran into situations where those suppliers would refuse to sign a quality agreement. They indicate that we are too small volume business or it is against corporate policy to sign a quality agreement. So in that situation, how do we handle or mange these suppliers?

Eltermann: You know that is always a difficult situation. From my perspective, it would depend on how critical that particular aspect of it is. If that is something that you really need the assurance either from knowing the compliance history or knowing if they are manufacturing according to GMPs and that is a critical aspect for you, you may need to walk away. If it is something that is less critical, the impact isn't going to be as great if something goes awry, you may have a little more flexibility there.

Becker: Bear in mind that as the manufacturer, you are responsible for the quality of your product. So you have to make your own judgment.

Shirey: I would add this from a practical standpoint: I recognize the limitations, and I think everyone understands that the pharmaceutical industry's position with some excipient suppliers… The first question I'd ask is, what is your program? Talk about 2020, what is the vision? We cannot repeat the events of the past, so we need to improve in the area of supply chain security. Each firm should develop a position, the industry for that matter, on where we think we need to be with oversight and develop risk-based approaches for doing that. We certainly don't have the resources to do everything everywhere. You need to focus—I agree—on where the risks are, and it may be that it is about the critical material of your process and they are not willing to sign something, you need to find another source, or you need to work your way around that. Doesn't have to be a 20-page quality agreement; it just may be simple quality terms, such as

notifications of changes. If they change a site, you need to know. Cannot let them just go operate however they want to. What is your firm's position on suppliers and how would you apply that? If it risk-based, that would help dictate to you in advance where you'd want to go.

Question: Do you recommend legal liability language in a quality agreement like a supplier agreement?

Zink: No, not at all. It is really like one paragraph. It is not really full-blown like it would be on a supply agreement. If there is any kind of overriding business decisions or anything like that, refer back to the supplier agreement on a technical agreement.

Question: How does Pfizer manage supplier oversight in cases when the DMF is closed regarding who you contract to supply you?

Shirey: First I will preference by saying I am not an expert in API. I have the Americas and there are not that many API manufacturers in the Americas anymore for anything. I know that is a problem… If you can leverage the situation to get that open or get it to the point where you have visibility to prior steps where prior materials are coming from. It is difficult for everybody, but you need to figure out a way to do that.

Schoneker: I just wanted to speak a little bit to the last two points that were made. One of the problems that we see at IPEC with getting agreements, especially with small suppliers, is the standardization piece. Excipient suppliers might be dealing with a thousand different users that all have their own agreement that they want to have taken care of. Many times [the company is selling small amounts to the customer.] The key, that you came up with, really the only way to make that happen is to standardize and get everybody to agree that you cannot have everything your way all of time. A good compromise based on good science that covers the key factors, like you were mentioning, is a way to success so that an excipient company or other type of smaller supplier can standardize what they are going to do and not have to put a lot effort into it.

Right with that is to your point Barbara, the legal liability piece. I think what we find many times is that people try to build in as much legal stuff into the quality agreement… That is one of the biggest reasons why you don't get an agreement, because if companies have to go back and forth with their lawyers to get a quality agreement in place, it is not about the business issues, that is why they back away. If as you mentioned, you can separate and just have a very minor legal piece that connects it to the supply agreement, let the business guys and lawyers play for years and years, but the quality people can get it done and get it done quickly and easily. That is the key, to try and get this done quickly. If you don't compromise that way, you are never going to have those agreements in place. And in today's world you really have to have them.

Question: What is FDA's viewpoint as it relates to supplier qualification when the API is provided by the licensed company? Should the contract manufacturer consider the license holder as a supplier when they are the actual manufacturer of the API, or would supplier qualification apply at all?

Eltermann: I think that might be one of the situations that depends on how you've written the agreement. Sounds like it is going from an API to a dosage form. In a situation like that, I can see it working either way considering the applicant ultimately is going to be responsible for that. However you as the contractor need to have enough information to be able to manufacture that according to GMP. I think there has to be a balance there… I can imagine a number of different scenarios coming up where I might have one answer versus another, just depending on the nature of the products.

Question: Please comment on the major differences of quality agreements for clinical suppliers of commercial products.

Shirey: Well to answer the first question, actually I think looking at my [clinical] Phase 3 supplies that I'm more familiar with, there is probably very little difference in all reality. A lot of the terms are similar. As I mentioned from the standpoint of stability, if you have a lot of shorter stability studies going on in R&D, you obviously want them tested sooner then you may for a commercial product that is older. From a GMP perspective, there are some minor differences, and validation is another area. Core GMP type things are very similar. My experience is more with Phase 3 and more commercial clinical supplies than they are early on.

Question: Quality Agreement for contract laboratories: Is it acceptable to release batches by the applicant based on CoA from a contractor, or would a review of raw data by the applicant be expected?

Zink: [Review the CoA and the raw data in detail for the first 5-10 batches.] Get a really good assurance that the contract manufacturer or the contract testing laboratory really knows what they are doing… and understands the GMPs, and then we back off and maybe just look at the QC results along with the batch record, but not actually go back to the raw data itself. And then, maybe on an annual basis, come in and do another detailed review of one or more batches.

Shirey: Overarching for all contract test labs, I would put a risk-based approach to it. I think it makes sense to understand what services they are providing, whether it is a contract sterilizer or something a little simpler. Once again, you need to demonstrate that you have good oversight from a quality perspective, but I don't know too many firms that are resourced to do everything for every service and every contractor.

Global Supply Chain Quality Problems — What Next?

Helena Champion, Ms, Mba, Drug Quality Assurance

Adulterated and defective products have made headlines in recent years, regarding contaminated heparin in drugs causing deaths, recalls of medical devices containing contaminated heparin, melamine in pet food and milk products, to name a few. Medical device companies have had problems with contractors not meeting specifications, sometimes with disastrous consequences to patients. The globalization ideal of lowering costs by sourcing materials and services from countries with low labor rates has turned out to have quality and safety risks which take a great deal of effort and expense to mitigate.

The observer may well ask – what next? Updated heparin standards, such as those in the United States Pharmacopeia effective October 1, 2009, should ensure detection of heparin contamination but that is only the tip of the iceberg. "What next" is a question that we have to explore proactively, to ensure all our products are safe and effective. We need to perform risk analysis to determine which components in our supply chain are at risk, and control risk as much as possible, to prevent problems.

The FDA has just published a cGMP Guidance "Pharmaceutical Components at Risk for Melamine Contamination," August 2009. Although melamine has not yet been found in the U.S. in drugs or components, the risk of melamine contamination does extend to materials used for drugs and the melamine Guidance requires that all drug product manufacturers determine whether the components they use are at-risk for melamine contamination and if they are at-risk, it recommends testing them for melamine before use. The components considered by the FDA to be at-risk for melamine contamination include commonly used materials such as albumin, ammonium salts, calcium pantothenate, caseinate, copovidone, crospovidone, gelatin, guar gum, lactose and povidone and others. They state that manufacturers need to know and monitor their supply chain for any at-risk components, and they need to know the identity and role of the actual manufacturer of such components and any repackers and distributors who handle the components before receipt by the manufacturer. Manufacturers should obtain certification from the manufacturer of at-risk components that these components are tested for the absence of melamine contamination as well as audit their component suppliers to ensure CGMP compliance.

In response to problems and increased trade in excipients and drug substances with China and India, the U.S. Food and Drug Administration has set up offices in those countries to facilitate FDA inspections and to help their authorities improve their regulatory capacity. While this is helpful, inspections only occur periodically and may not cover a particular company's product, so the onus will still be on the sponsor company to carefully qualify and audit all suppliers and regularly review their quality performance as well as their upstream supply chain.

The FDA is actively addressing the situation in other ways. In January 2009 a Draft Good Importer Practices Guidance, relating to consumer products in general, was published by the FDA and other Federal agencies, including the Departments of Homeland Security, Agriculture, Commerce, Transportation, the U.S. Consumer Product Safety Commission, U.S. Environmental Protection Agency and the Office of the United States Trade Representative. This Draft Guidance recommends that companies establish a well resourced Product Safety Management Program and emphasizes that corporate responsibility for product safety should start at the very top of the organization. The Product Safety Management Program recommended comprises many responsibilities already required for drugs and medical devices and the FDA recommends that a company use a system for communication and information that allows the sharing of relevant information on safety and compliance not only internally, but also with third parties and federal, state, and local authorities.

An international pharmaceutical supply chain consortium called Rx 360 is being developed by volunteers from the pharmaceutical and biotech industry and their suppliers, with the intention of improving the performance of supply chains and sharing supplier audits and sharing information on safety problems in the supply chain. Rx 360 should be a good resource for sharing information with third parties in the drug and device industries and this is one of its objectives.

The security of finished drug product supply chains and prevention of counterfeiting is also a challenge and the January 2009 Draft Guidance "Standards for Securing the Drug Supply Chain - Standardized Numerical Identification for Prescription Drug Packages" is an example of efforts by the FDA to address this.

There are numerous conferences and workshops this year on supply chain quality and the issue will grow in importance. Ensuring the safety of your supply chain is a challenge and will need close coordination between purchasing, operations and quality to successfully qualify and monitor suppliers and distributors. Considering the high stakes in terms of patient safety, company reputation and the enormous direct and indirect costs of product recalls, companies need to know much more about their supply chains and control them even more actively than before, to avoid problems.

Quality & Regulatory Snapshot

Meet Hee-Young "Hailey" Park—Our New Intern

Hailey Park, PDA

[**Editor's Note:** The following was written by Hee-Young "Hailey" Park, Korea Food & Drug Administration, who is interning at PDA as part of her Long-Term Fellowship Program for Overseas Study sponsored by the Government of Korea. She will be contributing to the *PDA Letter* for the duration of her internship.]

I am pleased to meet all of you through the *PDA Letter*. My name is **Hee-Young Park** from Korea Food & Drug Administration (KFDA). And some of you might remember me with the English name, Hailey. I became a new family member of PDA at its Bethesda location in December of 2009. I would like to tell you my story.

I have worked for KFDA since the summer of 2002, beginning with reviewing "me too" drug applications at the Gyeongin Regional office at Incheon, west of 17.4 miles from the Korean capital Seoul.

When I graduated from the school of pharmacy at the Kangwon National University with a Bachelor degree, I did not know much about pharmaceutical regulatory work. Most of the classes I had taken in the university were focused on the knowledge used for developing a new molecular entity rather than on the regulatory process required to place it as a new drug on a market.

I am here to learn how to establish a sound and reasonable regulatory system as a government employee

My first job was a pharmacist at a drug store in my small hometown. Except for a few days per week, I spent more time to waiting for patient orders than actually taking care of them. I spent hours reading drug insert papers. I began to wonder who wrote these labels and how they knew what to write on them.

In 2002, as luck would have it, KFDA, which was only four years old, needed to recruit more employees as their work increased. I happened to read the KFDA job advertisement. Although I did not understand exactly what I was going to do in this job, I felt it might give me an answer to my question. So, I decided to apply and dive into new world. I got the job!

After four years at the Gyeongin Regional office, I moved to the Biopharmaceuticals Bureau at the headquarters in Seoul. I was at the department in charge of new drug approvals and regular GMP inspections. The headquarter offices at KFDA are responsible for establishing policies and regulations and enforcing them. The six regional offices share parts of that function. However, the biopharmaceuticals affairs are only performed by the headquarters. Even though the regulatory field is similar to conventional drugs in a large view, some typical areas of each biopharmaceutical products looked strange to me at first but were also really interesting.

Working at the Biopharmaceuticals Bureau gave me a chance to look outside; whereas conventional drugs were predominantly manufactured by local companies, almost all of the biopharmaceutical products on the Korean market are imported from overseas. So, I had many opportunities to read foreign health authorities regulations/guidelines, inspect overseas manufacturing sites and study international industrial standards. This experience caused me to consider seeking new experiences in the foreign pharmaceutical industry.

Fortunately, the Korea Government runs various training programs for its employees. One of them, the Korean Government Long-Term Fellowship Program for Overseas Study, is aimed at developing the careers of young middle management officials by sending them abroad for a maximum of two-years for study. The KFDA sends about three

staff members annually through this program. I applied for it and luckily, I won.

My plan was to go to a school for one year and spend another year at a company in the United States. I arrived in the San Francisco bay area on December 2008. I had already known about the Bay area's reputation as a cluster for the biopharmaceutical industry. I wanted to pursue the Clinical Trials Design and Management certificate program provided by the University of California, Santa Cruz (UCSC). Their classes were qualified and practical, taught by experienced experts from the bay area and oriented to pharmaceutical regulatory affairs. These classes helped supplement my knowledge from my previous work.

After one year in California, I moved to Maryland this past December to begin an internship at PDA. All I knew about PDA at first was what I had found out when I was involved in GMP inspections. PDA has great expertise with parenteral products, which is a typical dosage form of a biopharmaceutical product. As I did not have any experiences in manufacturing drugs, PDA's technical reports and others publications helped me to understand the key issues. I was also interested how PDA made those documents itself, because I thought that they were very similar to a guideline or regulation of a government in terms of gathering experts' knowledge on sound scientific bases into an organized document. As much as I studied about clinical research at UCSC, I wanted to devote another year to learn about GMP compliances. As far as I could tell, PDA was the very place for my training.

I had not met anyone who worked at PDA's headquarter before, but I contacted Senior Vice President Dr. Richard Levy on the advice of Dr. Woo-Hyun Paik, the leader of the PDA Korea Chapter. Even though Dr. Levy did not know me, he considered my proposal positively and invited me to PDA. As PDA had not had any interns from the KFDA, and I had not worked in industry, Rich, my supervisor, and I developed a step-by-step program together, sharpening the intent of my training and discussing timeframes and content. We designed the internship to continue for a year from late December of 2009 to December of this year, as it would be good to go through an entire year of working at PDA.

As soon as I arrived at PDA, I joined the holiday party where we enjoyed bowling together. Even though I am poor at bowling (but not much worse than the *PDA Letter* Editors), it was a nice ice breaker. At the moment finishing the game, I felt like I was already one of PDA staff members.

I am here to learn how to establish a sound and reasonable regulatory system as a government employee. I know the system might be accomplished only over the mutual relationships of people who are working there. Therefore, I would like to have a chance to meet many members of industry as often as I can. In the coming year, you can see me at courses at PDA's Training and Research Institute or through articles which introduce more about the KFDA and my home country of Korea.

And I hope I can see all of you at PDA's annual meeting soon.

Harmonization *Report*

Official ICH Training for Q8, Q9 & Q10 in Europe

Integrated Implementation Training Workshop

- **June 2-4 • Tallinn, Estonia**
- **www.ispe.org/2010ICHworkshops**

Jim Lyda, PDA

Training endorsed by the International Conference on Harmonisation (ICH) endorsed training on integrated implementation of the ICH Q8, Q9 and Q10 guidelines will kick off on June 2-4 in Tallinn, Estonia. The training, cosponsored by PDA and ISPE is presented by members of the ICH Quality Implementation Working Group (Q-IWG), which consist of industry and regulator experts from the three ICH regions—USA, Europe and Japan—and also observers from Canada and Switzerland (EFTA countries) and WHO. The training will use a presentation and workshop format including a full day discussion with Q-IWG members. It is designed for all persons, regulator and industry, who have an interest in, or responsibility for, the integrated implementation of these guidelines. On the regulator side, the workshops should be valuable to assessors and GMP inspectors. The USA and Japan training workshops will be held in Washington, DC, October 6-8 and in Tokyo, October 25-27.

The workshops have been designed under the guidance of the ICH Q-IWG, and many of the faculty will be regulator and industry experts serving on the Q-IWG. Additional instructors will be industry and regulator experts involved in development of the actual ICH Q8, Q9 & Q10 guidances. **Jean-Louis Robert**, the Rapporteur/Chairman for ICH Q-IWG, is serving as the Chairman of the Faculty for the workshops.

Attendees will receive training on the integrated implementation of Q8, Q9 & Q10 and how they apply along the product life cycle. In addition to technical development and manufacturing details, the workshops will provide comprehensive information on regulatory aspects including regulator expectations, dossier preparation, assessment and GMP-inspections. Workshop features include:

- How Q8, Q9 & Q10 can benefit pharmaceutical development, manufacturing, regulatory assessment, scale up to commercial operations and GMP-inspection
- A case study on opportunities for combined implementation of Q8, Q9, Q10 in specific quality systems

continued on page 25

ICH

ISPE

PDA
Parenteral Drug Association

The ICH Quality Implementation Working Group (Q-IWG) Presents

Integrated Implementation Training Workshops for ICH Q8, Q9 & Q10

- Official ICH training
- For both regulators and industry
- Expert instructors from Q-IWG and authors of Q8, Q9 & Q10

2-4 June 2010
Tallinn, Estonia

Workshop

See the complete program at:
www.pda.org/europe – www.ispe.org

Register by 6 April 2010 and SAVE!

You are invited...

On behalf of the ICH Quality Implementation Working Group (Q-IWG) you are invited to attend a special training opportunity regarding the future of pharmaceutical development, manufacturing and quality. This workshop will provide comprehensive training on the integrated implementation of ICH Guidelines Q8, Q9 & Q10, and how they apply to drug (medicinal) products and related operations. In addition to technical development, manufacturing details, and pharmaceutical quality systems, this workshop will provide comprehensive information on regulatory aspects including regulatory expectations, dossier preparation, assessment and GMP-inspections. The instructors for the worshop will be members of the Q-IWG and authors of the ICH guidelines.

Please consider joining the Q-IWG for the Europe region training, the first of a series of three worldwide workshops, to be held in Tallinn, Estonia, 2-4 June.

I hope to see you there.
With very best regards,

Jean-Louis Robert
Rapporteur of the ICH Q-IWG & Chairman of the Faculty

Harmonization Report, continued from page 23

The workshops have been designed under the guidance of the ICH Quality Implementation Working Group, and many of the faculty will be regulator and industry experts serving on the Q-IWG

and operations

- Discussions among industry and regulators on solutions to implementation challenges
- Smaller breakout sessions for industy people in development and manufacturing as well as for regulators in assessment and inspections to explore possibilities over the product life cycle

Feedback from the workshops will be used by the Q-IWG to further facilitate the harmonized implementation of ICH Q8, Q9 & Q10 and included in the official Q&A (www.ich.org/LOB/media/MEDIA5783.pdf). The final workshop materials and outcomes will be summarized by regulators and industry from the ICH regions and made available to other regions as well. The workshop materials will be suitable for further internal training by industry and regulators.

For more information on the Europe region workshop, "Integrated Implementation Training Workshops for ICH Q8, Q9 and Q10," visit www.pda.org/europe or www.ispe.org/2010ICHworkshops.

ICH guidances on Pharmaceutical Development (Q8), Quality Risk Management, including the Q9 briefing pack (Q9) and Pharmaceutical Quality System (Q10) are available at www.ich.org.

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

Collection of Information on Postmarket Surveillance Activities for Medical Devices

Through the *Federal Register*, the U.S. FDA has announced a collection of information relative to postmarket surveillance activities for medical devices. The notice references the appropriate sections of the regulations and provides the Agency's estimate of the burden on the industry to comply with the reporting requirements.

If anyone desires to comment on the collection of information, comments are due by April 6, 2010.

Guidance to Assist Industry When Submitting Product Information

A guidance entitled, *Contents of a Complete Submission for the Evaluation of Proprietary Names* is now available. This guidance is intended to promote the prevention of medication errors. It will assist industry in the submission of complete product information; this will help the U.S. FDA evaluate the safety of proposed proprietary drug and biological product names by taking into account factors that can contribute to medication errors.

Agency Guidance to Help with Mechanical Calibration of Dissolution Apparatus 1 and 2

The Use of Mechanical Calibration of Dissolution Apparatus 1 and 2 – Current Good Manufacturing Practice (CGMP) guidance has been released by the U.S. FDA.

The guidance recommends an alternative method for manufacturers to comply with FDA's CGMP regulations that require laboratory apparatuses to be calibrated at suitable intervals in accordance with established written specifications. It is intended to aid drug manufacturers (including ancillary testing laboratories) in calibrating USP Dissolution Apparatus 1 (basket apparatus) and 2 (paddle apparatus) to help assure that critical parameters associated with the dissolution apparatus meet certain mechanical calibration tolerances.

Comments Needed For the Assessment of Abuse Potential of Drugs

The U.S. FDA has released a draft guidance entitled, *Assessment of Abuse Potential of Drugs*. It is intended to assist sponsors who are developing drug and other medical products with the potential for abuse that may need to be scheduled under the Controlled Substances Act.

Comments should be submitted by March 29, 2010 as FDA develops a final guidance on the subject.

Europe

Consultation Paper Proposals to Boost MHRA Authority Against Counterfeiters

The MHRA has published for consultation a proposal to better control the movement of medicines throughout the *legitimate* supply chain. Some of the provisions of the document provide for:

- An applicant for a Wholesale Dealer's license demonstrate that he/she is a "fit and proper person" to undertake such a role, with minimum requirements to be set out in guidance
- A disclosure is made by applicants of relevant criminal records
- Enabling the MHRA to decline a Wholesale Dealer's license if an applicant discloses a relevant criminal conviction
- Introduction of a "due diligence" obligation into the legislation, with a requirement to notify the MHRA of suspicious events

The consultation deadline for responses is March 12.

Key Regulatory Dates

Comments Due:

March 12
MHRA Consultation proposal on supply chain movement

March 29
U.S. FDA Assessment of Abuse Potential of Drugs

April 6
U.S. FDA Collection of Information relative to postmarket surveillance activities for medical devices

April 30
The European Medicines Agency Road Map Initiative on its strategic development of the agency

European Medicines Agency Requests Comment on Road Map Initiative

The European Medicines Agency has published a draft paper outlining its vision for the strategic development of the Agency for five years to 2015.

Building on the previous strategy paper of 2010, this paper, called The European Medicines Agency Road Map to 2015: The Agency's Contribution to Science, Medicines, Health, chart's the future direction of the Agency through developments in medical science and pharmaceutical research. It also looks at the evolution of the European and international regulatory environments.

Comments should be sent using the Agency's comments form by April 30, 2010 to roadmap@ema.europa.eu.

Parenteral Drug Association Training and Research Institute (PDA TRI)

2010 ASEPTIC PROCESSING TRAINING PROGRAM

2010 SCHEDULE:

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

Session 2:
Wee[SOLD OUT!]16
Week [illegible] April 19-23

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

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

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

The most comprehensive program in the preparation of sterile parenteral products

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

BENEFITS OF ATTENDING:

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

LEARNING OBJECTIVES:

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

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

FOR MORE INFORMATION CONTACT:

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

LOCATION:

PDA Training and Research Institute
4350 East West Highway, Suite 150, Bethesda, MD 20814
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Deadly Sins That Stunt Organic Growth

If you're like most business-to-business suppliers, you're probably making certain predictable mistakes that can greatly impact your ability to compete. Avoiding those mistakes can help you survive and thrive in a tough economy.

Dan Adams

You already know that organic growth makes for a stronger company. In today's tough economy, it just makes sense to grow from within by developing outstanding products and services that win over new customers and keep current ones coming back. (The alternatives are to grow via debt financing or an army of flush-with-cash buyers on a spending spree—and clearly, neither is easy to come by these days!) Problem is, your competitors are playing by the same rules. But you can outwit them… simply by putting a halt to the mistakes you (and they) are making right now.

Unless your company has smarter employees, some inherent unassailable advantage or a markedly different approach to satisfying customers, those competitors always seem to throttle your growth. But what if you and your competitors were committing some serious mistakes that stunt organic growth—and you corrected them? Wouldn't that be enough to propel you to the front of the line?

It makes sense. And I should know: I have spent my career helping some of the largest business-to-business (B2B) companies in the world overcome the obstacles that clog up their organic growth engines—the ability to develop new "stuff" that customers want to buy. In 20 years the common mistakes B2B companies make will be as glaring as trying to improve quality with inspectors rather than statistics. Correct them now, and you'll enjoy a substantial head start on years of healthy organic growth.

Here are the seven deadly sins that too many B2B companies commit:

1 Imagining Customers' Needs in Your Conference Rooms

Does your new product process begin with the word "idea," perhaps with a light bulb next to it? So whose idea is it: Yours or your customers? Unfortunately most suppliers start with their solution "validating" it by showing it to some customers and measuring market needs by watching sales results… after the product launch!

Companies should invert this process: Begin with customer needs and end with supplier solutions. While doing things in the wrong order may "feel" better to you, it is far less likely to result in sales and customer satisfaction. Besides, intelligent B2B customers can detect your "validation" a mile away. They correctly sense you are more interested in your idea than in them… and that doesn't do much for the long-term relationships you need to build.

2 Relying On Sales Reps to Capture Customer Needs

A salesperson is unlikely to uncover a full set of market needs if he is A) rewarded for near-term selling, B) unable to reach true decision makers or C) not calling on most of the customers in your target market segment. But put a good salesperson on a team with marketing and technical colleagues trained in advanced B2B interviewing methods and you'll run circles around your competitors.

Be wary of voice-of-the-customer (VOC) consultants who want to exclude your sales force from interviews because "they can sell but not listen." In the long run, your company will fall behind competitors that have taken steps to develop a team of engaged and enlightened salespeople.

3 Counting On Just a Few VOC Experts

Some companies rely on a handful of internal VOC experts to interview customers. You'll do far better training a critical mass of employees—who routinely interact with customers—to gather customer needs. Keep your VOC experts as coaches and trainers, but implement "VOC for the masses." You'll overwhelm competitors by turning a trickle of customer feedback into a torrent.

4 Using Hand-Me-Down Consumer Goods Methods

Traditional VOC methods rely on questionnaires, tape recorders and post-interview analyses. That's fine for consumer goods, but your B2B customers are insightful, rational, interested and fewer in number. They're smart and will make you smarter if you engage them in a peer-to-peer dialogue. Use a digital projector, let them lead you to their areas of interest, probe with skill and you'll be shocked at how much you'll learn you never knew.

5 Gathering Only Qualitative Customer Feedback

I once had a new client who came to me extremely frustrated. He had spent months interviewing customers, only to hear his boss say, "Nah, I don't think they want that; they want this." Unfortunately, interviewers often hear want they want to

hear… and then parade some customer quotes for support.

What you need is quantitative data, which measures customer importance and satisfaction on key outcomes. Skip quantification and your new product will be based on assumptions, bias and wishful thinking.

6 Listening Only to Immediate Customers

Unlike business-to-customer (B2C) producers, your product might be part of your customers' products, your customers' customers' products and so on. It's a mistake to interview only your direct customers, because they are usually unable or unwilling to disclose downstream customers' deepest needs. Also, B2C producers assign "one vote" per consumer… while you need to weight the buying power and value chain position of downstream customers.

7 Ignoring Competitors When You Design Your Product

I find most product development processes are far too casual—and late—in assessing competitive offerings. Your new product makes a lot of money only if two conditions are satisfied: A) it offers significant value to customers and B) customers cannot get this value elsewhere. Interviews tell you only about condition A. You need side-by-side testing to learn about condition B. This allows you to attack competitive weak spots, avoid getting blind-sided and optimize pricing.

So why is it so important to focus so intensely upon customer needs? Consider three points: First, the average new product success rate is only one in four. Over 30 years of research says the number one reason is inadequate market understanding.

Second, the "how" continues to get easier than the "what." You have twin goals of understanding what your customers want and then how to satisfy them with your solutions. In these days of open innovation and global access to technology, the "how" is easier than it's ever been… if you have a solid grasp of the "what."

Finally, you reap benefits beyond good product design when you use respectful peer-to-peer interviews. You engage customers in the design process, which primes them to buy your product later.

Our clients often enjoy benefits well before product launch. Their interviews cast them as caring, competent suppliers, so they have a better shot at other near-term business.

Never forget that relationship building is everything. We're living in an age where anyone, anywhere on the globe, at any time can start a business that competes with yours. By engaging customers in a respectful peer-to-peer dialogue and genuinely soliciting their ideas, you position yourself as a valuable partner and not just a vendor—and that in and of itself is a reason to stick with you.

About the Author

Dan Adams, president of Advanced Industrial Marketing, Inc., is passionate about B2B new product development. In over 30 years working within and with major B2B corporations, he has explored every aspect of product development, building New Product Blueprinting from the ground up. He is a chemical engineer and holder of many patents and innovation awards, including a listing in the National Inventors Hall of Fame. Adams was head of strategic planning for a billion-dollar company and has extensive experience in Fortune 500 marketing, business development and leadership positions. He is an award-winning speaker and conducts workshops in every region of the world.

Adam's book, *New Product Blueprinting: The Handbook for B2B Organic Growth* (AIM Press, 2008, ISBN: 978-0-9801123-4-4, $35.00), helps clients bring clarity to the "fuzzy front end" of product development. It is available at bookstores nationwide and from major online booksellers. For more information, visit www.newproductblueprinting.com.

Send in your feedback on *Tools for Success* section.
Email Emily Hough at hough@pda.org.

PDA WCC Hosts FDA Speaker at Dinner Meeting

West Coast Chapter Secretary Kristina Nordhoff, Genentech

PDA's West Coast Chapter (WCC) hosted their final event of the 2009 Professional Dinner Meeting Series on November 12, 2009 at the lovely Oyster Point Inn overlooking the Bay in South San Francisco, Calif. **Elizabeth Leininger**, Regulatory Affairs and Quality Consultant, Elizabeth Leininger Consulting and PDA West Coast Chapter President, opened the meeting by welcoming the guests, many of whom had braved Bay Area traffic around the San Francisco 49ers football game to attend, thanking the evening's sponsor, BioVigilant Technologies, and introducing the evening's presenter, **Mark Roh**, U.S.FDA Food and Drug Director for the Pacific Region. Mark was invited to present "A Revised Vision for Effective Enforcement and Benefits to the Public Health" to the chapter members and spread the word outlined by Margaret A. Hamburg, MD, FDA Commissioner, "to prevent harm to the American people" through swift, aggressive and effective enforcement of FDA laws and regulations. He highlighted six initial steps designed to hone the effectiveness and timeliness of the FDA's regulatory and enforcement system:

- Set post-inspection deadlines.
- Take responsible steps to speed the warning letter process.
- Work more closely with FDA's regulatory partners.
- Prioritize follow-up on warning letters and other enforcement actions.
- Be prepared to take immediate action in response to public health risks.
- Develop and implement a formal warning letter "close-out" process.

Mark began his presentation with the last decade of enforcement, stating that there has been a steady decline in enforcement actions due to Administration policies, staff shortages, decrease in expertise and past emphasis on voluntary compliance. He presented chart diagrams to demonstrate the decrease in FDA seizures, injunctions, warning letters, criminal arrests, convictions and recalled products over the fiscal years 1998–2008 and indicated that 2009 experienced similar declines. Mark emphasized that FDA enforcement is important to protect public health through law enforcement, fulfill FDA's mission, meet expectations of consumers and industry, achieve corrections and promote deterrence. Some of the compliance options described were enforcement actions, such as import refusals or civil money penalties that are common to receive. Product seizures, injunctions and prosecutions occur less frequently. Mark explained the current enforcement environment and gave examples of emergent public health hazards, such as food-borne illness outbreaks that are increasing due to the way we operate in business and the worldwide supply chain. There has been an increase in the volume and complexity of regulated products and in foreign manufacturing and distribution.

He emphasized that the line between "low risk" and "high risk" may shift, as demonstrated by peanuts that were a low risk product but now high risk due to salmonella outbreaks. There has been an increase in recalls, increase in congressional oversight and a loss of consumer confidence.

Mark gave examples of how public health protection would be improved through FDA's enforcement program, such as embracing the enforcement culture, reaffirming the agency's enforcement policy, articulating enforcement as a shared responsibility throughout the Agency and emphasizing corporate responsibility, such that industry needs to be enforcing their own standards and requirements. Strong enforcement would be accomplished through regulated industry's duty to meet FDA standards and comply with the law. Effective enforcement has benefits to public health, improves public confidence in FDA oversight and product safety.

Mark Roh, the presenter for the November Dinner Meeting, delivered a comprehensive presentation on the U.S. FDA's revised vision for effective enforcement and benefits to the public health

Confidence is critical to the long-term success of industry and FDA. Mark stated that "the consumer knows that the FDA is responsible for watching over products…this will lead to the consumer having confidence in your products, use them and not complain." Mark shared results from recent surveys that indicate the consumer has more confidence in the IRS, which drew a laugh from the participants at the chapter meeting and Mark mused that "collectively we are not where we ought to be." He said that FDA must be vigilant, strategic, quick and visible so that the consumer sees what they are doing; yet remain at arm's length from industry.

The new administration is very consumer-conscious, especially in light of recent episodes such as the May 2009 recall of cosmetic water-based face paints due to adverse event reports of skin reactions in children. These items were distributed nationwide. Significant microbial contamination was indicated in most of the products. Questions the Agency should ask while investigating new products such as these are: ➤

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

PDA Europe Upcoming Workshops April/May 2010

Container Closure Systems

This workshop will give an overview of components of container closure systems and their processing in a pharmaceutical environment. Experts will present on elastomeric components, glass and plastic containers. All aspects from producing the components to their physical, chemical and pharmaceutical properties will be discussed. Quality issues and latest concepts of sterile components which can be used without further treatment at the pharmaceutical facility are presented. A session will deal with the development of container closure systems: Selection of the right components, e.g. which hardness should the stopper have and what vial or syringe type should be chosen. What are the relevant tests to be performed, which methods can be used and what documentation and reports are needed for regulatory inspection and submission.

27-28 April 2010
Berlin, Germany

Flexible Immediate Containers for Pharmaceuticals

The workshop will give an overview of flexible polymer containers which are used for pharmaceuticals. Especially containers produced by blow-fill-seal , film-form-seal and related technics will be considered.

The sessions cover the whole range from polymer selection to final product testing:

- Selection criteria for polymer containers: product, user and process requirements
- Materials and test methods: resin types, extractables, generally chemical and physical properties
- Biotech applications
- Manufacturing and process topics: machines, IPCs, Leak and integrity testing
- Current containers and their technologies
- Regulatory update
- Case studies, examples from blood and and plasma, diluents, biotech products

The focus will be on new technologies and new applications for such containers.

5-6 May 2010
Berlin, Germany

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

"What is the product? Where did it come from? What are the ingredients? Where did the ingredients come from? What is the potential for harm?" Mark cited recent action of a warning to consumers concerning promotion of products to treat H1N1. As of August 6, FDA issued 65 warning letters to offending web sites covering >125 products. There has been increased action against manufacturers of body-building supplements containing steroid ingredients.

FDA's new pathways to effective enforcement were also presented. Companies must respond to significant findings no more than 15 days post-inspection or FDA will issue a warning letter. The company's response must address all findings adequately. If not, the Agency will issue warning letters in a more timely manner and facilitate prompt corrective action. Chief counsel review of warning letters will be limited to those with "significant legal issues." There will be a streamlined review process consistent with historical practice—companies will need to fix what was found. FDA plans to work with regulatory partners to develop effective risk control models and enforcement strategies and to use local, state and international authorities for quicker action. Partners are to take immediate action while FDA develops a long-term response. FDA will prioritize enforcement follow up, such as after warning letters or major recalls and commits to follow-up within six months to take appropriate action. FDA will act swiftly and aggressively, i.e., no more multiple warning letters. One will be issued and then, if necessary, enforcement action will follow. FDA will respond to firms after they have made necessary corrections. One item that pleased the crowd was that FDA is developing a warning letter close-out process. If and when all corrections are verified, FDA will issue a "close-out letter" and post it on FDA's web page. A template is being created that will say that the company fixed the problem(s), did a good job and provided closure.

Mark indicated that for a long time FDA has been under resourced and there has been an enormous gap between investigators with less than two years experience compared to those past retirement age but still active in the Agency. FDA is adding resources and new responsibilities with funding for increased headcount in fiscal years 2010 and 2011. The Pacific region includes nine western states and will hire approximately 100 more investigators by 2011, while ORA as a whole may hire as many as 600 more investigators. Mark encouraged members of the audience to apply for a position if it was something that they would consider. Industry can expect to see new food and tobacco authorities, and there are proposals for the revision of cosmetic, drug and medical device authorities.

Overall, FDA's new vision is one of "Outcomes Versus Outputs." The agency's success would be measured by impact on public health, not by number of enforcement actions. Enforcement is not the end, but a step toward improving public health. Metrics would include a Program Performance Management Initiative known as FDA Track to measure what FDA does and link that to public health outcomes.

In summary, Mark reemphasized the key points of FDA's new vision:

- Partnerships (Embark & Enhance)
- Inspection-Verification-Enforcement-Change
- New Strategic Framework
- Focus on Prevention
- Baseline Data
- Quicker Response
- Update and Integrate FDA Policies

Industry can expect FDA to be out in the field more often, and its actions to be quicker. Mark told the audience that FDA was interested in partnering with industry to help train investigators to be more aware of new technologies and methodologies. Interested companies could work with their local PDA chapter to suggest and coordinate the partnerships.

About the Chapter

PDA's West Coast Chapter (WCC) PDA primarily serves the Northern California region, the beautiful San Francisco Bay Area and beyond. The Bay Area is considered by many to be the birthplace and cradle of the world's biotechnology industry, with a high concentration of leading bioscience companies. WCC frequently draws attendees and support from local companies such as Affymax, Allergan, Amgen, Alza, Bayer HealthCare, BioMarin Pharmaceutical, Fibrogen, Genentech, Geron, Gilead Sciences, InterMune, Ipsen, MedImmune, Novartis Pharma, Proteolix, Roche, Solstice Neurosciences and Takeda San Francisco.

WCC's goal is to have six dinner meetings each year and to alternate presentation formats from a featured speaker to a multi-panelist discussion featuring a wide selection of local industry hot topics. Dinner meetings for 2010 are scheduled for February, April, May (Symposium), July, September and November with the topic and speakers to be announced on the chapter's webpage and via email. The meetings are open to the public and are held in South San Francisco, typically the third Thursday of every other month from 6p.m.– 9:30p.m.

For additional information or to signup for future event announcements, visit the Chapter's website at www.wccpda.org or contact Kristina Nordhoff at kris@wccpda.org.

James Agalloco Headlines NEPDA Dinner Meeting

Past President of NEPDA Mark Staples, Cusp PharmaTech Consulting

The PDA New England Chapter (NEPDA) kicked off its dinner seminar schedule for 2010 with a presentation by **James Agalloco** on "USP Activities Impacting Sterilization & Sterility Assurance." Jim's update on upcoming changes to the USP sterilization chapters encompassed critical topics of interest to any professional involved with parenteral therapeutics. After registration and the social hour, a buffet dinner was followed by Jim's talk.

The January 13 meeting was well-attended with 110 registrants and nine vendor sponsors (Accugenix, Baxter Healthcare Corporation, BioVigilant Systems, GE Sensing & Inspection Technologies, Genesis Packaging Technologies, Masy Systems, Millipore, NSF/David Begg Associates and Seidenader Equipment).

The event was hosted at the Hotel Marlowe in the Kendall Square neighborhood of Cambridge, Mass, one of the highest concentrations of biotechnology and pharmaceutical companies in the world.

As a member of USP's Microbiology & Sterility Assurance Expert Committee, Jim is well-equipped to provide perspective, prospects and implications for the planned changes in the USP sterilization chapters. His presentation drew on in-process drafts currently in preparation within the committee that has substantially revised and reorganized the original USP sterilization chapters. The rationale for the changes as well as considerations of extensive industry experience were described in the context of reshaping the USP chapter structure to provide more specific and more scientifically-based guidance regarding sterilization processes. In particular, the impact on Chapters <71>*Sterility Testing* and <1211>*Sterilization & Sterility Assurance of Compendial Articles* was described.

Members are welcome to visit the NEPDA page on the PDA website to access a copy of Jim's presentation. (View http://www.pda.org/MainMenuCategory/Chapters/New-England/Presentations.aspx for a copy of his presentation.) It has been the chapter's practice for several years to archive speaker presentations at this site as a member service.

Contact Chapter President **Jerry Boudreault** (Drug Development Resources) at boudreault@ddres.com or visit the New England Chapter web page (www.pda.org/NewEngland) for Chapter details.

Volunteer Spotlights

Mihaela Simianu, PhD, Research Advisor in Manufacturing Science and Technology— Parenteral Product Network, Eli Lilly

PDA Join Date: 1997

PDA Areas of PDA Volunteerism: Midwest chapter and focus groups member; Member of the Paradigm Change in Manufacturing (PCMO) task force; Speaker and organization committee member for PDA in the USA and Europe; 2009 PDA/FDA Asia Pacific Pharmaceutical Ingredient Supply Chain Conference committee member; *2009 PDA Annual Meeting* speaker; 2008 PDA Annual Meeting speaker; *2008 PDA/FDA Pharmaceutical Ingredient Supply Chain Conference* committee member; 2007 PDA Europe/Italy Best practices in Aseptic processing committee member and speaker; 2005 PDA France- Extractables and Leachables speaker

Interesting Fact about Yourself: I am Transylvanian…a real one! I was taking the less-traveled roads or starting a new one whenever I found myself at crossroads in my professional work. I have had a very diverse work and life experience. I was born in Romania as the only daughter of a doctor who was also a life-long diabetic; he passionately cared for his patients for many decades. He was and still is inspiring to me. I discovered biochemistry at the end of my college years and later biotechnology when such a technology was just a "dream" in that part of the world. I was fascinated by the potential to understand, one day, diseases at molecular level and have better tailored therapies; the interest may have been "contagious" because my two sons also decided to study biochemistry/biotechnology and continue on, one with studying medicine and the other with business studies. The highlight of my starting years, spent mostly in research and academic positions in my home country, is the time I was teaching clinical biochemistry at the Medical School in Cluj.

I arrived, as a family of 4, in the USA in 1991 and completed a PhD and post doctoral studies related to structural characterization of different metalloenzymes. I joined Lilly Research Laboratories in 1997 and contributed to the development and commercialization of several biopharmaceutical products. My last six years spent in manufacturing, in United States and outside the United States, added a very valuable experience and perspective on the challenges encountered during pharmaceutical product life cycle.

Of your PDA volunteer experiences, which stand out the most?

I enjoyed every PDA event in which I participated as speaker or moderator. However, getting to be part of the program planning committee for the PDA/FDA Supply Chain Conference on September 12, 2008 stands out to me as a unique and very valuable experience. It was transformational to be part of a committee that gathered several PDA and FDA leaders and subject matter experts and was put together in a very short time. It was an outstanding program that was replicated rapidly in the United States, Europe and Asia.

Which member benefit do you most look forward to?

All PDA periodic publications (*PDA Letter*, PDA technical reports and the PDA Journal), are key sources of technical and regulatory information. A very useful benefit is the access to the presentations at different conferences that one may not be able to attend in person.

Which PDA event/training course is your favorite?

The agenda and the program for PDA conferences has become so rich and diverse (in the United States and overseas) that it is more and more difficult to select few to attend. The annual conference and PDA/FDA regulatory conference remain the leading events with the largest influence.

How has volunteering with PDA benefited you professionally?

In the first years after joining PDA, I used the membership in particular for getting and learning from its publications. Networking and being part of discussions at different interest groups was the next step, which became a source of learning and reference for specific tasks or project phases during my assignments in product development. My involvement with PDA was more focused on validation and quality issues after being involved with the transfer (out of the United States), commercialization and manufacturing of parenteral products. PDA networking and the conferences in the United States and Europe helped me greatly in maintaining alignment with emerging or active regulations, quality trends and best practices in industry.

The information I collected from my activities with PDA help with the decisions I had to make and/or direction I had to lead inside the corporation. Meeting and having direct conversations with world-wide experts that PDA gathers at different forums is equally a pleasure and a source of new perspective on different activities in our industry. PDA also provided me the opportunity to share with others the approaches taken internally that led to successful results.

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

James Vesper, President, LearningPlus

PDA Join Date:1995

Areas of PDA Volunteerism: PDA Biennial Training Conference program/planning committee (2010, 2008, 2006); FDA/PDA Joint Meeting presenter (September 2002); Biennial PDA Training Conference presenter (October 2002); Biennial PDA Training Conference presenter (May 2004); Biennial PDA Training Conference presenter (May 2006); Biennial PDA Training Conference presenter (May 2008)

Interesting Facts about Yourself: I enjoy traveling as part of my work, which has allowed me to acquire a collection of almost 100 different airline air-sick bags.

Of your PDA volunteer experiences, which stand out the most? Working with the other planning committee members for the PDA Biennial Training Conference is something I very much enjoy. It is a fun, creative, professional group. We've had some great support from the PDA staff. For the past two years, we made the first session of that conference different from any other PDA event with a unique opening that involved the entire committee (and me in an outrageous costume).

Which PDA event/training course is your favorite? I have two: The Biennial Training Conference and the annual PDA/FDA meeting in Washington are both very important to me. Not only are the speakers knowledgeable and the presentations topics very timely, the meetings are a terrific way for me to recharge professionally and reconnect with colleagues and friends.

How has volunteering with PDA benefited you professionally? Volunteering with PDA has had several benefits. I enjoy the other volunteers with whom I collaborate. They are smart, connected with what is happening in the industry, and are a resource for questions or opinions. Corresponding with a colleague–and now a friend–on the PDA listserv (PharmSciTech) has had some very interesting results. It was how I got connected with the editor of a WHO guideline on training that I helped write. There's also a very helpful network of professionals within PDA that helps us all as we continue to learn.

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: Shin-Yi Hsu
Email: shinyi.hsu@otsuka.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 New PDA Members

Michele Augustine, Baxter
Kevin Austin, Total Validation Services
David Barry, Eli Lilly
BethAnne Bort, Pfizer
Amy Bosch, Lyophilization Technology
Bjoern Breth, Greiner Bio-One
Jacqueline Briskin, Takeda
Robert Buenaga, Johnson & Johnson
Chantal Bullot, Sanofi-Aventis
Ralph Bush, King Pharmaceuticals
Marsha Cummings, Eli Lilly
Gabriele Dallmann, Pharmatching
Corinne de la Foata, Biomerieux
Vivian Denny, Peak to Peak Pharmaceutical Associates
Benjamin Frey, ProPharma Group
Lelia Fuentes, Cardinal Health
Shaun Gittard, North Carolina State University
Jonathan Goulet, Merck
Jacob Grana, Opal Group
Amy Grenham, MedImmune
Vickie Hall, Ben Venue
Thomas Hendershot, Aramark Cleanroom Services
Darold Hill, PharmaSys
Joanne Hough, Novartis
Heloise Imbault, Seppic
Zak Iqbal, Life Technologies
Kenneth Jordan, ValSource
Julian Kay, Glaxosmithkline
Kwang Jong Kim, Chong Kun Dang Pharmaceutical
Sofia Kovalevskaya, Millennium
Jim Landers, Wentworth Institute of Technology
Karl Lutkewitte, Steriflow Valve
Elizabeth Lyons, Particle Measuring Systems
Sharon Ma, Genentech
Darshan Makhey, Dr. Reddys Laboratories
Yabuki Mami, PMDA
Samuel Manzanares, Care Fusion
Bruce McGathey, Eli Lilly
Robert Miller, JHP Pharmaceuticals
Gianluca Minestrini, F. Hoffmann-La Roche
Misako Nakamura, Japan
Darren Nolen, CryoLife
Yasser Nshed-Samuel, Amgen
Joana Oduro, Baxter Healthcare
Thomas Patton, Institute of Technology Sligo
Jon Petrone, Pall Life Sciences
Charmaine Porter, Baxter Bioscience
Joseph Potvin, Pfizer
Stephanie Rainsford
John Ramunas, Stanford University
Lorianne Richter, Genentech
Jennifer Roche, Three Rivers Pharmaceuticals
Joseph Roman, Prime Technologies/ITS
Meghan Samberg, NCSU-CVM
Veronica Santiago, Baxter
Markus Schneider, Novartis
Norbert Schulze, Biotest
Art Stoneking, Boehringer Ingelheim
Alexander Ushakov, Termo-Kont MK
Bjorn Van den Sanden, Institute of Tropical Medicine
Earl Wall, Hyde Engineering and Consulting
Kim Wan Soo, Ildong Phrmaceutical
Bernard Willis, Merck
Pierrette Wright Jenkins, Baxter Healthcare
Kun Yao, MedImmune
John Zaremba, Vistakon
Fujun Zhang, Life Technologies
Sandra Zoghbi-Gay, Biomerieux

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

Two Vaccine Workshops Upcoming in U.S. & Europe

Bethesda, Md. • May 17–19 • www.pda.org/vaccines2010
Berlin, Germany • June 16 • www.pda.org/europe

Program Committee Member Maik Jornitz, Sartorius Stedim Biotech

In 2002, it was SARS, followed by the avian flu and now H1N1, which made the world hold their collective breath, but it also has provided an opportunity for regulators and the vaccines industry to work closely together to overcome these threats. The recent H1N1 pandemic showed that these joint efforts can result in rapid and robust activities to stifle the spread of the disease. The vaccine industry has been fast and flexible in producing desired vaccines, and the regulators responded with focus and speed to approve the vaccines that have been required. As a vaccine recipient, it has been pleasant to see the joint efforts of regulators and industry to overcome a very real threat.

Having said this, there are lessons learned from it and these lessons are of high value for any member of the vaccine industry and regulatory authorities. Once again, PDA facilitates such learning and network venues and has planned two vaccine conferences in Bethesda, Md. and Berlin, Germany.

These conferences will not only address the lessons learned from the H1N1 pandemic but will encompass a multitude of topics, which are currently discussed within the vaccine field. Topics like new production technologies, for example, single-use equipment or cell culture based vaccine developments, new adjuvant development and potential therapeutic vaccine application will be addressed. The H5N1 threat and H1N1 pandemic showed the need for the acceleration of vaccine supplies. Multiple vaccine manufacturers have been working on cell culture based flu vaccine technologies. These new developments are essential to advance manufacturing processes and will hopefully in the future speed-up supplies to the patient. Single-use process equipment support such fast turn-around, since cleaning and set-up times are reduced. In addition, this equipment reflects containment advances, as they function as closed, interconnected unit operations. Concepts of single-use technology facility lay-outs have been presented recently, which show the potential reduction of clean-room floor space utilizing isolators in conjunction with disposable components. The containment advances will help to utilize production facilities, possibly as multi-product facility. The flexibility advances shall not be underestimated, as we have seen the need of production capacity during the pandemic threats. Containments mean production staff protection, especially when live viruses are processed. The conferences will address these advanced process devices in case studies presented, which show the use of single-use systems and the validation exercises required.

New adjuvants are currently being tested to enhance the potency of many types of vaccines. These new adjuvant developments are necessary and desirable to create a solid supportive basis and flexibility when other pandemics occur.

Storage and transport, typically under the umbrella of cold chain, will be a among the topics addressed. This topic becomes more and more relevant with the increasing distribution of vaccines into the African and Asian continents. Vaccine qualities and efficacies need to be maintained once the vaccine leaves our facilities. How do we assure an appropriate cold chain distribution? Current approaches and expectations will be presented and discussed at the conference.

The described topics are just a glance of a very complete vaccine conference program. Others are bioassay development, therapeutic vaccine developments, comparability or post approval change procedures, regulatory initiatives, inactivation or removal of potential contaminants.

Vaccine development and production is on the increase, not only triggered by the Anthrax scare of 2001 but also by the inevitable occurrences of new pandemic pathogens. Since PDA's membership voiced their desire to have an information and network platform, naturally PDA not only reacted with the continuous support of the Vaccine Interest Group but realized that dedicated focus conferences are required to fulfill the demand of vaccine professionals.

The program committee invites you to join us in Bethesda, Md. on May 17-19. PDA Training and Research Institute courses will follow the conference on May 19-20. In Bethesda, some of the topics covered will be on growth of live organisms, containment, facility design for multiuse, aseptic processing for

Extend your Time and Knowledge

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

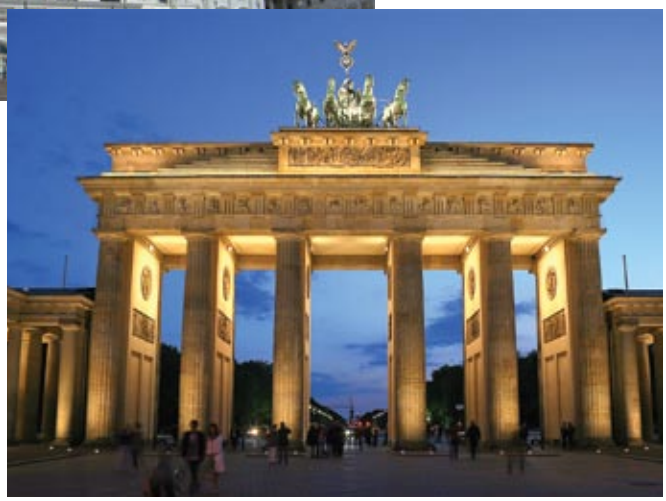
Check the TRI website (www.pdatraining.org) for details and registration information for these courses. We look forward to seeing you there.

bulk manufacture, adventitious agent contamination, removal of host cell DNA, adjuvant and potency measurement.

In Berlin, Germany, a conference on this topic will be held on June 16 which will enable you to exchange your experience and knowledge with your peers. This meeting will cover topics on applying new vaccine technology to old problems, cancer vaccines, new developments in conjugated vaccines, cell based assays for prediction of vaccine efficacy and new developments with veterinary vaccines.

To learn more about the Bethesda conference, please visit www.pda.org/vaccines2010. For details on the Germany conference, please visit www.pda.org/europe.

No gridlock at our meetings — join us in Washington for the Vaccines workshop and TRI courses



Join PDA in tearing down the barriers to vaccine development and manufacturing in Berlin

The Parenteral Drug Association presents

2010 PDA Vaccine Conference

May 17-20, 2010 | Marriott Bethesda North | Bethesda, Maryland

Register before March 6 and save up to $200!

Due to recent threats and pandemics, there is a **serious need to get available vaccine supplies to the patient without delay.** Discuss solutions with industry experts who will share their experiences, case studies and advice for navigating the global product development and regulatory waters regarding vaccines at this conference!

Topics will include:

- Application of Quality by Design (QbD) principles and challenges of process validation
- Supply chain complexities
- Challenges of analytical methods development (stability indicating and potency assays)
- Novel adjuvants, substrates, expression and delivery systems
- Technical bridging of changes during development and application of comparability protocols
- Update on 21 CFR 601.12 Changes to be Reported
- Expanding requirements for preclinical testing
- Impact of biosimilars
- Challenges of developing therapeutic vaccines for non-infectious disease indications

FDA representatives will also share insight into their expectations for generating the appropriate data and information to support robust manufacturing processes that are approvable and sustainable into the future.

The PDA Training and Research Institute (PDA TRI) will offer courses on May 19-20 to complement what you learn at the meeting.

For more details visit: www.pda.org/vaccines2010

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

PDA Europe Upcoming Workshops 2010

PDA Workshop on Advanced Therapy Medicinal Products:
ATMPs – 21st Century Pharmaceuticals, a New Paradigm

With the revision of the GMP Annex 2, and the European directive on Advanced Medicinal Therapy Products, PDA will host its first exclusive work workshop on Advanced Therapies, how and where they are produced, and how they are affected by the new GMP guidance. This workshop is clustered with our Vaccine and Monoclonal Antibody workshops to give you the latest information in this new and emerging area of medicines manufacturing.

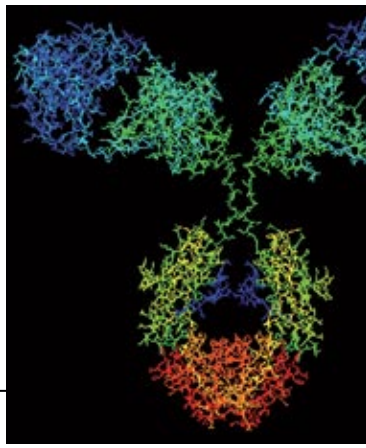
15 June 2010
Berlin, Germany

PDA Vaccines Workshop 2010
New Technologies for 21st Centry

Derived from our conferences on Deve-lopment and Production of Biopharmaceuticals the last 3 years, this workshop will be dedicated exclusively to the development, manufacturing and regulatory supervision of vaccines in today's market. It will provide information on the latest issues driving vaccine development, and the regulatory aspects affecting GMP and approval for marketing.

16 June 2010
Berlin, Germany

PDA 3rd Monoclonal Antibodies Workshop:
Managing the Challenges of Comparability: Scientific and Regulatory Considerations for Monoclonal Antibodies



Reflecting PDA's commitment to the area of Monoclonal Antibody manufacturing, our 3rd annual workshop will be built on our interactions with the regulatory authorities in those areas of acute interest in both the manufacturing and development domains. As the third part of our biotechnology cluster in Berlin, attendees will be privy to the industry leaders discussion the robust future this well understood manufacturing technology.

17-18 June 2010
Berlin, Germany

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

Learn About Compliance Training and Performance in a Changing Environment

2010 PDA Biennial Training Conference • Baltimore, Md. • October 11-13 • www.pda.org/biennial2010

Planning Committee Chair Joyce Winters, J Winters Consulting

On behalf of the Program Planning Committee and PDA, I would like to invite you and your staff to attend the *2010 PDA Biennial Training Conference,* October 11-13 in Baltimore's Inner Harbor. You'll want to be a part of this exciting opportunity to enhance your skills and network with others in your field of interest.

Recognizing many of the challenges trainers face today, the Program Planning Committee has selected *Compliance Training and Performance in a Changing Environment* as the 2010 conference theme. We will offer concurrent sessions featuring topics that are designed for all levels of training individuals. These sessions, plus keynote speakers and an interactive format will provide a forum to learn from the experiences and successes of your fellow trainers.

We are pleased to announce that **Allison Rossett**, PhD, Professor of Educational Technology, San Diego State University, will be a featured speaker. Her topic will be on job aid and performance support.

Rebeca Rodriguez, National Expert Investigator, U.S. FDA, will provide the regulatory perspective on current training issues. Hear about the latest trends and have your questions answered.

The conference will also provide an exhibition where you can see what's new in training and available for your use. PDA Training and Research Institute courses are scheduled to accompany this conference and balance out your educational experience. Courses include:

- "Designing and Presenting Effective GXP Training Programs to Meet New FDA Training Requirements" (Oct. 14)
- "Introduction to Competency-Based Training" (Oct. 14-15)
- "FDA Inspection Readiness for a Training Systems Audit" (Oct. 15)
- "Developing and Using Virtual Learning Opportunities" (Oct. 15)

With a location like Baltimore's Exciting Inner Harbor, dynamic programs by outstanding training professionals, networking opportunities galore and more, we have all the ingredients for a successful conference in 2010!

We look forward to seeing you in Baltimore on October 11-13. For more details on the conference and to register, please visit www.pda.org/biennial2010.

2010 PDA/FDA Pharmaceutical Supply Chain Workshop

Enough Talk: Let's Find and Implement Solutions

April 26-28, 2010

Hyatt Regency Bethesda | Bethesda, Maryland

Register before February 14 and save up to **$400**!

A reliable supply of high quality, safe and effective drug products and drug ingredients depends upon a series of controls across the entire supply chain from sourcing of incoming starting materials to distribution controls to the market. Recent experiences in the market have highlighted the need for effective regulations and controls.

Attend the *2010 PDA/FDA Pharmaceutical Supply Chain Workshop* on April 26-28, 2010 and you'll be able to:

- Hear from senior FDA personnel on the current regulatory environment
- Share improvements in programs and technology
- Identify any barriers and associated actions to enable implementation of good solutions

An exhibition featuring supply chain technological advances and programs from today's leading companies will complement the skills and knowledge gained during this meeting.

For more details and to register, visit www.pda.org/supplychain2010

Cold Chain Course to Follow Conference

Bethesda, Md. • April 14-15 • www.pdatraining.org/coldchain2010

Stephanie Ko, PDA

The PDA Training and Research Institute will offer a two-day lecture course immediately following PDA's Pharmaceutical Cold Chain Management Conference titled, "Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging, Testing, and Transport Systems." The course will be taught by **Rafik H. Bishara**, PhD, the leader of PDA's pharmaceutical Cold Chain Interest Group (PCCIG), and **Tom Pringle**, Industry Consultant and Educator, Pharmaceutical and Biomedical Temperature-Controlled Transport Packaging. The course will give you two full days of lecture, discussion and case studies that expand upon what you learn at the conference and much more.

The general theme of day one covers global regulations and standards that influence cold-chain distribution practices. Global governance and oversight will be discussed along with industry consensus practices and a review of PDA's Technical Report No. 39. In addition, IATA regulations for air transport and good cold-chain management practices will be covered, which includes global citations for non-compliance. At the end of the first day, there will be group discussion of case studies on regulatory citations related to cold-chain activities.

Day two focuses on the development and testing of cold-chain transport systems, specifically excursion and deviation analysis in qualification and monitoring. You will learn the 10-step process to a qualified thermal container and understand the package handling environment; e.g., development of defensible temperature profiles for thermal package testing. There will be a lecture and exercise on thermal package performance testing, from design to qualification to monitoring of actual shipments (PQ). Towards the end of the presentation, participants will engage in a group discussion on deviations and acceptable/non-acceptable temperature excursions during transport, using PQ results from the exercise.

There will be enhancements to the course with two new topics: Cold Chain Risk Management and Last Mile, PDA TR No. 46. The instructors will also be developing some modules to be used according to the audience.

By the end of the course, you will be able to describe global practices and ➤

PARENTERAL DRUG ASSOCIATION TRAINING AND RESEARCH INSTITUTE (PDA TRI)

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3-4: Elements of Risk Management
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23-25: Fermentation/Cell Culture Technologies Training Workshop
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The PDA Training and Research Institute is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education.

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

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

Participate at the Innovative Aseptic Technologies Conference

Innovative Aseptic Technologies • Basel, Switzerland • June 10-11 • www.pda.org/europe

Siegfried Schmitt, PhD, Parexel Consulting and Volker Eck, PhD, PDA

There are many conferences on aseptic technologies, but the one by PDA combines practical aspects and regulatory requirements to maintain continual compliance.

As an example, take the Pharmaceutical Inspection Cooperation Scheme (PIC/S) document published on January 8 called, *GMP Annex 1 Revision 2008, Interpretation of Most Important Changes For the Manufacture of Sterile Medicinal Products*. There are 16 sections of Annex 1 discussed and interpreted. With regards to crimp-capping, the interpretation given emphasizes that it is valid for all aseptically filled vials. So requirements are put forth for the environment to be established from the moment onwards when such vials leave the aseptic processing area to be crimped. Grade A air supply is expected for conveyor tunnels that connect the aseptic process area to the crimping station. Grade D classification is the minimal requirement for the clean room where the crimp-capping machine is located. There is no requirement for aseptic conditions up to crimp capping.

The document defines grade A air supply as something that is *specifically used to describe a supply of air which is HEPA filtered and at the point of supply meets when tested, the non-viable particulate requirements of a grade A area.*

Then, some qualification requirements are defined, in particular: *Qualification is done only under at rest conditions: For the crimp-capping machine the at-rest state is achieved when the air supply is switched on, the crimp-capping machine is operating (feeding of vials and crimp caps is not considered necessary) and there is no interference by operators. For the conveyor tunnel for liquid products the at-rest state is achieved when the air supply is switched on, the conveyor belt is switched on and there is no interference by operators. Non-viable particles should be measured and are expected to meet grade A requirements. The probe should be located at the point of supply of the filtered air. Smoke studies should be performed. Whilst unidirectional air flow is not required, efficient protection of the vials should be demonstrated and the absence of air entrainment from the surrounding room should be demonstrated. Limits for air velocity should be in place and justified.*

To have a clear picture of what should be in place to fulfill such interpretation and to know about innovative technologies to remain compliant with those and other requirements, the PDA conference on Innovative Aseptic Technologies in Basel, Switzerland, is the place to go.

Therefore, your expectations in this event should be high and we aim to please. Our lecturers are seasoned industry professionals and regulatory agency experts, who are openly sharing with you their successes and challenges. Even better, one-half day of this two day conference will be dedicated to a workshop around your issues. You ask us your nagging questions and we will aim to answer them.

As we only have two days for this conference, we are concentrating on three main topics:

- The API session will focus on aseptic compounding, sterilization techniques and use of disposables.
- The Transfer session will concentrate on connection systems, vial transfer solutions and new technologies.
- The Fill and Finish session theme will cover capping (Annex 1 issues), containment designs and inspection techniques.

If you had enough of lectures that tell you what you already knew or what you can read for yourself and instead want interactive, challenging and open lectures on real life industry experience, then this is the event for you.

Hope to see you in Basel, June 10-11.

Cold Chain, continued from page 42

regulatory requirements for cold chain distribution as well as explain the guidance and regulatory requirements of the manufacturer for distribution and packaging of products.

You will be knowledgeable in the cold chain pharma distribution network by identifying where mistakes are made, discussing common materials used for cold chain distribution and explaining acceptable and unacceptable product temperature excursions in transit. And most importantly, you can apply immediately what you learn on the job by defining a prioritizing a list of action items for your organization to be cold chain compliant.

For more information about the course and how to register, please go to www.pdatraining.org/coldchain2010.

PDA Parenteral Drug Association

Connecting People, Science and Regulation®

2010 PDA Europe Workshop

Biofilms

The Impact of Biofilms on Pharmaceutical and Biopharmaceutical Manufacturing

20-21 April 2010
Frankfurt, Germany
Workshop/Exhibition

See the complete program at:
www.pda.org/europe

Register by 19 March 2010 and SAVE!

Biological contamination of water systems continues to present significant challenges to the pharmaceutical, biotechnology, and medical device industries. Bacteria, in particular, are well adapted to survival in purified water systems. Their presence leads to the contamination of process equipment, raw materials, and—in some cases—product adulteration leading to recalls. Effective control of bioburden in water systems requires an understanding of those factors that promote microbial growth and biofilm formation. The presence of biofilms associated with wetted surfaces gives rise to both bioburden and associated endotoxin (pyrogen) contamination. This two-day workshop will focus on the genesis, detection, prevention, and treatment of biofilms (including mycoplasma biofilms) in pharmaceutical and biopharmaceutical fluid-handling systems.

PDA
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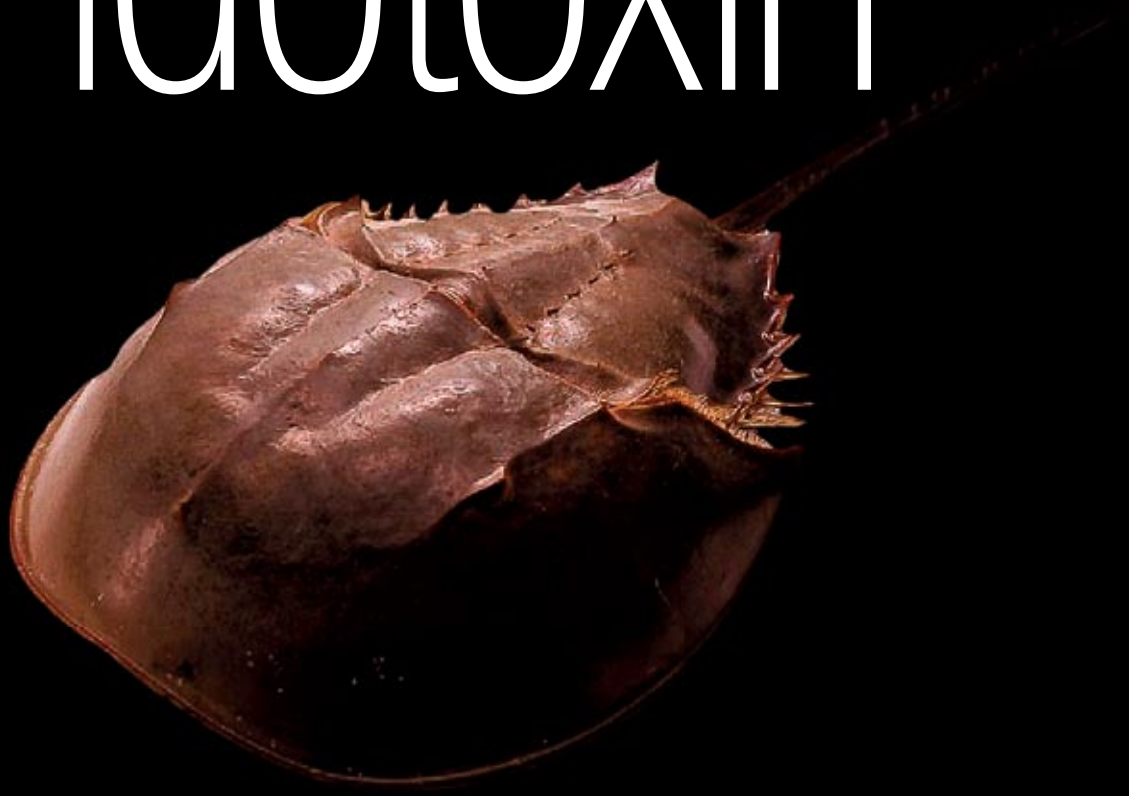
2010 PDA Europe Conference on

Endotoxin



13-14 April 2010
Barcelona, Spain

Conference/Exhibition

See the complete program at:
www.pda.org/europe

Register by 16 March 2010 and SAVE!

This edition focuses on the results achieved by the PDA and SFSTP experts working on a document that will give an overview on best practices regarding Endotoxin detection, removal and Bacterial Endotoxin Testing (BET) as well as GMP issues.

Aspects discussed will be: correlation between Endotoxin and Pyrogens • regulatory background, expectations and trends • removal, sampling, detection and testing of Endotoxin for non-conventional samples • how to reveal and determine Endotoxin in APIs, excipients and auxiliaries • practical issues in removal, detection and testing of Endotoxin on immediate container components like plastic surfaces, vials and stoppers • best practices in monitoring Endotoxin levels • requirements and technologies for Endotoxin removal • practical definition of alert and action levels during manufacturing • detection and determination of Endotoxin in non-aqueous matrices • handling potential interferences with for example biotech products • alternative methods (e.g. Monocyte Activation Test) • future trends. This two-day interactive program includes case studies, workshops, problem solving strategies and round table discussions.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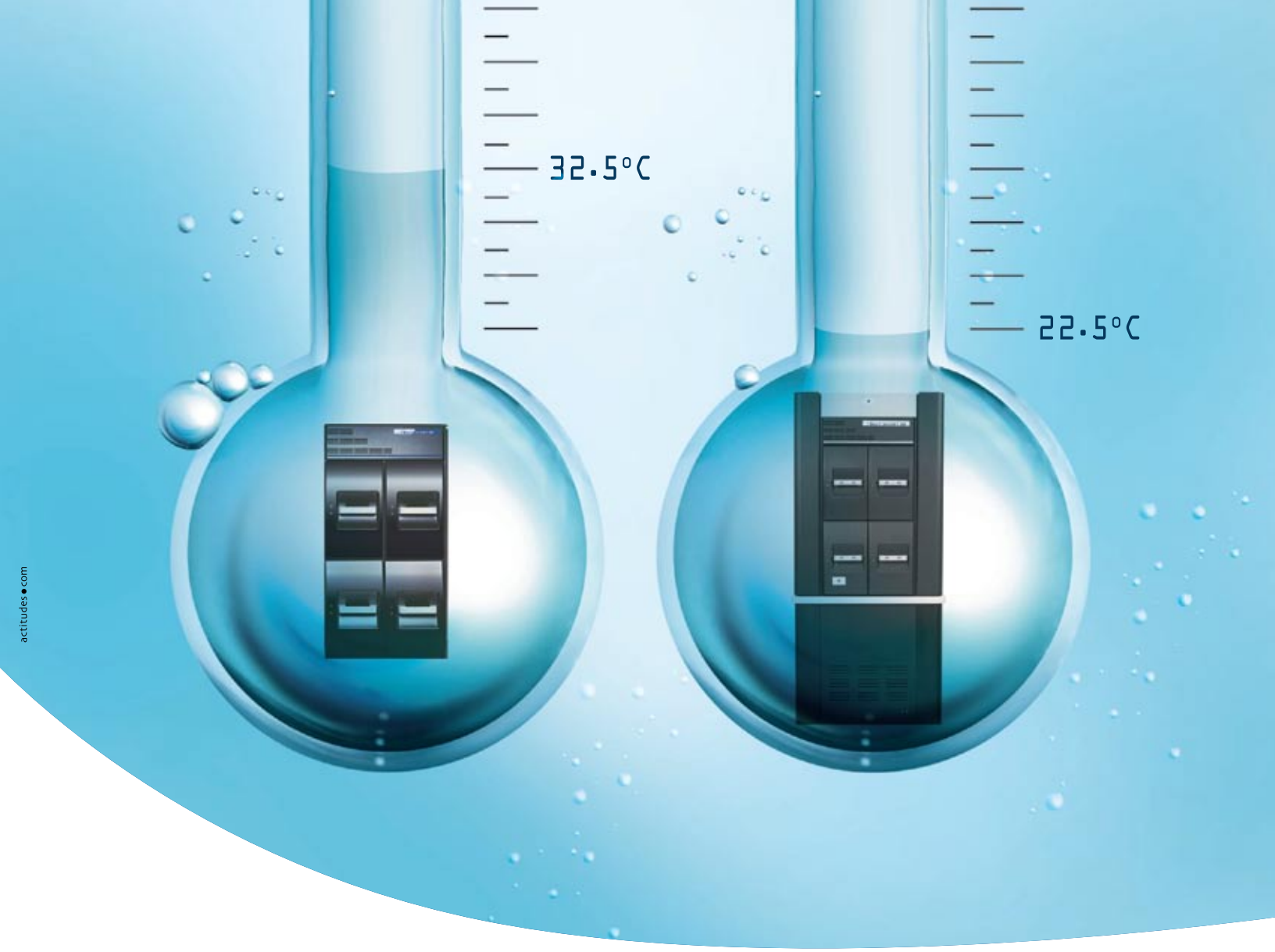

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