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PDA Letter

Volume XLVI • Issue #2

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February 2010

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PDA
Parenteral Drug Association

Connecting People, Science and Regulation®

Knowledge Management: A Key Aspect of ICH Q8, 9 and 10 Implementation

Walter Morris and Emily Hough, PDA

Do you know how your company is managing its knowledge? Is it comprehensive, corporate-wide or a fully integrated knowledge management system? Most importantly, is your system ready to withstand regulatory scrutiny?

A session at the *2009 PDA/FDA Joint Regulatory Conference* last September was organized to answer these and other questions about knowledge management (KM). Experts representing the U.S. FDA, F. Hoffman-La Roche and World Bank provided instructive case studies on how to convert large amounts of data into usable and valuable organizational knowledge during the session.

Knowledge management is an important concept, though not a new one, that is rising in prominence mainly because of the existence of the International Conference of Harmonisation (ICH) quality guidelines Q8, Q9 and Q10, which cover pharmaceutical development, risk management and quality systems, respectively. Q10 states that knowledge management is a *systematic approach to acquiring, analyzing, storing and disseminating information related to products, processes and components.*

In its twentieth year, ICH has evolved from a facilitator of harmonized existing regulatory and technical requirements to a catalyst for the implementation of new, more advanced industrial practices, a remarkable accomplishment for a process spun out from efforts to improve international trade.

As with risk management, process analytical technologies and QbD, knowledge management is an area in which the pharmaceutical industry has fallen behind others. A look at how the World Bank has implemented KM systems is indicative of how far other industries have gone.

According to **Charles Mignosa**, President, Business Systems Architects, a firm that works with the World Bank, knowledge management is "a proposition that responsiveness and innovation can be improved through the leveraging of collective wisdom and experience." To do this, companies need processes specific to the management of knowledge, organizational structures that create accountability for knowledge management, applications to

REPORT FROM THE 2009 PDA/FDA JOINT REGULATORY CONFERENCE

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

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ICH weaves together technical standards from three regions to create harmonized regulatory expectations

Coming Next Issue:
Securing the Supply Chain

Editor's Message

ICH: Two Decades of Success

When I first broke into this industry as a writer for *"The Gold Sheet"* in 1995, the International Conference on Harmonisation (ICH) was just getting going. Only five years into its existence, the ICH already had a number of quality documents in the pipeline. As each came out, it was exciting tracking how they impacted the industry and the regulatory authorities. By the close of its first decade, ICH had entered a round of revision to refresh some of its earliest documents.

As the next ICH decade got underway, the true power of the organization was being felt. First, it published a GMP document for APIs which actually forestalled the publication of regional API GMPs. The *PDA Letter* was pleased to interview key members of that working group back in the September 2009 issue. Next, ICH created a common technical document for the submission of drug applications, complete with safety, efficacy *and* the quality (CMC) sections. ICH also served as a catalyst to get the three major pharmacopeias—USP, EP and JP—to make a serious effort in aligning their respective testing standards.

Then, ICH became involved in the regulatory programs to change the entire paradigm for pharmaceutical manufacturing and control with its Q8/9/10 guidelines. These documents are helping regulatory authorities and industry around the world grapple with the challenges associated with the implementation of stronger drug development sections to the marketing authorization applications, risk management and quality systems. Soon, a document specific to APIs will be completed.

Even more impressive is the infrastructure ICH has developed to ensure harmonized implementation of its guidelines in the three ICH regions and to facilitate the use of its guidelines across the world. The Quality Implementation Group will be partnering with PDA and ISPE to hold three workshops in 2010 on the Q8/9/10 trio. The ICH Global Cooperation Group is working with international organizations across the globe to spread the ICH standards.

PDA members have been involved with ICH from the very beginning, and the Association played a major role in the international training effort for Q7A. The PDA PCMO initiative (www.pda.org/pcmo) is aimed at continuing PDA's efforts to support harmonization.

So as ICH approaches its 20th birthday in April, I'd like to salute it and all the people who've made it a success over the last two decades!

PDA Letter

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PDA Welcomes David Hall as Vice President of Sales

With 20 years of sales and association management experience, the new Vice President of Sales, **David Hall**, came to PDA in December looking for a new challenge and a place where he could utilize his knowledge of the industry. During his tenure at ISPE, he was instrumental in growing supplier-related products and services, including electronic and Web advertising opportunities, sponsorship packages and exhibitions, as well as building a solid global sales structure to meet the needs of this growing segment of the industry.

One of David's goals for PDA is to create value-added opportunities that align with the association's mission and strategy. He believes that to be successful, it is imperative to listen to the PDA supplier community, establish and maintain long-term open relationships with this integral segment of the organization, and build programs to meet their needs. He sees significant opportunities to provide resources to better connect suppliers with pharmaceutical science and manufacturing professionals by leveraging PDA's strong global brand.

Even though he has only been here a short time, David has already been involved in many productive, collaborative meetings with both staff and members who are open to new ideas and share a commitment to PDA's continued growth and success. "PDA members, leaders, and volunteers are a dedicated group representing all facets of the pharmaceutical science and manufacturing industry," said David. "I'm looking forward to working with them and the PDA staff to implement new strategic initiatives and position PDA to successfully overcome the challenges ahead."

He concluded, "as a membership organization, we can never forget that what we do is for the members. The more closely we align our products and services with our members' needs, the more successful we'll be."

David Hall, PDA

2010 PDA Pharmaceutical Cold Chain Management Conference

From Cold Chain to Good Distribution Practices – Integrated Supply Chain Management

April 12-15, 2010

Bethesda, Maryland

Conference | Exhibition | Course

Register by March 2 and save up to $200!

The ***2010 PDA Pharmaceutical Cold Chain Management Conference*** and training course will provide guidance on the handling and distribution of temperature-sensitive pharmaceuticals as it relates to patient safety and product integrity.

Following the theme, "From Cold Chain to Good Distribution Practices – Integrated Supply Chain Management," this conference will cover:

- New compendial standards for storage and shipping of medicines
- ISTA's certification of thermal laboratories for cold chain
- Cold chain packaging sustainability
- Mean Kinetic Temperature (MKT)
- Radio frequency energy and biopharmaceuticals
- Case studies on excursion data and shipping outside labels, etc.
- Proactive risk management to enhance supply chain integrity
- Recent advances in the development and implementation of sea transport
- And more!

PDA is also offering an exhibition during the conference. Let your company's products and services become a valuable tool or resource for attendees!

Advance your cold chain knowledge by attending the PDA Training and Research Institute (PDA TRI) course, *Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems*, which will immediately follow the conference.

www.pda.org/coldchain2010

PARENTERAL DRUG ASSOCIATION TRAINING AND RESEARCH INSTITUTE (PDA TRI)

Early 2010 Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

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

February 2010

22-24: San Diego Course Series — LAST CHANCE TO REGISTER
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Courses Include:
- Biotechnology: Overview of Principles, Tools, Processes and Products
- CGMP Biotechnology Facility Design and Validation
- Implementing CGMPs in Biopharmaceutical Manufacturing
- Sterilizing Filtration of Liquids
- Virus Clearance - New Course

March 2010

3-5: Pharmaceutical Water System Microbiology Lab Course
Bethesda, Maryland
www.pdatraining.org/watersystems

10-12: Developing an Environmental Monitoring Program
Bethesda, Maryland
www.pdatraining.org/DEMP

18-19: PDA Annual Meeting Courses
Orlando, Florida
www.pdaannualmeeting.org/courses

Courses Include:
- Applying Lean to Aseptic Processes - New Course
- Bioprocess Validation - New Course
- Change Control: A Practical Workshop
- Clean Room Design, Contamination Control, & Environmental Monitoring for Controlled Environments
- Fundamentals of Lyophilization
- Isolators: From Concept through Qualification - New Course
- Risk Mitigation Solutions: The Response to Risk Assessment - New Course
- Role of the Quality Professional in the 21st Century
- Use of HACCP for Microbiological Control in Pharmaceutical Manufacturing

22-26: Aseptic Processing Training Program - Session 2
(Week 2: April 19-23) — SOLD OUT!
Bethesda, Maryland
www.pdatraining.org/aseptic

April 2010

6-8: Saint Louis Course Series
Saint Louis, Missouri
www.pdatraining.org/stlouis2010

Courses Include:
- Environmental and Utility Monitoring in a Classified Facility - Developing the Regulatory Rationale - New Course
- Managing Quality Systems
- Process Validation for Pharmaceuticals: Current and Future Trends with Emphasis on Implementation of the New FDA Guide
- Risk Management for Aseptic Processing
- Single-Use Technologies in Downstream Processing: A Blueprint for Implementation – New Course

7-9: Cleaning Validation
Bethesda, Maryland
www.pdatraining.org/cleaning

14-15: Global Regulations and Standards: Influences on Cold Chain Distribution, Packaging Testing and Transport Systems
Bethesda, Maryland
www.pdatraining.org/coldchaincourse

28-30: Development of Pre-filled Syringes
Bethesda, Maryland
www.pdatraining.org/prefilled

May 2010

5-7: Environmental Mycology Identification Workshop
Bethesda, Maryland
www.pdatraining.org/mycology

22-26: Aseptic Processing Training Program - Session 3
(Week 2: June 14-18)
Bethesda, Maryland
www.pdatraining.org/aseptic

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

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

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.

Science & Technology Snapshot

2010 PDA Annual Meeting Interest Group *Briefing*

13 PDA Interest Groups Sessions

Monday March 15, 4 – 5:30 P.M.

IG1 – Clinical Trial Materials: The Clinical Trial Materials Interest Group offers members an opportunity to discuss topics of interest associated with the development and manufacture of clinical supplies. This includes the pre-clinical phase (involving pharmaceutical development operations), the manufacture of all phases of clinical supplies (including both API and drug product), and the ultimate transfer of the manufacturing process to the commercial manufacturing site.

IG2 – Lyophilization and Sterile Processing: As a constantly developing field there are always new perspectives in the science, technology and compliance realms. This interest group provides an open forum for discussions on current topics. Topics are identified at the onset of the meeting for open discussions among participants. This provides a unique opportunity to learn from a variety of experiences and perspectives and provides an excellent benchmark for current industry practices.

IG3 – Visual Inspection of Parenterals: The Visual Inspection of Parenterals Interest Group provides a forum to discuss topics related to the visual inspection of injectable products. Past topics have included selection and qualification of human inspectors, validation of automated inspection systems, recent regulatory activity and country specific inspection requirements. This group has also initiated activities to survey industry inspection practices, organize special meetings on visual inspection and to provide scientific guidance on compendial requirements for the inspection of injectable products.

IG4 – Process Validation: Participate in an on-going forum for the exchange and dissemination of information and ideas for the purpose of education, innovation, and compliance related to the validation of critical processes and those activities which support the validation of critical processes. The interest group should be a forum for presenting and discussing issues and trends in validation. These discussions should result in a better understanding of PDA member needs. This in turn results in better programs, more useful publications, and appropriate areas of advocacy.

IG5 – Biotechnology: The Biotechnology Interest Group meets the mission of PDA of advancing understanding of existing and cutting edge biotechnology internationally by promoting scientifically sound, practical technical information and education for industry and regulatory agencies.

IG6 – Prefilled Syringes: The Prefilled Syringe Interest Group provides a forum for discussions of actual topics related to prefillable injection system components such as cartridges or syringes and combinations thereof with injection and safety devices. Members come together to exchange in an open discussion latest information about technological improvements in the universe of prefillable syringes and injection devices, covering production, filling, handling and regulatory aspects.

Tuesday, March 16, 4:15 – 6 P.M.

IG7 – Combination Products: This interest group provides a forum for discussion of topical issues concerning submissions and compliance matters related to a variety of combination product types with emphasis on drug delivery devices and functional pharmaceutical packaging. The format of the Combination Products Interest Group meetings includes open discussions of hot topics and formal presentations by industry and government experts on a variety of topical combination product quality and regulatory issues.

IG8 – Vaccines: The Vaccines Interest Group (VIG) focuses on issues that affect the biological, biotechnology and vaccine industry. The interest group has previously discussed regulatory issues, new technologies and emerging industry trends. Resent issues include vaccine availability and supplies, homeland security, and inspection trends. The group also issues a newsletter. All PDA members are welcome to attend VIG meetings, which are held in conjunction with PDA events. A roundtable discussion will be held during PDA's *2010 Annual Meeting*. Intended speakers will be named after the *2009 PDA/FDA Joint Regulatory Conference*.

IG9 – Inspection Trends/Regulatory Affairs Quality Systems: The Inspection Trends/Regulatory Affairs Interest Group provides a forum for sharing experiences and knowledge in the subject areas. Data on current inspection findings and trends are presented, as well as discussions on new regulatory and compliance initiatives. The PDA Quality Systems Interest Group is a network of Quality Assurance/Quality Control Professionals. Past topics have dealt with issues ranging from systems based inspections, to Quality Assurance/Quality

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Journal *Preview*

Bio's CEO writes on Biotech Public Policy

Volume 64, No. 1 (January/February) of the *PDA Journal of Pharmaceutical Science and Technology* is now available online. This issue has a guest editorial from James Greenwood, President and CEO, Biotechnology Industry Organization, on the public policy that is needed to advance biotechnology innovation. In addition, results from an FDA-sponsored study on the risks of changing sterile drug manufacturing sites are published.

The January/February Journal Table of Contents:

Editorial

"Advancing Biotechnology Innovation Depends on the Right Public Policies" – James C. Greenwood

Commentary

"Assessing Risks of Changing Sterile Drug Manufacturing Sites" – Stephen E. Langille and Cliff Campbell

Research

"Root Cause Analysis of Tungsten-Induced Protein Aggregation in Pre-filled Syringes" – Wei Liu, Rob Swift, Gianni Torraca, Yasser Nashed-Samuel, Zai-Qing Wen, Yijia Jiang, Aylin Vance, Anthony Mire-Sluis, Erwin Freund, Janice Davis, and Linda Narhi

"In Vitro Iontophoretic Delivery of Nicorandil" – Bijaya Ghosh, Rashmi Baser, Uma A. Patil, and B. M. Dinesh

"Influence of Simulated Gastrointestinal Fluids on Polymorphic Behavior of Anhydrous Carbamazepine Form III and Biopharmaceutical Relevance" – S. B. Bhise and M. Rajkumar

"Comparison of Solute-Binding Properties of Plastic Materials Used as Pharmaceutical Product Containers" – Dennis Jenke, Tom Couch, and Amy Gillum

"Matrix-Type Transdermal Drug Delivery System of Trandolapril: In Vitro and Ex Vivo Characterization" – Mamatha Tirunagari, Venkateswara Rao Jangala, Mukkanti Khagga, and Ramesh Gannu

"Thermosensitive Drug Permeation through Liquid Crystal-Embedded Cellulose Nitrate Membranes" – Afrouz Yousefi, Elham Khodaverdi, Fatemeh Atyabi, and Rassoul Dinarvand

"Impact of Different Elastomer Formulations on Moisture Permeation through Stoppers Used for Lyophilized Products Stored under Humid Conditions" – Hitoshi Sasaki, Jun Kikuchi, Terutoshi Maeda, and Hitoshi Kuboniwa

"How and Why Would You Do a Pressure Holding Test on an Aseptic Installation for which You Want to Check the Integrity? Theory and Practical Example" – Olivier Chancel, Raoul Grissely, Magnus Stering, and Luc Pisarik

Make sure you go to http://journal.pda.org to access the latest Journal.

Technical Report *Watch*

First Technical Report Compilation Available In February!

Over the years, PDA expert task forces have developed several technical reports on various aspects of filtration. Now you can own all five of them in one easy-to-use hardbound volume.

PDA Technical Series: Filtration – A Compilation of Technical Reports on Filtration bundles the following five PDA technical reports:

- *Technical Report No. 15 (Revised 2009): Validation of Tangential Flow Filtration in Biopharmaceutical Applications*
- *Technical Report No. 26 (Revised 2008): Sterilizing Filtration of Liquids*
- *Technical Report No. 40: Sterilizing Filtration of Gases*
- *Technical Report No. 41 (Revised 2008): Virus Filtration*
- *Technical Report No. 45: Filtration of Liquids Using Cellulose-Based Depth Filters*

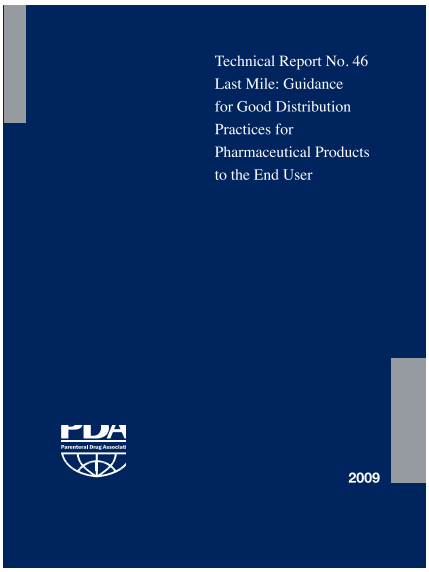
This volume is a convenient and powerful reference for anyone working with filtration processes for water and virus removal. To order, go to the PDA Bookstore (www.pda.org/bookstore) or contact Janny Chua at chua@pda.org.

In Publication

Now Available at www.pda.org/bookstore.

Technical Report No. 46: Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User

Managing shipments of product in the "last mile" to the point of patient administration can prove difficult, but PDA's Last Mile Task Force has sorted through the various distribution regulations in major markets to provide guidance on the proper handling of controlled-temperature medicinal products and devices along the final legs of the distribution chain. This follow-up document to Technical Report No. 39 on cold chain management is an invaluable tool to all involved in the "last mile."



Recent Sci-Tech Discussions: Micro Growth Promotion Tests and Microbiology Method Validation

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

Micro Growth Promotion Tests

My first question is how do you interpret the "factor of 2?" I assume that if the previously qualified media had 50 colonies on it this means the new media should have between 25 and 100 colonies on it (divide by 2 and multiply by 2)? How do you decide if the new media is acceptable?

2. Do you test previously qualified media and the new media at the same time and compare results?

3. Do you compare the results that you got earlier with the previously qualified media to the results you get on the new media?

4. Do you expect to get within a factor of two of the manufacturer's stated value? For example, if the assay value for a product is stated to be 5.0 E+ 02 CFU per mL, when it is reconstituted do you expect to be within a factor of 2 of 50 colonies if you inoculate an agar plate with 0.1ml?

Last question: Do most labs calculate the mean and the standard deviation of the control when they perform growth promotion testing (like a daily process control)?

Respondent 1: [Questioner], My answers are inserted in your text. "My first question is how do you interpret the "factor of 2?" I assume that if the previously qualified media had 50 colonies on it, this means the new media should have between 25 and 100 colonies on it (divide by 2 and multiply by 2)?" You are right.

"How do you decide if the new media is acceptable?" 2. "Do you test previously qualified media and the new media at the same time and compare results?" No, that is not necessary.

3. "Do you compare the results that you got earlier with the previously qualified media to the results you get on the new media?" In this case, the previously qualified media and the new media would be tested at different times, but in both tests the same lot of microorganism product would be used. For example, the previously qualified media may be tested in August and the new media in October, but in both cases the microorganism lot is lot 63. One day the standardized inoculum will be past its expiry data and automatically you will have to go to batch number "64." If possible, you could test the two batches of micro-organisms simultaneously, alternatively, your third option should be acceptable.

4. "Do you expect to get within a factor of two of the manufacturer's stated value? For example, if the assay value for a product is stated to be 5.0 E+ 02 CFU per mL, when it is reconstituted do you expect to be within a factor of 2 of 50 colonies if you inoculate an agar plate with 0.1ml?"

Last question: "Do most labs calculate the mean and the standard deviation of the control when they perform growth promotion testing (like a daily process control)?" I don't know.

Respondent 2: I did construct a control chart of the counts and recoveries for 12-15 incoming lots of SBCD and SAB agar plates. The variables were inocula, lot and technician. The data was statistically well -behaved, and the plot would be used in assessing the performance of future incoming lots.

Microbiology Method Validation

Dear Colleagues,

I have a question regarding submission of a microbiology copy of an ANDA to the U.S. FDA in addition to a chemistry copy. If all methods I used for the sterility and bacterial endotoxin test are per USP<75> and <85> general procedures, is there a requirement to put the Microbiology Method Validation package in to CTD 3.2.R.P.2 as these are just the "verification" of compendial methods? Note: CTD 3.2.R.P.1 is my HPLC Method Validation package.

Respondent 1: [Questioner], It depends on how cocky you want or not to be. I have seen some submissions simply claiming that so so test is compendial, and they just place a copy of the official monograph page in the method description/validation sections of the ANDA for that test method. To this approach, some FDA divisions (not all) have come back to request for some partial validation data on such compendial test methods, in accordance with the method validation guidelines.

Yet others (my preference), have duly provided a copy of the official monograph in the method description section of the ANDA and a copy of abridged validation report in the method validation section of the ANDA.

Method/system suitability and precision and/or accuracy suffice for validation of compedial test methods. But if you don't have time to pare down your full validation report and you choose to submit the full report, it won't hurt you in anyway.

Questioner: Yes, I do agree with you that eventually we are going to be asked

to show suitability. That is why I plan to submit a Method Verification package in the CTD 3.2.R.3.P.2 (Microbiology Validation) right next to 3.2.R.3.P.1 (Method Validation for HPLC). Is this what everyone is doing? The verification of microbiology test method for sterility and endotoxin has no precision or accuracy issue, only sensitivity and viability of microbes.

Respondent 2: Validation/verification package for compendial methods need not be submitted in applications. You may claim that these methods are duly validated/verified and package is available for review at site. You may submit it if FDA requests you to do so.

Interest Group Briefing,, continued from page 8

Control organizations to Risk Analysis. The Quality Systems Interest Group also sponsors a Quality Systems Forum on the PDA website for daily networking opportunities. Members participate in Task Forces on compliance and Quality related topics.

IG10 – Microbiology/Environmental Monitoring: The Microbiology/Environmental Monitoring Interest Group addresses topics in pharmaceutical microbiology, rapid microbiology, environmental monitoring, and compendial issues. The group typically has a guest speaker followed by a group discussion. If warranted, task forces are established to respond to issues relevant to microbiologists.

IG11 – Packaging Science: The Packaging Science Interest Group (PSIG) is a venue for the exchange of knowledge and ideas about pharmaceutical packaging. Members come together to develop presentations for PDA programs, organize special meetings on current topics, review USP and FDA proposals and regulations, work on task forces on focused topics and educate each other. Meetings are held in conjunction with PDA meetings.

IG12 – Facilities & Engineering: The Facilities and Engineering Interest Group provides a forum for the discussion of topics and interests related to the design, construction, operation and maintenance of the production and research facilities used for GMP and GLP purposes. Discussions are held in conjunction with two of the PDA meetings: the Annual Meeting and the PDA/FDA Joint Conference, as well as a discussion forum on the PDA website. The format of the Facilities and Engineering Interest Group meetings are an open forum for discussion, where attendees select the topic for discussion and the leader moderates the discussion of peers seeking to reach a better understanding of regulatory expectations and opportunities to share and learn best practices. Where appropriate, the Facilities and Engineering Interest Group will compile these understandings and best practices into technical reports with the contributions and review of interested members.

IG13 - Filtration: The PDA Filtration Interest Group provides a forum for discussion of topics and issues related to filtration in pharmaceutical and biopharmaceutical applications, including sterilizing filtration of liquids and gases, depth filtration of process streams and process systems, and viral removal and purification. Discussions are held in conjunction with PDA meetings (e.g., the Annual Meeting and PDA/FDA Joint Conference) and via discussion forum on the PDA website.

Interest group leaders frequently invite special guest speakers to their sessions

PDA Interest Groups & Leaders

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

SECTION TITLE

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16-17 March 2010
Cologne, Germany

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18 March 2010
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Knowledge Management: A Key Aspect of ICH Q8, 9 and 10 Implementation, continued from cover

support these processes and enabling technologies.

Besides identifying and managing the knowledge, the integrated approach taken must ensure that the "information assets of the enterprise" are shared, Mignosa stressed.

Knowledge management allows the World Bank to streamline its efforts and avoid reinventing the wheel with each new situation. Sharing of information across various functions is a key element of the Bank's streamlining goals.

We must publish

"The program called knowledge sharing [is] very important," Mignosa explained. "You have to share the knowledge. [The World Bank has] a collaborative, multi-directional, international, continuous and active knowledge sharing and learning process. It is available across the board."

Before tackling how to share knowledge, the organization first had to address other elements of a sound KM process. These elements should be considered add-ons to existing information management procedures and include improved information access, alignment of intellectual assets with strategic direction, developing a KM culture (trust, autonomy, collaboration and innovation), and identification of subject matter experts.

Share What Works

Once these were in place, the Bank had to figure out how to build a collaborative environment and culture, as well as integrate KM into the normal workflow and functions of the workers. "Boy, how many times do people hold on to things? They don't share." Mignosa asked rhetorically. "This gets to that one person that knows how to do it better than everybody else. You have five people doing the job, only one person gets the best product out the door, and what do we do in industry? We promote the guy. No! Have him train everybody else to do it the same way."

Companies need to encourage employees to share what works. "We must publish," Mignosa explained. "I guess it is a problem, because people don't like to write, [but] we need to publish [and] get the information out there."

All boiled down, the KM system implemented by the World Bank is playing a key role in helping it achieve its daunting and complex mission, which is to end poverty and improve living standards worldwide.

In the past, when a country needed help, the Bank would form a team to study the problem before solutions could be recommended. Today, when a country needs help, a Bank task manager contacts a community of practice expert to ask for advice on applying technologies and global experience. The resulting solution is stored in database for future use.

Mignosa pointed to a recent example of this process in action. The government of Pakistan asked the Bank for help in acquiring technologies for a deteriorating highway system. Instead of taking a long time to study the problem, the Bank drew upon the knowledge of its 110 communities of practice around the world that it has connected with each other to provide the appropriate help and guidelines. "So instead of just going over there and doing it, they said, 'What's worked around the world? What's worked in different environments? What is this environment and does it fit in anywhere with something we already know? What can we use?'"

Pointing to this example, Mignosa rhetorically asked, "Do you know how much time this can save instead of reinventing the wheel every time?"

FDA Publishing KM Success

The U.S. FDA is recognizing many of the lessons that can be drawn from the World Bank's example. Writing down and publishing what works is currently one aspect of the Agency's KM efforts.

Joseph Famulare, former Deputy Director, Center for Drugs Evaluation and Research, told the PDA/FDA audience that CDER is drafting a new Manual of Policies and Procedures (MaPPs) to capture the lessons learned from the process of transitioning therapeutic biologics from FDA's biologics center to drugs. From the outset, Biologics Licensing Applications (BLAs) were handled slightly differently than New Drug and Abbreviated New Drug Applications (NDA/ANDAs).

"Biotech products very much have an integrated approach to CMC review and inspection," said Famulare, who is now Senior Director of External Influence & Compliance at Genentech. "Part of the CMC [Chemistry, Manufacturing and Control] review is done in CDER's Office of Compliance. Part of the inspection is performed by our expert CMC reviewers in the Office of Biotechnology Products."

The level of integration in the biotech review "is a really good example…of how we wanted to harness…what we learned on our preapproval and post-approval inspections and have that integration with our CMC reviewers, and vice versa, how we can get that knowledge from CMC reviewers over to compliance and inspection."

The MaPPs being developed is essentially an FDA SOP for this process. When completed "this integrated approach will be available not only for all to see within FDA, but more transparent for folks outside FDA," noted Famulare. ➤

Knowledge Transfer Initiative Maps Product Lifecycle

FDA is embarking on a broader "Knowledge Transfer Initiative" to create a formal process of sharing product-specific knowledge from application review under the preapproval inspection program across all products handled by the drugs center. CDER's well-publicized growing review workload, which includes BLAs, NDAs, ANDAs and the burgeoning number of application supplements, is the main driver behind this initiative, but is a valuable case study for any organization trying to get a grip on knowledge management.

"We really need robust systems to understand which applications going through are really most important to cover during our inspections."

The Division of Manufacturing and Product Quality (DMPQ) within CDER's Office of Compliance plays a central role in this process. Working with the review divisions, the group put together a process for the flow of information "from review to inspection, from CDER to our Office of Regulatory Affairs [ORA]," Famulare said.

One aspect of the Knowledge Transfer Initiative is the issuance of Knowledge Transfer Memos from DMPQ to help focus an ORA investigators efforts. In the past, investigators received the CMC section of an NDA and were told to go inspect—which is akin to handing someone a Manhattan phonebook and saying, "here go figure this out," Famulare said. Knowledge Transfer Memos provide the investigators guidance from Headquarters on important areas, like supply chain issues, data integrity questions, questionable or unclear manufacturing controls, process analytical technology use, real-time release testing plans, new validation approaches, etc.

In two years, the number of Knowledge Transfer Memos issued nearly doubled, Famulare reported. "Feedback from the memos will be used to refine and continually improve the program," he said.

FDA's process can be translated to how firms can close the loop internally to ensure knowledge flows down through its various processes, and then back up to product development.

The Q10 definition is "wide-scoped," Famulare said, "but it is also important to think about how we could best harness knowledge to take advantage of all the things that we've talked about in Q8, 9 and 10 and [the forthcoming] 11."

Famulare presented an image depicting the flow of information back and forth between the development of products, commercial manufacturing and the monitoring of process performance and product quality. The Quality System, as defined in Q10, should be set up to ensure the information is flowing between these distinct aspects of the product life cycle, resulting in continuous improvement of commercial manufacturing and the feeding of that knowledge back to the development of similar products in the future.

Too much data collection could hurt, not help

For these kinds of feedback loops to be successful, knowledge management is extremely important. "Certainly, there is a lot of data and information to get to the knowledge that is actually usable," Famulare stated.

IT and People Manage Knowledge

KM is not just about IT systems, an idea stressed by the three speakers.

Famulare stated, "The importance of people in a culture cannot be overemphasized."

Lothar Hartmann, PhD, Head, External Relations, F. Hoffmann-La Roche, said that you must have a strong foundation in order to manage your knowledge successfully. Employee management and IT infrastructure were two of the key factors to successfully manage knowledge.

Hartmann presented an eight-step KM module, similar to the case study presented by Mignosa, that can help a company take its information and create understanding (see **figure 1**). The eight steps are:

- Knowledge identification
- Knowledge acquirement
- Knowledge development
- Knowledge sharing
- Knowledge utilization
- Knowledge preservation
- Knowledge review
- Knowledge goal

Identification of knowledge is dependent on the issue at hand. Once defined, a company must understand its competencies, the processes and people involved and the technology to be used.

Knowledge acquirement is the process of identifying where the right knowledge will come from. "Is it something I have in-house…or do I need to hire consultants or extra people for resolving the problem?" Hartmann explained.

Knowledge development is the process of spreading knowledge acquired to groups or the organization. Echoing Mignosa, Hartmann said it is important to make sure that the company captures the best practices of its employees and disseminates it to other, relevant employees. "Implicit knowledge must be transferred to explicit knowledge."

Knowledge sharing, the next step, is broader. Here, companies must make sure that hierarchical and functional barriers within an organization do not block the transfer of knowledge. "We still have metrics organizations that lead to fragmented islands," Hartmann said. Overcoming this involves the systematic linking of knowledge islands. IT systems are an important aspect in this.

Knowledge utilization forms a key element of lean processing and product life cycle, including QbD applications.

The sixth part of the knowledge management module is knowledge preservation. The challenge with this is to retain essential knowledge within the organization. In order for that to occur, people who possess the knowledge,

matrix units (islands), documentation management and appropriate IT systems are needed to ensure that knowledge does not get lost.

Linked to the ICH Q10 section on management review, knowledge review should challenge the system. Hartmann elaborated on the questions that should be asked: "Do I have the right knowledge available in the right time? Do I need more to increase competence? If it is not possible, what are the alternatives? Are the right key performance indicators in place? Does knowledge management contribute to the effectiveness of processes?"

Hartmann said it was important to know *what* is important to your company. "We cannot know everything, so we should apply quality risk management to filter out what our company feels does not add value to its business."

Mignosa weighed in on this during his presentation, warning that too much data collection could hurt, not help. Speaking from a past experience, he said that in his 25 years at IBM, the company would collect data on everything, but it was never used. "I can remember [IBM] collected 25 cases of data for every disk that they made. [But], all they needed was the serial number." He said when IBM needed a serial number from the disks, it could not generate it from the database. "It was garbage in, garbage out. We had more data than you could shake a stick at and it took a long time to get out of the mindset that you collect everything."

KM and Management Goals Must Align

Hartmann's last step, the knowledge goal, ensures that goals are aligned according to the results of the review, defines knowledge that will be captured, supplements the company's goals, sets new goals, and adjusts the key performance indicators, if needed.

Firms must recognize there is a value chain for knowledge, and the overall value chain of an organization includes both its business processes and its KM processes. "This is where your executive management comes in. If they are not going to protect this chain, it is just going to fall apart. It is unfortunate that this happens too many times when we change upper management," Mignosa said.

It soon could be a matter of regulatory importance. Hartmann noted that an "ambitious" inspector from the MHRA told him that "European inspectors will very soon start to inspect according to how good a company is utilizing the knowledge in this area."

Famulare ended his presentation by telling the audience that knowledge management needs to be implemented within the industry. "There is really no more 'over the wall' transferring from development to tech transfer to commercial manufacturing," he maintained. FDA had a rising expectation for its investigators to see connections across a drug product's life cycle.

[Editor's Note: Turn to the next page to see the Knowledge Management portion of the ICH Q&A document that the Quality Implementation Working Group released in 2009.]

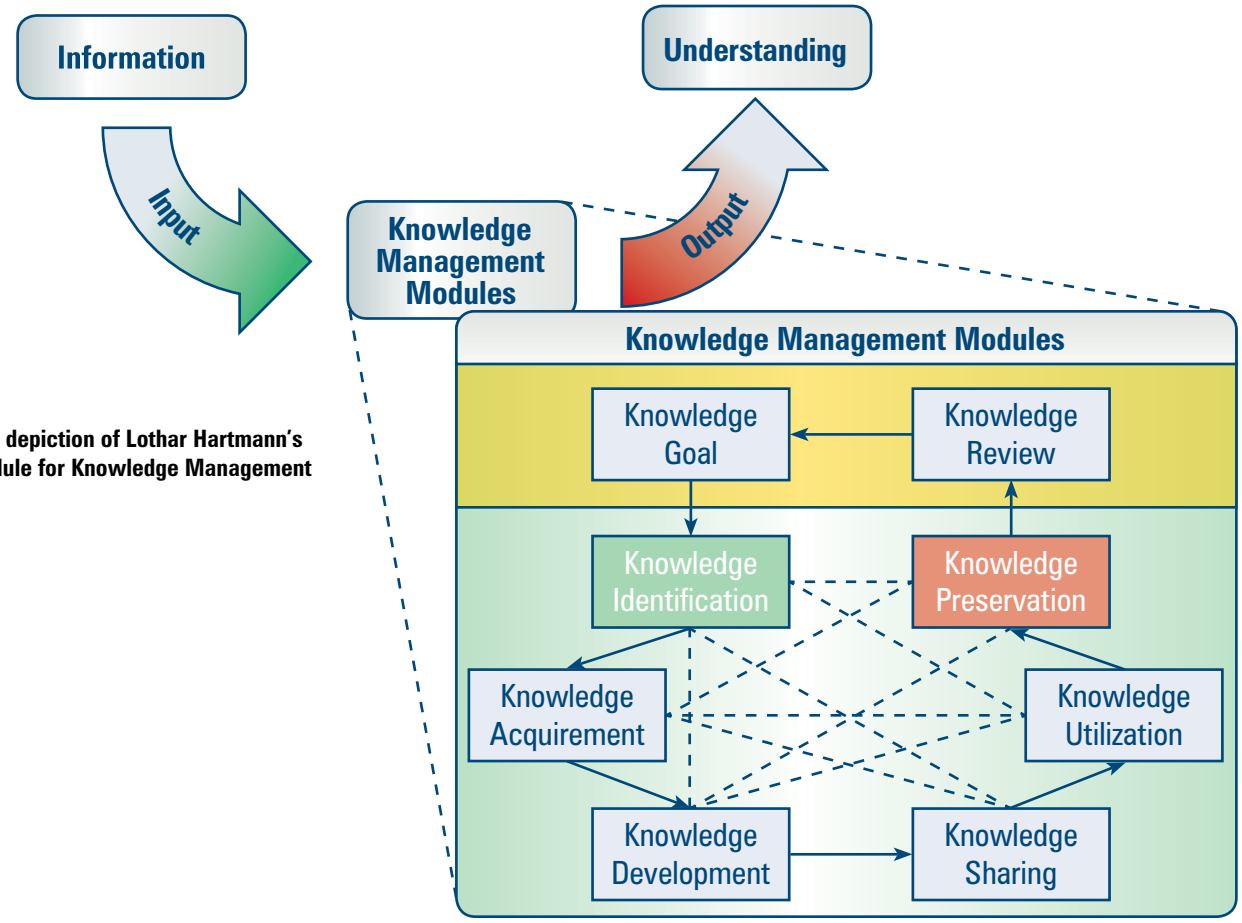

Figure 1: A depiction of Lothar Hartmann's 8-step module for Knowledge Management

Uncertain about Knowledge Management? You're not alone…

The ICH Quality Implementation Working Group (see related story, page 22) developed a Q&A document to help with the implementation of Q8, 9 and 10. The document included the following five questions and answers pertaining to knowledge management.

How has the implementation of ICH Q8, Q9, and Q10 changed the significance and use of knowledge management?

Q10 defines knowledge management as: 'Systematic approach to acquiring, analyzing, storing, and disseminating information related to products, manufacturing processes and components'.

Knowledge management is not a system; it enables the implementation of the concepts described in ICH Q8, Q9 and Q10.

Knowledge Management is not a new concept. It is always important regardless of the development approach. Q10 highlights knowledge management because it is expected that more complex information generated by appropriate approaches (e.g., QbD, PAT, real-time data generation and control monitoring systems) will need to be better captured, managed and shared during product life-cycle.

In conjunction with Quality Risk Management, Knowledge Management can facilitate the use of concepts such as prior knowledge (including from other similar products), development of design space, control strategy, technology transfer, and continual improvement across the product life cycle.

Does Q10 suggest an ideal way to manage knowledge?

No. Q10 provides a framework and does not prescribe how to implement knowledge management. Each company decides how to manage knowledge, including the depth and extent of information assessment based on their specific needs.

- Prior knowledge based on experience obtained from similar processes (internal knowledge, industry scientific and technical publications) and published information (external knowledge: literature and peer-reviewed publications)
- Pharmaceutical development studies
- Mechanism of action
- Structure/function relationships
- Technology transfer activities
- Process validation studies
- Manufacturing experience e.g.,
  – Internal and Vendor audits
  – Raw material testing data
- Innovation
- Continual improvement
- Change management activities
- Stability reports
- Product Quality Reviews/Annual Product Reviews
- Complaint Reports
- Adverse event reports (patient safety)
- Deviation reports, recall information
- Technical investigations and/or CAPA reports
- Suppliers and contractors
- Product history and /or manufacturing history
- Ongoing manufacturing processes information (e.g., trends)

What are potential sources of information for Knowledge Management?

Some examples of knowledge sources are:

Is a specific dedicated computerized information management system required for the implementation of knowledge management with respect to ICH Q8, Q9 and Q10?

No, but such computerized information management systems can be invaluable in capturing, managing, assessing and sharing complex data and information.

Will regulatory agencies expect to see a formal knowledge management approach during inspections?

No. There is no added regulatory requirement for a formal knowledge management system. However it is expected that knowledge from different processes and systems will be appropriately utilized.

Note: "Formal" means it is a structured approach using a recognized methodology or (IT) tool, executing and documenting something in a transparent and detailed manner.

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Twelve Q4B Analytical Tests Harmonized—Four to Go

The *PDA Letter* takes a look at Pharmacopeial Harmonization

Emily Hough, PDA

Since it's inception twenty years ago, the International Conference on Harmonisation (ICH) has been instrumental in creating unified chemistry, manufacturing and control submission criteria in three regions—Europe, Japan and the United States—and a host of other areas that "observe" the ICH guidelines. This has led to a savings of time, effort and cost to industry.

In November 2003, ICH created the Q4 expert working group to address eleven general test chapters discussed within the development of the ICH Q6A guideline on drug product specifications. Leading the effort is a group called the Pharmacopeial Discussion Group (PDG). The ICH Steering Committee expanded the scope of the project in November 2008, and approved five new general chapters to the Q4b process.

Progress with harmonization has been slow, however. Currently, out of the 16 general test chapters, nine have reached the consensus stage, Step 5 and three have reached Step 3 (proposal). Four tests are currently working their way through the PDG process. The PDG undertakes a similar process than the ICH (see box below).

2009 was a remarkable year for the PDG, as a number of chapters advanced along the process. In October, three chapters reached Step 5 of the ICH process and two reached Step 3 of the process.

When asked about the Q4 process, **Sue Schniepp**, Director, Pharmaceutical Quality, Quality Systems, Antisoma, said, "Pharmacopeia harmonization is

The Pharmacopoeial Discussion Group Process

Stage 1 Identification: Based on feedback from users, the PDG identifies topics to be harmonized among PDG pharmacopeias and nominates a coordinating pharmacopoeia for each subject.

Stage 2 Investigation: The coordinating pharmacopeia for the subject retrospectively collects the information on the existing specifications in the three pharmacopoeias. Then it prepares a draft monograph or chapter accompanied by a report giving the rationale for the proposal with the validation data. This stage ends with a proposal draft; this draft is accompanied by supporting comments or data that explains the reasons for each test method or limit proposed and is sent by the coordinating pharmacopeia to the secretariats of the other two PDG pharmacopoeias.

Stage 3 Proposal for Expert Committee Review: The three pharmacopoeias forward the proposal draft to their expert committee. Comments by the experts resulting from this preliminary survey are sent to their respective pharmacopoeias. The coordinating pharmacopoeia reviews the comments reviewed and prepares a harmonized document accompanied by a commentary discussing comments received regarding the previous text and providing reasons for action taken in response to those comments.

Stage 4 Official Inquiry: The harmonized document and the commentary are published in the forum of each pharmacopoeia in a section entitled, *International Harmonisation*. The draft is published in its entirety. Comments regarding this draft are sent by readers of the forum to their respective pharmacopeial secretariat. Each pharmacopeia analyzes the comments revised and submits its consolidated comments to the coordinating pharmacopoeia within two months of the end of the review/comment period. The coordinating pharmacopoeia reviews the comments received and prepares a draft harmonized document accompanied by a commentary discussing comments received regarding the previous text and providing reasons for action taken in response to those comments.

Stage 5 Consensus: The draft harmonized document is reviewed and commented on by the other two PDG pharmacopeias within four months of receipt. The three pharmacopeias do their utmost to reach a full agreement with a goal to reach a final consensus document. If a consensus has not been reached, the coordinating pharmacopeia prepares a revised version by taking relevant substantiated comments from the original draft harmonized document from the two other pharmacopoeias into consideration. The revised document together with the commentary is sent to the secretariats of the other two PDG pharmacopeias. The revised document is reviewed and commented by the other two PDG pharmacopoeias within two months of receipts. This review/comment and revision process of the draft harmonized document repeats until the three PDG pharmacopoeias reach a consensus or until the coordinating pharmacopeia considers that harmonization by attribute should be applied.

If the coordinating pharmacopoeia considers that certain attributes in the monograph or certain provision in a general chapter are such that it will not be possible to harmonize within a reasonable time period, then harmonization by attributes/provisions are applied. If this is applied, the text only includes harmonized attributes/provisions.

Stage 6 Regional adoption and implementation: The document is submitted for adoption to the organization responsible for each pharmacopoeia. The pharmacopoeias inform each other of the date of implementation in the particular region.

Stage 7 Inter-regional acceptance: Following the Q4B evaluation process, a formal notification of regulatory acceptance is posted by ICH.

Timeline Of The Harmonized Q4b General Test Chapters

Test	ICH Step	Date
Dissolution	5	October 2009
Polyacrylamide Gel Electrophoresis		
Tablet Friability		
Analytical Sieving	3	
Capillary Electrophoresis		
Disintegration	5	June 2009
Sterility		
Microbiological Examination of Nonsterile Products (3 Tests)	5	November 2008
Uniformity of Dosage Units	3	
Test for Extractable Volume of Parenteral Preparations	5	June 2008
Test for Particulate Contamination		
Residue On Ignition/ Sulphated Ash	5	November 2007

2009 was a remarkable year for the PDG, as a number of chapters advanced along the process

slow and has been for years. That is why people rely more on ICH Q6A—it is generally accepted, is a little bit quicker and gives a little more latitude sometimes."

The Head of the Analytical Development within the Product Development Department at APP Pharmaceuticals, **Pearle Torralba**, PhD, said it was an "accomplishment" that so many of the original chapters have now been harmonized, but thought it was "inconvenient" for the others to remain out of harmony. "It simply means one will have to apply separate criteria and/or standards to that attribute specific to one's needs."

Torralba told the *Letter* that she would like to see other compendia tests added to the guideline. "Heavy Metals testing is currently very unpredictable. There just seems to be no cohesive guidance on container closure testing. Leachable and extractable [testing] is very controversial, as well." **[Editor's Note:** ICH is developing a guideline on metal impurties, refer to p. 25 for more details.**]**

In 2009, during the ICH meeting in Japan, PDG based on industry feedback named five areas of testing for addition to the PDG process, but not those mentioned by Torralba. The areas targeted are chromatography, infrared absorption spectroscopy (including near IR), pH and water determination (volumetric and coulometric).

Harmonized Implementation is a Key ICH Target

Walter Morris, PDA

The International Conference on Harmonisation (ICH) is taking its implementation efforts to a new level in recognition of the complexity of topics involved in the latest wave of quality guidances—Q8, Q9 and Q10.

Over its first two decades (ICH turns 20 in April), the ICH Steering Committee has consistently demonstrated its willingness to ensure harmonized and consistent interpretation and implementation of its documents, not only in the three primary regions, but in other regions looking to adopt the ICH guidelines. The roll-out of the guideline on GMPs for active pharmaceutical ingredients (Q7) is a primary example. Q7 Expert Working Group members participated in numerous training sessions on Q7, many of which were managed by PDA, to help both industry and regulators work towards a unified approach.

The paradigm-changing nature of the guidances on drug development, risk management and quality systems requires a whole new approach, and the ICH Steering Committee responded with the creation of a Q8, 9 and 10 Implementation Working Group (Q-IWG). ICH recognized in the Q-IWG sanctioning document (Nov. 2007) that "deviating views have been observed, setting up non-harmonized interpretation and new expectations beyond the intention of these ICH guidelines."

In a relatively short period of time, the Q-IWG has been able to put together a comprehensive Q&A document covering a variety of topics important to the implementation of the three Q-documents. The group first met in June of 2008, and the first version of the Q&A document reached Step 4 by April 2009. Additional questions were added to the document and approved by June 2009, and the document was corrected two times by October 2009.

Topics covered in the Q&A document are:

- QbD
- Pharmaceutical Quality System
- ICH New Quality Guidelines' Impact on GMP Inspection Practices
- Knowledge Management
- Software Solutions

So many questions were addressed under the QbD umbrella, the topic was subdivided into three, more specific categories: Design Space, Real Time Release Testing and Control Strategy.

The Q-IWG is still receiving questions for the document. According to the ICH website, "The Quality IWG will continue to develop a Questions & Answers which will be submitted for adoption by the ICH Steering Committee." Those wishing to submit questions or comments can send them to Q8-9-10@ich.org.

The Q-IWG is working on an "enhanced implementation training program" for 2010, according to group member **Stephan Rönninger, PhD**, Global Quality Manager, Global Quality, F. Hoffmann– La Roche, who discussed the activities of the group at the *2009 PDA/FDA Joint Regulatory Conference* in September.

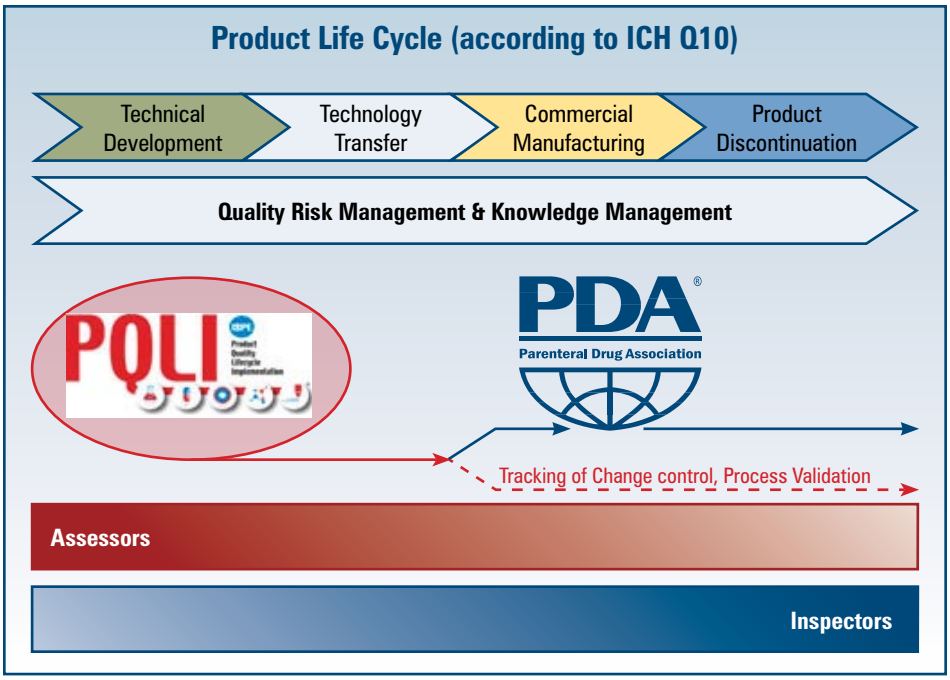
Three, two-day workshops are currently being planned for each of the primary ICH regions. The first will be in Europe in June, the second will be in the United States in October, and the third will be in Japan late in the year.

PDA and ISPE are cosponsoring the workshops in Europe and the United States with the IWG. Already PDA has scheduled the workshop in the United States for October 6–8 in Bethesda, Md. More information will be provided in the *PDA Letter* and on the website about these workshops in the coming months.

The Q-IWG recognizes the important role organizations like PDA will play in facilitating the harmonized implementation of Q8, 9 and 10, and indeed, helping to establish the new paradigm for manufacturing, control and regulation.

Rönninger is involved with PDA's "Paradigm Change in Manufacturing

Figure 1: Stephan Rönninger illustrated how ISPE's PQLI and PDA's PCMO fit into the implementation strategy for ICH Q8/9/10



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EFPIA
Georges France (Wyeth)
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Operations" (PCMO) initiative and discussed how it will help facilitate the adoption of Q8/9/10 concepts into the manufacturing area. The goal of PCMO is to drive the establishment of "best practice" documents and/or training events in order to assist pharmaceutical manufacturers of Investigational Medicinal Products (IMPs) and commercial products in implementing the three quality ICH guidelines. The project facilitates communication among the experts from industry, university and regulators, as well as experts from the respective ICH Expert Working Groups and Implementation Working Group. See the box below for PCMO's objectives.

Likewise, Rönninger credited the ISPE Product Quality Lifecycle Implementation project for facilitating the uptake of Q8/9/10 principles into the product development/technology transfer areas. It is important that both of these initiatives complement, rather than compete with each other.

PDA PCMO's Objectives

PCMO follows the product lifecycle concept and has the following strategic intent:

- Enable an innovative environment for continual improvement of products and systems
- Integrate science and technology into manufacturing practice
- Enhance manufacturing process robustness, risk based decision making and knowledge management
- Foster communication among industry and regulatory authorities

For more information, go to www.pda.org/pcmo.

ICH Global Cooperation Group: Expanding Harmonization Worldwide

The ICH Global Cooperation Group (GCG) is entering its second decade of existence, and never has its mission been more important. As the international drug market and supply chain expands to all areas of the world, the raising of national standards in every region is a critical component to ensuring the availability of safe and effective products and supplies.

The GCG's mission is to *promote a mutual understanding of regional harmonization initiatives in order to facilitate the harmonization process related to ICH guidelines regionally and globally, and to facilitate the capacity of drug regulatory authorities to utilize them.*

One way GCG works to fulfill this goal is by linking with regional harmonization initiatives, like the Asia-Pacific Economic Cooperation (APEC) group, the Association of the Southeast Asian Nations (ASEAN), and the Gulf Cooperation Council.

In 2008, the GCG invited drug regulatory agencies to participate in the effort, expanding the group's ability to spread the ICH guidelines. The group strategically invited authorities from countries with advanced understanding of ICH concepts, with significant participation in multinational clinical trials and/or important centers of API/drug product supplies. Authorities involved so far are: Australia, Brazil, China, Chinese Tapei, India, Korea, Russia and Singapore.

To help these regions understand ICH guidelines, they are invited to participate in ICH meetings and comment on Step 2 guidelines.

Since 2008, the GCG has endorsed and contributed to a growing number of workshops, particularly in Asia.

ICH Q11 on Track for Step 2 in 2010

Development and Manufacture of Drug Substances Guideline to Fill ICH Gap

Walter Morris, PDA

The Expert Working Group (EWG) developing ICH Q11 on the development and manufacture of drug substances is moving steadily towards submission of a draft for Steering Committee scrutiny later this year. If accepted, the document will reach ICH Step 2 and will be published in the three ICH regions for public comment.

It is the goal of the Q11 Expert Working Group to cover both traditional chemical APIs and biotechnology ingredients.

According to the group's work plan, approved by the Steering Committee in 2007, the proposed guideline *fills a gap in the regulatory framework and describes the suggested contents for the 3.3.S.2.2 "Description of the manufacturing process and process controls," 3.2.S.2.3 "Control of materials," 3.2.S.2.4 "Control of critical steps and intermediates," 3.2.S.2.5 "Process validation and/or evaluation" and 3.2.S.2.6 "Manufacturing process development" sections of a regulatory submission in the ICH M4 Common Technical Document (CTD) format.*

The document is intended to reduce the time and effort spent by regulators *searching for missing or misplaced manufacturing development information as a result of firms' misunderstanding of regional differences.* In turn, the document is supposed to help companies reduce the resources they spend answering such queries from regulators by helping them prepare a more effective submission at the outset.

At ICH's public Japan Symposium in 2009, Q11 rapporteur **Brian Withers**, EFPIA, provided an update on the EWG's progress. He announced that the working structure of the document closely follows the aforementioned CTD sections.

Priority harmonization subjects currently under discussion include starting materials, process validation, control strategy and the development section.

Following his presentation, Withers answered questions from the audience. The discussion was captured on a "Proceedings" document from the meeting, which is available at the ICH website. The questions to Withers on Q11 are reproduced here:

Question: I think the speed of the harmonization process is very slow. Of course, I know it is very difficult. But, if we could divide the guideline into chemical compounds and biotechnological products, it is easier to develop such a guideline. What is the merit of combining the biotech products and chemicals?

Withers: I think that is a very good question. The question that you asked is one that impacted on the time it took to get agreement to prepare the guideline in the first place. However, within the expert working group, we have members who have an interest in biotechnological products and others with an interest in chemical compounds. What we discovered in our discussion is that we have more in common than there are differences. We found that the principals apply to all molecules and there are some things where there is more emphasis on one molecular type than another molecular type. We are finding more agreements than differences.

Question: You showed us the Priority Harmonization Subject List in which five items from the starting material to the process validation are listed. Among the five items on the list, which one do you think is the easiest to harmonize, or has the least gap within the three regions?

Withers: I can probably tell you which one is the hardest. Currently, the hardest one might be starting materials because at the moment it is a difficult subject since there are different views between the regions, so I think that might be the hardest. The easiest one might be guidance for process validation. Principals are already generally accepted across the three regions.

Question: Two years ago, I attended the Quality of Biotech Products meeting. At that time, the SC asked us to incorporate the idea the "Quality by Design" into the guidance. I am surprised with your lecture because the word of the Quality by Design is no where. So, I would like to know what has happened.

Withers: For Q11, there is definite interest in expressing the principals outlined in Q8R and to give examples of how different approaches to the development could be followed and that will include the Quality by Design. One of the challenges is that we must make a balance so that the guideline can be applicable to a company whichever approach they choose for the development. So, it has to cover a wide spectrum of approaches to the development. Certainly, a lot of the discussion within the expert working group has been done about the principals of the Quality by Design and how they apply to the development of the molecule irrespective of the complexity. So, it is certainly vey much on our agenda.

Harmonizing Metal Limits is Latest ICH Effort

Steering Committee Adopted Q3D Project at October Meeting

Walter Morris, PDA

The ICH Steering Committee has decided to expand its Q3 series of guidelines on impurities by sanctioning the development of Q3D on metal impurities.

ICH's current impurities guidelines cover organic impurities (Q3A and Q3B) and residual solvents (Q3C), but none yet exists for inorganic impurities, the category into which metals fall.

The Final Concept Paper for Q3D states:

A harmonized approach for control of metal impurities, including a list of specific metals to be limited and appropriate limits for these metals, would be beneficial to help avoid uncertainty and duplication of work for industry to meet requirements that may otherwise differ between the ICH regions.

Currently, the only regulatory guidance on specification limits for residues of metal catalysts and reagents is provided by the European Medicines Agency, according to the concept paper. Similar guidance is not provided by the U.S. FDA or the Japanese MHLW.

The paper states that the guideline would emphasize the control of supply chains and risk management. The intended guidance *would be outside the usual scope of pharmacopeias and would require significant input from regulatory authorities.* However, in support of the guideline, *harmonized analytical procedures should be established by the pharmacopeias for determining levels of metal impurities.* Regarding such compendial procedures, the concept paper was careful to add the caveat *with allowance for use of any appropriate validated procedure for a particular application.*

This topic was first broached at the November 2008 ICH meeting in Brussels. There it was discussed that a process similar to Q3A, B and C was not only an instructive model but a preferable model for Q3D, with the end result being the incorporation of the ICH guideline into the pharmacopeial standards dealing with impurities.

The Q3D Expert Working Group will be composed of chemists with backgrounds in quality assurance and regulatory affairs and toxicologists. The concept paper notes that the group can start with the EMEA guideline, thus making it feasible for the project to be completed within a one to two years of initiation of work.

Quality & Regulatory Snapshot

Health Authority *Special Report*

Present & Future of European GMP/GDP: Update from the Dec. Interested Parties Briefing Meeting

Martyn Becker, Martyn Becker Associates; Stephan Rönninger, F. Hoffmann-La Roche; Tesh K Patel, Astellas Pharma

[**Author's Note:** The three authors represented PDA at the December 2009 Interested Parties Briefing Meeting at the European Medicines Agency offices in London, at which a number of industry organizations were represented. The following is an informal summary of the meeting prepared by the PDA delegates and is organized by topics covered. While every effort has been made to be accurate and the summary has been shared with the Agency, readers should not use this information to make compliance or GMP decisions. For more information on this meeting, see the box at the end of the article. PDA's **Jim Lyda** contributed to this report.]

GMP Guidance Update

An overview was presented by the European Medicine Agency Inspectors' Working Group on developments in GMP and related guidance:

- EU GMP Chapters 1 and 2 have been updated in light of ICH Q10. The revised drafts were released for consultation on the European Commission's website at the end of November 2009 and are now open for comment until May 31, 2010. It is understood that the EU GMP guide was to be complemented by the addition of ICH Q10 as Annex 21.
- Chapters 3 (Premises and Equipment) and 5 (Production) would be updated regarding dedicated facilities using a strategic approach, following input from toxicology experts. When finished, this would be shared with the U.S. FDA under the Transatlantic Simplification Process. [**Editor's Note:** See related Regulatory Brief, p. 32]
- Chapter 7 (Contract Manufacture and Analysis) will be updated to reflect the current situation of outsourcing. A concept paper has been published with comments expected by the end of January 2010.
- Annex 2 (Manufacture of Biological Medicinal Products for Human Use) has been redrafted into its second edition, which will be released for a second public consultation in the near future.
- Annex 11 on computerized systems is expected to be available in mid 2010, together with consequential changes to chapter 4.
- Changes to Annex 13 on Manufacturing of Investigational Medicinal Products (IMPs) have been made regarding QP certification and requirements for QC independence.
- Annex 14 on blood-derived products has been revised and is anticipated in mid-2010.
- The EU GMP Part II on active substances has been updated to include Quality Risk Management principles and is now awaiting publication.

API Inspection Pilot Program

Participating countries in the pilot program include the United States, France, Germany, Italy, UK and Australia. Common sites in territories outside their jurisdictions have been identified for collaboration, including common inspection, with some already having been undertaken. Inspection reports from inspections of interest to more than one party have been requested by the European Directorate for the Quality of Medicines & Healthcare (EDQM), European Medicines Agency, the U.S. FDA and Australia's TGA. The European Medicines Agency has proposed conducting up to 20 joint inspections, one of which has already been completed with the FDA. The pilot has been extended to the end of 2010. A report will be published at the end of the pilot project.

Other GMP-Related Items

The new GDP guide was still under development, with no fixed release date as of yet.

Work had been undertaken on Site Master Files (SMF) in collaboration with the Pharmaceutical Inspection Co-operation Scheme (PIC/S), which was awaiting public consultation. Guidelines on Site Master Files are expected to form a new Part III in the GMP Guide.

Industry topic – Risk-based Scheduling of Audits

Stephan Rönninger, co-Chair of PDA's Regulatory Affairs and Quality Committee, presented the potential to harmonize the way that industry undertakes scheduling supplier audits and the way that regulators

undertake scheduling of inspections (the outcomes and planning processes are the same). There are different approaches to risk-based inspection scheduling. The MHRA and European Medicines Agency processes cited as examples of models that other regulators were now using.

The presentation discussed models for audit determination published in the Novermber/December *PDA Journal of Pharmaceutical Science and Technology* (S. Rönninger, M. Holmes, "A risk-based approach to scheduling audits," vol. 63, pp. 575-588, http://journal.pda.org). This paper shows a process to determine when an audit of a supplier or inspection of a manufacturer should take place. Included is a "black box" system involving a data calculator for determining the trigger point for an inspection. Risk-based inspections are welcomed, although the provision of many long questionnaires by different inspectorates is a concern.

Much of the information requested in the questionnaires is already available in the PIC/S Site Master File. A system is proposed that will focus on high-risk suppliers and is based on the ICH Q9 processes, taking into account severity, probability and detection. A document is being published by PDA on this topic.

Regarding suppliers, some necessary aspects of tracking and decision-making regarding the scheduling of audits are complexity, availability and history. This concept is part of the Paradigm Change in Manufacturing Operations (PCMO) project (www.pda.org/pcmo) currently being undertaken by PDA.

Response

The Inspectors' Working Group responded positively to the process presented, indicating that it was a well-thought out application of ICH Q9 in relation to audit/inspection scheduling. The European Union is to adopt the Site Master File concept formally into the EU system in due course. Some of the data currently requested by authorities does not exist in the SMF, and there is also a perceived variability of data in the SMFs.

Industry topic – Quality of Guidance Documents

The European Federation of Pharmaceutical Industries and Associations (EFPIA) has proposed that a training system could be developed to ensure production of guidance documents that are effective, efficient, within resource constraints and are developed via industry and regulator collaboration. This relates to Annex 2 development and the development of an Annex 1 summary document by Swissmedic following the 2008 PDA-ISPE-PIC/S Workshop in Geneva that identified a harmonized interpretative stance by the EU member states and PIC/S countries. Guidances could be developed collaboratively by face-to-face meetings rather than by the circulation of pre-formed drafts. This would facilitate a mutual understanding so that the ongoing process of re-drafting and public consultation would be more

efficient. In summary, the process could consist of a stakeholder pre-draft meeting, consensus drafting, roll-out and training with Q&A-type documents to address specific concerns. Opportunities exist for scientific input by organizations such as PDA and ISPE.

Response

It is agreed in principle that it is important for there to be a better exchange of GMP information. However, there is a potential resource issue. For certain types of documents, first contact with industry would be important on a limited basis. Otherwise, response to concept papers would be the time and place for input of alternative proposals and discussions. Regarding interpretations and training—there is experience already with Q8-10 and there is also much resource implication, which would mean currently that this may not always be possible. As indicated earlier, there has been a PIC/S, European Medicines Agency and Swissmedic interpretative document regarding Annex 1 as an example of a document that can be used for training. It should perhaps be discussed whether a face-to-face meeting is appropriate at the start of a particular process.

Industry topic – Role of the QP

The QP Association presented results of a survey regarding whether audits of API manufacturers should be undertaken by QPs. This is currently the requirement of some member states although this function should be capable of being delegated. It should be accepted that QPs can never have all available detailed process knowledge. Differences in interpretation by different member states were being observed, especially with issues such as batch-specific variations. There should be the potential for more than one QP to be nominated on the Manufacturing Authorization in some member states, since QPs can delegate responsibility but not accountability.

The reporting structure of QPs should be clarified since it was possible for a QP to report to the Head of Production, although in small organizations this was sometimes inevitable. Uniform enforcement is also an issue and should be incorporated into Annex 16. QPs are required to be pharmacists in some member states, such as France and Germany, whereas a relevant scientific discipline was acceptable in the United Kingdom. This approach should be harmonized if possible so that the European Medicines Agency and the Commission could ensure consistent application across Europe.

Response

The European Medicines Agency published Q&A document indicates that audits of IMPs can be undertaken by experienced auditors rather than QPs. The QP however must be satisfied with the process. The level of detail in the reflection paper is inappropriate to be included in Annex 16. Annex 16 does not feature on the 2010 work plan for the GMP/GDP IWP. ➤

Parenteral Drug Association Training and Research Institute (PDA TRI)

2010 ASEPTIC PROCESSING TRAINING PROGRAM

2010 SCHEDULE:

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

Session 2:
Week 1: March 22-26
Week 2: 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

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

LEARNING OBJECTIVES:

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

- Demonstrate an increased proficiency of techniques and skills relating to aseptic processing
- 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:

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Regarding the acceptance of a deputy QP, relative national and European Union responsibilities would need to be defined. IMP assessments are normally undertaken using a risk-based approach by competent authorities. The position and role of QPs is assessed on a case-by-case basis particularly in small organizations.

National legislation for different member states has specific requirements for experience of QPs that cannot be changed by the European Medicines Agency. Based on the above issues and the desire for consistency on both the role of the QP and interpretations between Member States, there is perhaps a strong case to support a review of Annex 16.

Industry Topic – Process Validation

A white paper presented by EFPIA builds on current references within the EU GMP Guide. It is similar in concept to the current FDA draft paper on process validation, focusing on ICH Q8-10 and the use of holistic science and risk-based approaches to validation throughout the product life cycle. The process uses the same three-phase approach as FDA regarding process development, flexibility and continuing process verification based on Quality Risk Management, making it potentially possible that a single "validation batch" could be appropriate. Benefits are better understanding of processes, continual improvement, PAT support and real-time-release, as well as guidance for inspection, although it is essential that scientific rationales exist which would be available at inspection. This could be useful in the updating of the EU GMP guide process validation guidance update in 2010 and also an update of Annex 15.

Response

Inspectors would define their own methods on how to inspect process validation. The Quality Working Party (QWP) has already initiated revision of the process validation guidance, and this document has been shared with the GMP/GDP IWG. It is recognized that it is necessary for inspectors and assessors to continue to work collaboratively in this area.

The Interested Parties Meeting is sponsored by the European Medicines Agency Inspections Sector and is usually held once per year in conjunction with a meeting of the Agency's GMP/GDP Inspectors' Working Group. Attending the current meeting were representatives of the inspectorates from each of the 27 European Union Member States, from accession countries and the European Economic Area countries, Switzerland, and the European Commission. The meeting was chaired by David Cockburn, Head of the Manufacturing and Quality Compliance unit of the Agency's Compliance and Inspection Sector.

Industry Topic—Atypical Actives

The Association of the European Self-Medication Industry (AESGP) has developed a paper promoting a unified position on atypical actives. Atypical actives are materials also used in other industries that were not keen to adopt pharmaceutical GMP principles (although a definition has been proposed by industry), therefore providing an issue for QPs. The European Medicines Agency Q&A document is helpful, but it is not being followed by some member states. Of responses from twelve member states requesting feedback on acceptance of risk-based approaches associated with the QP declaration, two indicated that risk-based approached were not being accepted. Guidance is suggested from the Inspectors' Working Party (IWP) regarding risk-based approaches and inclusion of some kind of reference in EU GMP. Additional "points to consider" documentation, such as MHRA has on its website may be useful for other agencies to consider.

Response

The group pointed out that QP declarations are a dossier matter and GMP/GDP is not the lead for this topic. However, it was confirmed that a declaration is always needed and it was also noted that some declarations are of poor quality and perhaps it is this that causes problems. QWP is currently working on a recommended format, which might help.

Industry Topic—Supply Chain Security

ISPE is developing a white paper on supply chain security with requests for collaboration and contribution from regulatory authorities. This is a global paper covering all suppliers and geographic regions and will be published as an ISPE guidance document. The draft provides guidance on subjects such as signal detection, deterrence and prevention of adulteration, counterfeit, diversion and so on and will serve as an initial teaching and discussion document. The document would also address some elements of Good Distribution Practice. The guidance should be issued by the end of January 2010.

Other Business

The European Medicines Agency is considering development of a concept for the institution of a "pedigree" system for Active Substances used, such that documentation would be available at inspection to identify each active and its supply chain as known. This concept is still in early discussion stage and requirements were being considered regarding a format that could facilitate this process. There will be a consultation opportunity should such guidance be proposed.

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Regulatory Briefs

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

North America

U.S. FDA Wants Feedback on draft ICH Q4B Annexes 11 and 12

The Federal Register has announced that comments are due by February 16 on draft ICH Q4b guidances: Annex 11 on Capillary Electropheresis and Annex 12 on Analytical Sieving.

The draft guidances convey recognition of the three pharmacopoeial methods by the three ICH regulatory regions and provides specific information regarding the recognition.

U.S. FDA Clinical Trail Workshop Registration Available

The U.S. FDA has announced a public workshop on Clinical Trial Requirements, Regulations, Compliance and Good Clinical Practices on March 3-4, 2010 at the Wyndham Orlando Resort in Orlando, Fla.

Guidances Covering Annex 5, 8 published by the U.S. FDA

The U.S. FDA has published two guidances that are a part of the Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions. One guidance contains information about sterility testing (Annex 8) and the other conveys information about disintegration testing (Annex 5).

The guidances convey recognition of the three pharmacopoeial methods by the three ICH regulatory regions and provide specific information regarding the recognition. The guidances recognize the interchangeability between the local regional pharmacopoeias, thus avoiding redundant testing in favor of a common testing strategy in each regulatory region.

U.S. FDA Guidance on PET Drugs Published to Provide Clarity to Final Rule

A Final Rule, by the U.S. FDA, providing regulations on cGMP for Positron Emission Tomography (PET) drugs has been published. The regulations will apply to approved PET drugs. For investigational and research PET drugs, the requirements to follow CGMP may be met by complying with the GMP regulations and/or by producing PET drugs in accordance with the USP General Chapter on compounding PET radiopharmaceuticals. The regulations are effective December 12, 2011.

A guidance entitled, *"PET Drugs – Current Good Manufacturing Practice (CGMP)"* has also been published in the Federal Register to help producers of PET Drug products better understand FDA's thinking concerning compliance with the PET cGMP regulations.

Registration should be made by February 26, 2010.

Europe

European Commission Regulation Expands Variation Application Procedure to Mutual Recognition and Centralized Procedure

An application form for variations to a marketing authorization for medicinal products will now be used in the mutual recognition and the centralized procedure in accordance with Commission Regulation (EC) No. 1234/2008.

This variations regulation aims to establish a simple, clearer and more flexible legal framework for variations to marketing authorization while ensuring a high level of protection of public and animal health.

European Medicines Agency Consults Toxicological/Pharmacological Experts Regarding Dedicated Facilities Policies

The European Medicines Agency is making progress in its effort to align its dedicated facilities policies with the ICH guidance, Q9, Quality Risk Management, according to a recent update.

Key Regulatory Dates

Comments Due:

Feb. 16
Annex 11 and Annex 12

Workshops:

Feb. 26
Aspects of Clinical Trials

New Regulation/Guidance:

Dec. 12, 2011
Final Rule on PET Drugs

The Agency is looking to clarify the dedicated facilities language in the existing GMP guide. Specifically, Chapters 3 (Sec. 6) and 5 (Sec. 18, 19) were singled out in a 2005 Concept Paper as lacking clarity with respect to when a medicinal product should be manufactured in dedicated, self-contained facilities.

In looking at the different aspects of the issue, an Agency drafting group has received input from toxicologists and pharmacologists. The Agency recommends companies also consult with toxicologists whenever introducing a product into a shared facility for product types covered by GMP Annexes that do not contain language on dedicated facilities. Currently, only new draft Annex 2 (biologicals), which is due out for comment later this year, and Annex 4 (veterinary products) address this issue.

PDA
Parenteral Drug Association

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At this conference you will interact with experts in vaccine development, manufacturing, quality and regulatory science from both the industry and the FDA. A complementary mixture of plenary, focused break-out and breakfast sessions will examine case studies that illustrate real-life vaccine development challenges such as the recent lessons learned from the pandemic flu experience. Additional focused topics 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 substrates, expression and delivery systems
- Technical bridging of changes during development and application of comparability protocols
- Challenges of developing therapeutic vaccines for non-infectious disease indications

Sessions will also examine advances in vaccine technology and applications, paving the way for new options for disease prevention and treatment.

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Coming Out Of The Recession – Creating An Opportunity Mindset

Joe Calloway

Hopefully you didn't miss it. It's dominated the news for a year. It's been described as difficult, daunting and even devastating. People have referred to it as a meltdown and a disaster. It's the recession. But no crisis can last forever. One day soon, we'll wake up and the recession will be nothing but a memory. If you act expeditiously, you will be able to capitalize on the business opportunities that the recession has created.

The recession that we are currently emerging from continues to present what may be the greatest opportunity you'll ever have to advance your business, accelerate your strategy, and gain significant market share over your competition. There are three reasons this is true:

Some of your competitors checked out. They dug in, hunkered down and chose to ride it out, leaving an opportunity for your business to garner market share. Motivational speakers told everyone to "refuse to participate in this recession." You should hope that your competition did just that. Recessions create incredible opportunities but you have to jump in and take advantage of them.

Change in the economy creates changes in leadership. In a recession, customers, whether business or retail, gravitate toward strength and leadership. Drastic change can cause existing market leaders to hesitate or falter, creating a vacuum for you to move into. It can also give market leaders their best opportunity to extend their lead, showcasing their strengths as the also-rans run for cover. In marathons the lead usually changes hands or is extended in the toughest parts of the race.

Mindset becomes more important than ever. Mindset, or the way you think about business, becomes even more important in a recession. A company with a mindset, or culture, of everyday innovation and relentless improvement can improve its position more quickly now than ever before. It's been said that a recession is a reallocation of money from the timid to the bold. Be bold.

There are those that will say that to talk of the opportunity of a recession isn't being realistic. They are wimps. Nothing is more realistic than to act on the opportunity presented by economic upset. A real estate broker who worked through the great economic meltdown of 1980 (when the prime rate reached upwards of 20 percent) said, "God has given our competition the opportunity to find another line of work. It's our job to help them do just that."

It's all about your mindset. If you refuse to see the opportunity of the recession, or any other circumstance for that matter, there's no way you can take advantage of it. The following are key components in creating an opportunity mindset that can make the recession work for you:

Begin with the end in mind. Most companies execute business strategies without having a clear, compelling idea of what they are aiming for or how to get there. Know exactly where you want the new economy to take you. Clarity of your vision and your goals is the starting point for an opportunity mindset.

Stop talking about it – take action. Successful organizations and individuals have a great propensity to action. While others talk about what to do, leaders do it. Don't let the after effects of the recession freeze you into inaction.

Be willing to fail. If you are waiting until you are 100 percent sure of success before you try a new idea, then you'll never do anything. Winners know that even if an idea fails, they gain new information, which puts them on the correct path. The recession changed all the rules. The marketplace is looking for new ideas.

Give up being an expert. Experts get caught in the "I know how to do this" trap. If you are successful, all that means is that you know how things used to work. It means that you can compete and win in markets that no longer exist. Today's a new day with new challenges that will require new approaches. The best lessons are learned after you know it all. Be passionately curious and always look for the new best idea. Recessions create new realities. Be open to them.

Improve relentlessly. No idea gets more lip service than this: "To be competitive we have to be better tomorrow than we were today." What did you do so far today that made you better than you were yesterday? It's a tough question because even though our intentions about improvement are good, it's difficult to actually take action that improves your performance. Look at everything you do

with the permanent question in mind of "how can I make this better." You can't take advantage of the end of a recession if you do things the way you've always done them. Look at what you do with renewed vision.

It may seem slightly preposterous, but there are beneficial byproducts that are yielded to those who embrace a recession as a premier opportunity to both grow and succeed rather than a time to hunker down and take cover. Understanding that the recession, ironic as it sounds, could be the most opportune time to grow your business and command more market share is essential. Then, taking ownership of a new, multi-faceted mindset will help your business flourish, regardless of the economic climate.

About the Author

Joe Calloway is a partner in Engage Consulting Group, and author of several best-selling business books including the newly revised edition of "Becoming a Category of One," (August 2009, Wiley). Corporate heavyweights BMW, American Express, IBM and many more have sought his insight into today's marketplace. Joe provides consulting to help companies accelerate their strategies and make their visions reality. To purchase his books or hire him as a consultant, visit www.joecalloway.com or call (615) 383-2249.

Recipients of the 2008 Honor Awards

www.pda.org/2008honorawards

This is the final installment of the *PDA Letter's* coverage of the 2008 Honor Award winners, who were announced a the 2009 Annual Meeting banquet. The 2009 honorees will be announced next month at the 2010 Annual Meeting. Coverage of the winners will begin in May.

PDA/DHI Editor Award

This award is presented annually for the best editor/author of PDA/DHI co-published books as selected by PDA members.

Anne Booth

Siegfried Schmitt, PhD

James Agalloco Award

The James P. Agalloco Award is presented annually to the PDA faculty member who exemplifies outstanding performance in education. The slection is based on student and faculty evaluations and is named for James P. Agalloco in honor of his work in developing the PDA education program.

Harold Baseman

Special Recognition

The Special Recognition Award was presented for the first time to Richard Levy, PhD, for his outstanding contributions to the advancements of pharmaceutical science for PDA.

Richard Levy, PhD

President's Award

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

Hassana Howe

Jason Brown

The honor awards have been bestowed to esteemed PDA members since the first award was given in 1958.

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.

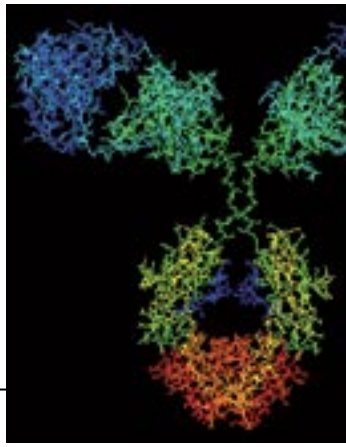
15 June 2010
Berlin, Germany

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

Chapter Contacts

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

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Learn What PDA Has to Offer

2010 PDA Annual Meeting

New Member Breakfast

Monday, March 15

7:00–8:00 a.m.

Welcome new PDA members! If you joined PDA on or after April 1, 2009, you are invited to kick-start your PDA membership by attending the New Member Breakfast hosted on-site at the *2010 PDA Annual Meeting*. This is a wonderful opportunity to learn more about PDA and to meet other new members, board members and staff.

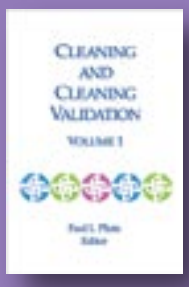
Please RSVP by February 28, 2010. For more information and to RSVP, please contact Hassana Howe at +1 (301) 656-5900 ext. 119 or howe@pda.org.

Note: You must be a full conference attendee to attend this event. RSVP is required.

Space is limited.

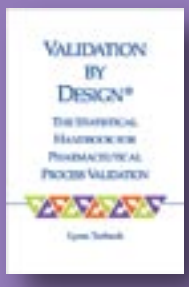
New Releases

from the PDA Bookstore



CLEANING AND CLEANING VALIDATION, VOLUME 1

Edited by Paul L. Pluta, PhD
(Item No. 17288)



VALIDATION BY DESIGN®: THE STATISTICAL HANDBOOK FOR PHARMACEUTICAL PROCESS VALIDATION

By Lynn D. Torbeck
(Item No. 17266)

PDA Technical Report
PDA Technical Report No. 46 Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User
(Item No. 01046)

White Paper
Use of Interactive Voice Response or Web Systems to Manage IMP Retest Dates
(Item No. 43800)

PDA Parenteral Drug Association

FEBRUARY FEATURED TITLES

PDA Members save 30% on select bestselling PDA/DHI publications every month at the PDA Bookstore.

Microbiology in Pharmaceutical Manufacturing, Second Edition, Volume 1 and II
Edited by Richard Prince, PhD
Item No. 17280
Member: ~~$375~~ $325, Nonmember: ~~$465~~ $420

Risk-Based Compliance Handbook
By Siegfried Schmitt, PhD
Item No. 17281
Member: ~~$210~~ $180, Nonmember: ~~$259~~ $235

**All prices in US dollars*

www.pda.org/bookstore

Please Welcome the Following Industry

Farhana Alavi, Itercell
Annie Ben Shoshan, Novartis
Jeffrey Bordin, Aramark Cleanroom Services
Tony Budianto Bee, Sartorius Stedim
Eileen Choi, Biotest Pharmaceuticals
Heymans Chris, GlaxoSmithKline
Martina Christiansen, Hoffmann Neopac
Matthew Cline, Genentech
Aimee Cousoulis, GxP Pinch Hitting
Thomas Damratoski, Bristol Myers Squibb
Brendan Decelles, Millipore
Junil Dhanpaul, CibaVision
Linda Di Martella-Orsi, Kedrion
Michael Dosmar, Sartorius Stedim
Xin Dun, State Food Drug Administration Training Center
Margarita Efthymiopoulou, VIiofar
Omar El-Ahmady, Eipico International Pharmaceutical Industries
Willem Ennik, Covidien
Annie Enriquez, Genentech
Jeanne Fiore, Pharmalucence
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Ronald Garrell, Cephalon
Andreas Geiger, Hoffmann Neopac
James Glover, Bayer Healthcare
Igor Gorsky, Shire Pharmaceuticals
Andriy Goy, Farmak
Alessandra Grifoni, ALFA Wasserman
Michael Gross, Biogen Idec
Gerardo Gutierrez Angel, Laboratorios Grossman
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Karen Kingsley, Kingsley Consulting
Jani Koskinen, FIT Biotech
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Sheng-Wen Lin, Taiwan Product Quality Research Institute
Harry Liu, CQ International
Anastasia Lolas, FDA
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Sarah Malain, ISTA Pharmaceutical
John Maslowski, Fibrocell Science
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Terri Mays, Kimberly-Clark
Joseph McGranaghan, Microtest Laboratories
Louise McKenna, Bioniche Pharma Teo.
Suzanne Mecalo, Commissioning Agents

Leaders to the PDA Community

Michael Metoyer, Biotest Microbiology
Etienne Michel, GlaxoSmithKline
Saeed Moshashaee, BioMarin Pharmaceutical
Robert Nichols, Genentech
Mario Nimac, GlaxoSmithKline
Toru Ogawa, Daiichi Sankyo
Naama Or, Novartis
Mehul Patel, Accugenix
Olivier Paul, EMA Pharmaceuticals
Giuseppe Pimpinella, Agenzia Italiana del Farmaco
Gabriel Ponce, Baxter Healthcare
John Sakai, Sakai International
Isabel Schulte, Meridian Medical Technologies
Jim Seely, Amgen
Gary Shifflett, Validation Technologies
Yann Simon, Ferring
R. Terry Smith, Boehringer-Ingelheim
Russell Soobrian, Novopharm
Gladys Speaker, Bayer Healthcare
Torben Svensson, Novo Nordisk
Paul Vina, GE Healthcare
Christina Waller, Global Compliance Solutions
Mary White, Ispen BioPharm
Jeff Wodrich, AcuTemp Thermal Systems
Diane Wojtaszek, Endo Pharmaceuticals
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Christine Wu, Baxter Healthcare
Frederick Wu, Deltatrak
Ilan Yaakon, Dexcel Pharma
Aron Yaeger, Genentech
Irem Yarli, PharmaVision Sanayi Ve Ticaret
Dane Zabriskie, Amgen
Gene Zhang, Bayer Healthcare

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

New members learn about PDA at the *2009 Annual Meeting*

2010 PDA Annual Meeting Showcase Your Products and Services

Visit www.pda.org/annual2010 for a complete listing of Exhibitors and Sponsors

For two days during the *2010 PDA Annual Meeting* (Monday, March 15 and Tuesday, March 16), hundreds of today's leading pharmaceutical and biopharmaceutical companies will gather to showcase the emerging technologies, trends, services and products driving the industry. Take advantage of this opportunity to compare the latest innovations, network with company representatives and learn about the future of the industry. And don't forget to join us in the exhibit hall for refreshment breaks, networking receptions and prize drawings.

Exhibitors include Eisai Machinery U.S.A. Inc.; Genesis Packaging Technologies; Lonza, Inc.; Sartorius Stedim Biotech; West Pharmaceutical Services, Inc. and more!

There are still exciting sponsorship and exhibition packages available at this conference. Gain on-site exposure in front of upper-level professionals with purchasing power in the pharmaceutical and biopharmaceutical industry. Connect and make new contacts with representatives from government agencies and industry professionals.

Potential clients attend the meeting to:

- Get updates on new trends and regulatory initiatives
- Network with experts in the bio/pharmaceutical industry
- Gather facts on innovative products and services

The *2010 PDA Annual Meeting* offers you numerous exciting sponsorship opportunities, including an exhibitor raffle drawing, refreshment breaks, long exhibit hours and more to showcase your company's products and services.

To take advantage of these marketing opportunities, please contact David Hall at +1 (240) 688-4405 or hall@pda.org.

Lean/Six Sigma – Fad, Craze or Here to Stay?

Lean/Six Sigma Workshop • Orlando, Fla. • March 17 • www.pda.org/leanmanufacturing

For much of the last decade, the pharmaceutical literature has been replete with articles about Lean/Six Sigma and how it relates to the new paradigm of manufacturing control under development with the advent of the ICH Q8, 9 and 10 documents. Wading through it all can leave one scratching their head and wondering what it all means.

Seen any Six Sigma Master Black Belts around your facility recently?

If so, perhaps your firm has embraced the concept. Indeed, maybe you already are involved with your firm's Lean/Six Sigma program. If not, you might wonder if your firm is behind the times or has it decided there are alternatives that better suit your firm's processes and/or culture.

Either way, the conference co-leaders want to hear from you at a workshop called, *What is the State of Lean/Six Sigma in Pharma and Biotech?* on March 17, which we expect to be a perfect bookend to the 2010 PDA Annual Meeting. This workshop represents a great opportunity for PDA members brainstorm a topic and help establish potential future PDA deliverables, i.e., courses, meetings or publications.

This is a problem solving workshop. It is your opportunity to discuss issues and problems with industry experts and peers in an effort to help meet your operational excellence challenges. We endeavour to create an atmosphere that workshop Co-Lead **Jeff Baker** calls, a "power point free zone." Rather than a standard workshop with presentations, panel discussions and Q&A, the agenda will be set around 5 topics with participants alternating between table and group discussions.

The five topics include:

1. How would you define the state of Lean/Six Sigma in the pharma and biopharma industries?

2. How do you measure value?

3. How would you evaluate your company's implementation of tools and management systems to analyze risk? What have been the potential pitfalls and unintended consequences?

4. If we as an industry know we need to improve the efficiency of our systems and operations, why has Six Sigma not become routine business practice in the pharma and biopharma industries? What are practical barriers? What are practical enablers?

5. How do you maintain a state of control of sustainability while always in a state of continual improvement?

We do not intend this workshop to be a Lean "revival." There are many who have not embraced Lean practices, and the workshop is not intended just for converts. True progress is only really synthesized through dialogue, and we trust this workshop will bring together the skeptics and the advocates for thought provoking debate. The guidance that Q10 brings to the industry is an excellent example of where we see the support for Lean/Six Sigma occasionally bifurcate and and provides an expected topic of discussion for participants. Some see the tools and methods for Lean as solely belonging in the manufacturing domain with no express purpose or value in the overall context of quality systems. Some see its value holistically, while others still see it as the flavor ➤

Manufacturing Excellence: Linking Academic Science to Industrial Science

2010 PDA Annual Meeting

Orlanda, Fla. • March 15-19 • www.pda.org/annual2010

Program Committee Member Marsha Hardiman, BSI Management Systems

In March 2010, PDA's Annual Meeting will be held at the Gaylord Palms Resort and Convention Center in Orlando, Fla. The program planning committee has been very busy working with the excellent panel of presenters we have selected, as we put the finishing touches on the conference and events which we have planned for you.

This year's meeting will take place March 15-19. We believe this program has the perfect blend of education, excellence in science and fun! This is PDA's "flagship" event and continues to be considered as the year's most valuable networking opportunity. This is the meeting that you look forward to going to every year and once again, this year's meeting won't disappoint you. We look forward to seeing you there. Come network with old friends and meet new ones.

The Program Planning Committee has selected *Manufacturing Excellence* as the theme for our 2010 event. In these times, it has never been more important to utilize manufacturing excellence and Lean practices in our companies. Our presenters will be discussing cutting edge technologies and advances in science that help move us towards these goals. Coupled with the presentations will be state of the art technology options which you will explore in the exhibition hall as you talk with the vendors.

The meeting will be conducted in the traditional format with three parallel conference tracks with additional time added in to each session for questions and answers. We really want this conference to be as interactive as possible. The exchange of thoughts and ideas creates the drive to influence change as we move forward in science and technology. We encourage you to not just come to this year's meeting but to come and engage in this exchange and influence someone! This year's tracks are:

- Manufacturing Process Science
- Development Science
- Quality Science

This meeting will hold a dialogue on the ways and means to achieve manufacturing excellence and productivity in the regulated healthcare product industry. With 24 individual conference sessions, 13 interest group meetings, a Lean manufacturing workshop and related TRI courses, this event has so much to offer to everyone.

At the opening plenary session on Monday, March 15th the committee is excited to present two keynote addresses, first up will be a presentation from **Janice Meck**, PhD, Director, Cardiovascular Laboratory, NASA–Johnson Space Center. Here we will hear about the link between science and industrial productivity. In our second keynote presentation, Nobel Prize winner **Per Carlson**, PhD, Professor, Elementary Particle Physics, KTH and former member of the Nobel Prize Selection Committee, will be speaking about the link between academic science and industrial science.

On Wednesday, March 17, we will enjoy a closing plenary session from **Martin Lafleur**, Project Director, AéroMontréal, who will discuss Manufacturing Excellence from an industry perspective.

In addition to the formal conference proceedings, we have put together an impressive choice of optional and fun events beginning with the PDA Annual Golf Tournament and the 3rd Annual Fun Run on Sunday, March 14th. Orlando has many family friendly entertainment options available, and we have information about Disney World, Sea World and Universal Studios in the program brochure online. Family members can participate in the Fun Run and Golf Tournament. Make your conference experience a well rounded one by taking part in these networking activities.

The committee appreciates your continued commitment to this meeting and in return we are committed to presenting you with a valuable, highly informative and fun program.

We all look forward to seeing you in Orlando in March.

Lean/Six Sigma, continued from previous page

of the month, a fad who will see its day eventually come to an end.

Whatever you position, we expect this meeting to bring together content experts and industry practitioners in a workshop environment to discuss the current state of Lean/Six Sigma in the industry and the barriers/hurdles to its implementation. This interactive workshop will capture the experiences of the participants, as well as sharing the experiences of leaders and facilitators to create process knowldge around the state of Lean/Six Sigma in our industry. We hope to see you there!

Visit www.pda.org/leanmanufacturing for more details about this unique workshop scheduled for March 17, 2010 in Orlando, Florida.

PDA and FDA Seek Supply Chain Solutions

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

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

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. There is a surge in global cooperation and efforts toward harmonization of Good Manufacturing and Distribution Practices (GMPs and GDPs) and controls pertaining to the supply chain among members of industry and the regulatory agencies. Understanding and securing the entire ingredient manufacturing and distribution chain increases confidence in and helps ensure the quality and safety of medicines for our patients.

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

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

The emphasis of the workshop will be to focus on solutions to reduce 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 to their specific programs and to improvement more generally across the market.

Learn About the Technical and Regulatory Challenges Facing Vaccines

2010 PDA Vaccine Conference • Bethesda, Md. • May 17-19 • www.pda.org/vaccines2010

Program Planning Committee Member Anthony M. Luttrell, Raland Technologies

On behalf of the program planning committee, we are pleased to announce the *2010 PDA Vaccine Conference* at the Bethesda Marriott in Bethesda, Md. on May 17-19, 2010. The theme of this upcoming meeting is *Today's Challenges, Tomorrow's Opportunities.*

Please join us for this valuable two-and-a-half day workshop designed to examine the technical and regulatory challenges currently being faced by the vaccines industry to ensure rapid development of high quality vaccines for the global market. Our focus will be on challenges and opportunities being experienced by vaccine manufacturers in the U.S. regulatory framework.

The pharmaceutical industry took the lead in developing vaccines against smallpox and polio and strongly contributed to the eradication of these dreaded diseases. In the past several years, the development of vaccines for prophylactic and therapeutic applications has once again become a focused effort for the pharmaceutical industry, the healthcare industry in general and the global public. We now face challenges such as the potential threat of a biological attack, and the industry is responding by developing investigational vaccines against anthrax and smallpox. Many clinical studies are also underway for new vaccines against HIV, hepatitis viruses and West Nile Virus.

Because our world is smaller, hotter, flatter and more crowded, we also have new and emerging threats such as West Nile virus, "Mad Cow Disease," Severe Acute Respiratory Syndrome (SARS) and a pandemic influenza (H1N1). And these are only the threats that we know about!

As a result of these challenges as well as technological advances within the industry, we must learn quickly to produce vaccines for human use even more rapidly, efficiently and more safely than in the past. The development of safe and effective vaccines carries its own set of technical, clinical and regulatory challenges, some of which are shared with other pharmaceutical sectors and others that are unique to the biologics and specifically the vaccines arena.

The conference will contain plenary sessions that will examine case studies, including lessons learned from the seasonal and pandemic flu manufacturing experience, summaries of highlights of concurrent breakout sessions, as well as a review of a companion vaccines session focused on development in the European regulatory framework that was given at the PDA Biopharmaceuticals Conference in Europe. These sessions should help all of us to understand the current vaccines landscape. Many relevant breakout sessions and breakfast roundtables are also scheduled, which will allow for concept exploration and interactive discussion on a variety of current issues facing the vaccine industry, such as:

- Application of Quality by Design principles and challenges of process validation
- Supply chain complexities, including methods for control, monitoring and cold chain management
- Updated technologies for control and containment during manufacturing
- Challenges of developing and validating analytical methods (stability indicating and potency assays)
- Novel substrates, expression and delivery systems
- Technical bridging of changes and scale-up manufacturing during development and application of comparability protocols
- Update on 21 CFR 601.12 changes to be reported
- Novel adjuvants
- Expanding requirements for preclinical testing
- Impact of biosimilars on the industry
- Challenges of developing therapeutic vaccines for non-infectious disease indications

These interactive discussions will focus on product development, quality, compliance and regulatory aspects. Industry representatives will share experiences, case studies and recommendations for navigating the U.S. product development and regulatory waters applicable to vaccines. U.S. FDA representatives will share insight into their current expectations for generating the appropriate data and information to support robust manufacturing processes that are approvable and sustainable into the future. Helpful hints for market applications for vaccine licensure in the United States, today and into the future will be discussed.

This conference is a tremendous opportunity to network with experts in all areas of public health, vaccine development, manufacturing and regulatory affairs. Additionally, you will be able to meet key vendors of manufacturing equipment and services and many worldwide regulatory/compliance professionals.

For more meeting information and to register, visit www.pda.org/vaccines2010.

2010 PDA Annual Meeting TRI Offers Nine Training Courses

Orlando, Fla. • March 18-19 • pdaannualmeeting.org/courses.php

Stephanie Ko, PDA

The PDA Annual Meeting is quickly approaching which means you won't have to wait long to have opportunities, such as conference sessions and networking at your fingertips, as well as in-depth training. PDA's Training and Research Institute (TRI) is preparing to deliver nine training courses on March 18 and 19. These one and two day courses will be held immediately following the conference and center around the theme of *Manufacturing Excellence*. If you attended a training course last year during PDA's Annual Meeting, you'll have a completely different selection of courses to choose from this year.

We are excited to present a unique and exclusive two-day course that has never been offered before—**"Risk Mitigation Solutions: The Response to Risk Assessment."** The course was developed by two industry experts, **Anne Marie Dixon**, President, Cleanroom Management Associates and **J. Scott Kemp**, Principal, JSK Consulting Services. While the concept of the course came to fruition awhile back, Dixon and Kemp made the decision to give the Training and Research Institute the honor of its debut.

A variety of topics will be covered and divided into ten sections as follows:

- **Session 1:** Project Initiation and Management
- **Session 2:** Risk Evaluation and Control
- **Session 3:** Controls/Safeguards to Prevent/Mitigate Loss Potential
- **Session 4:** Developing Risk Mitigation/Disaster Recovery Strategies
- **Session 5:** Risk Mitigation/Disaster Recover Solutions for Cleanrooms
- **Session 6:** Business Impact Analysis
- **Session 7:** Emergency Response and Operations
- **Session 8:** Training and Awareness
- **Session 9:** Maintaining and Exercising Risk Mitigation/Recovery Plans
- **Session 10:** Coordination with External Agencies

Course attendees will be able to prepare a full Risk Mitigation/Disaster Recovery Plan after attending this course. We encourage you to go to our website pdaannualmeeting.org/courses.php for the full details of this course and a listing of the other relevant training courses being offered.

We're further pleased to provide three other brand new, never offered before TRI courses centered on operations and manufacturing excellence. Consider a one-day introductory course on **"Applying Lean to Aseptic Processes,"** developed and taught by **Mike Long**, Director and Principal, KPM International Associates. This course is a natural follow up to the PDA Workshop on Lean Manufacturing: What is the State of Lean/Six Sigma in Pharma and Biotech being held Wednesday afternoon, immediately following the Annual Meeting. If you're attending this workshop, you won't want to miss this course; although, non-workshop attendees will also derive benefit from participating in the course. Another fundamental course is **"Isolators: From Concept through Qualification,"** where you'll receive 2 days of in-depth training from **Eddie Ballance**, Senior Manager, Parenteral Pilot Plant, Eisai. If you're more interested in a more advanced course centered around the validation of biological manufacturing processes, we recommend **"Bioprocess Validation"** taught by **Trevor Deeks**, Senior Director, Manufacturing Operations and Engineering, Emergent Biosolutions.

In addition to these four all-new courses, the following previously-offered TRI courses that remain amongst the core of our educational offers will also take place in Orlando.

- "Clean Room Design, Contamination Control, & Environmental Monitoring for Controlled Environments"
- "Role of the Quality Professional in the 21st Century"
- "Fundamentals of Lyophilization"
- "Change Control: A Practical Workshop"
- "Use of HACCP for Microbiological Control in Pharmaceutical Manufacturing"

To keep our course listings fresh and allow our instructors time to update courses, there is a possibility that these lecture courses may not be offered next year, so don't miss your chance to get in on the learning now!

So there you have it—plenty of opportunities during PDA's *2010 Annual Meeting* to enhance your professional growth. If you are unable to join us in March, the Training and Research Institute has no intention of limiting your training opportunities to just this particular event. While the mentioned lecture courses will only be scheduled once in 2010, they can be available year-round as in-house training for your company. Just find us at www.pdatraining.org and send a quick email to convey your interest. Otherwise, we'd be pleased to meet you in Orlando!

TRI Exhibit Demonstrations

Monday, March 15
Two demonstrations will take place at the TRI booth from 10:15a.m. – 10:30 a.m. and 3:30p.m. – 3:45pm.

Tuesday, March 16
Two demonstrations will take place at the TRI booth from 10:00a.m. – 10:15a.m. and 3:45p.m. – 4:00p.m.

PDA Parenteral Drug Association

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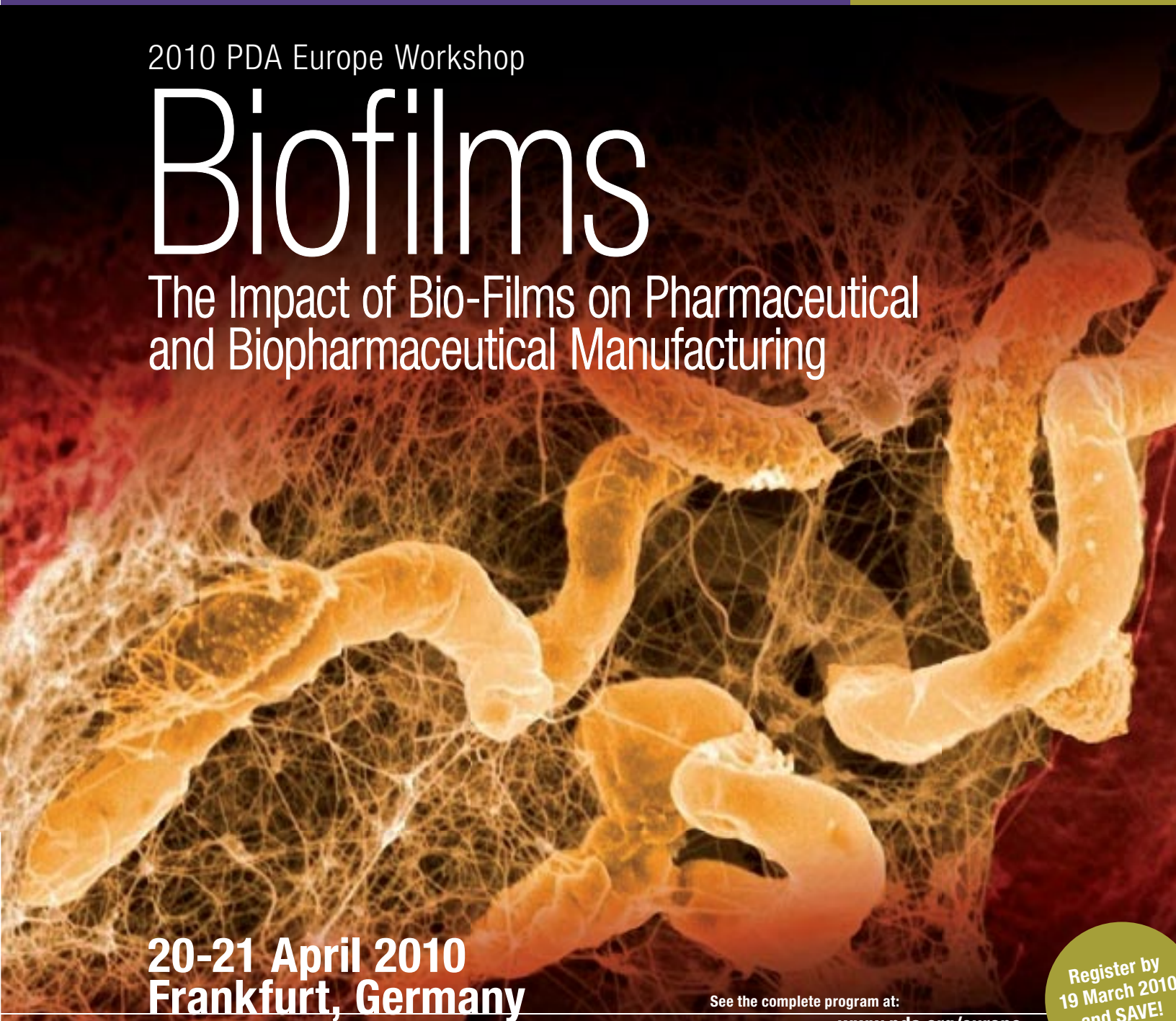
2010 PDA Europe Workshop

Biofilms

The Impact of Bio-Films 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 in pharmaceutical and biopharmaceutical fluid-handling systems.

The Heat is On: Endotoxins Reviewed at PDA Meeting

PDA's 2nd Conference On Endotoxins • Barcelona, Spain • April 13-14 • www.pda.org/europe

Philippe Gomez, Sartorius-Stedim Biotech and Volker Eck, PhD, PDA

The PDA conference on Endotoxins, supported by the French association, "French Society of Pharmaceutical Science and Technology" (SFSTP), took place in Paris on March 17-18 2009. Based on the input of a working team consisting of about 20 members from Europe and North America, this event drew 80 delegates from Europe, the United States and Japan to hear 22 speakers from industry and health authorities. Four lecturers from the French Health Products Safety Agency (AFSSAPS) demonstrated the involvement and support the team received from the French Agency both in participation as well as in disseminating the results for discussion.

During these two days, a complete picture on Bacterial Endotoxin Testing had been presented. Fundamentals including the molecular structure and lipopolysaccharides (LPS) properties; a 360 degree overview on reference and other standards necessary to conduct the Limulus polyphemus amebocyte Lysate-test (LAL-test) and its various testing methods; and testing methodologies for raw materials, small molecule and biotech finished products, primary packaging items or medical devices were discussed.

Depyrogenation techniques and the evolution of LAL test methods had been specifically addressed during a breakfast session. The new methodology, the Monocyte Activation Tests (MAT), and its potential applications had also been presented and lectured on.

Interaction between the delegates had been intense, demonstrating the vivid interest in this topic. Attendees and speakers have underlined that current techniques are suffering from inherent limits. Experts from industry, as well as regulators and controlling bodies, are exposed to these in their daily work and face identical issues worldwide. One of them being for instance the demonstration for a reduction of pyrogens greater than factor 1000 (3 log reduction) to qualify successful cleaning and disinfection procedures.

In conclusion, interested people felt invited to share their experiences and advice with the audience and specifically the team. Several volunteered to join the working group and participate in elaborating of a reference document that will constitute a practical guidance regarding endotoxins. Based on the numerous and very positive feedback, PDA is organizing a follow-up event on April13-14 in Barcelona, Spain.

To find out more, visit www.pda.org/europe.

Attend Three Berlin Workshops in June

Jim Lyda, PDA

Come to Berlin in June and take your pick of three timely PDA workshops addressing current topics in **biopharmaceutical development and production.** These workshops were developed by PDA volunteer experts from industry and health authorities and will address issues of interest to manufacturers, suppliers, vendors, service providers, regulators and academics. There will be ample time for discussion and networking. **Choose one, two or all three workshops for a special discount rate.**

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

June 15

This one-day workshop focuses on the **current developments in Advanced Therapy Medicinal Products (ATMPs)** from a European perspective. The emergence of gene therapy, cell therapy and tissue engineering offer great promise for such products used as medicinal products. To initiate regulation of ATMPs, the European Medicines Agency published EC Regulation 1394/2007 on December 10, 2007 and it came into effect on December 30, 2008. For sound regulation and technical resources, the Committee for Advanced Therapies (CAT) was also organized by the Agency to operate in parallel with the CHMP. In the workshop, regulatory perspectives are provided by European regulators who are members of the CAT who can speak about current issues. There are technical sessions which highlight a range of common manufacturing and production issues. Practical examples are illustrated through case studies presented by industry representatives.

Vaccines Workshop: New Technologies for the 21st Century

June 16

This one-day workshop focuses on the **current developments in the area of vaccine development and production.** Advances in research are leading to development of new vaccines for new and old diseases. The application of immunotherapy to diseases, such as cancer and allergies, has come to the forefront in recent years. While some vaccines can be manufactured using traditional production platforms, others may require unique technologies and specialized processes. Challenges associated with manufacture of live organisms, bulk aseptic processing steps, novel expression systems and variable bioassays can require special knowledge and controls. In the workshop, a regulatory perspective is provided by European regulators speaking about current issues. Technical sessions will highlight a range of common manufacturing and production issues illustrated through case industry studies.

3rd Monoclonal Antibodies Workshop: Managing the Challenges of Comparability

June 17-18

This one-and-a-half day workshop focuses on **comparability investigations for monoclonal antibodies** and is intended to provide useful insight into protocol planning, study execution and data evaluation.

When there are changes to therapeutic monoclonal antibody processes or products, a comparability exercise is usually conducted to demonstrate that the change does not adversely impact the product's established quality, safety or efficacy profiles. Despite internationally recognized guidance (e.g., ICH Q5E) comparability remains a complex issue for companies due to uncertainty about analytical tests, specific data requirements, acceptance criteria, data analysis and expectations of regulatory bodies. In this workshop, a European regulatory perspective is provided through presentations by regulators drawing on their experiences with comparability submissions.

Topics include:

- Regulatory expectations for comparability data packages
- Strategies to bridge product quality across late-phase manufacturing changes
- Selection of analytical tools for assessing comparability
- Implementation approach for single use technology
- Changes related to new dosage forms… and more.

For more information on all three workshops and other PDA conferences in Europe, go to www.pda.org/europe

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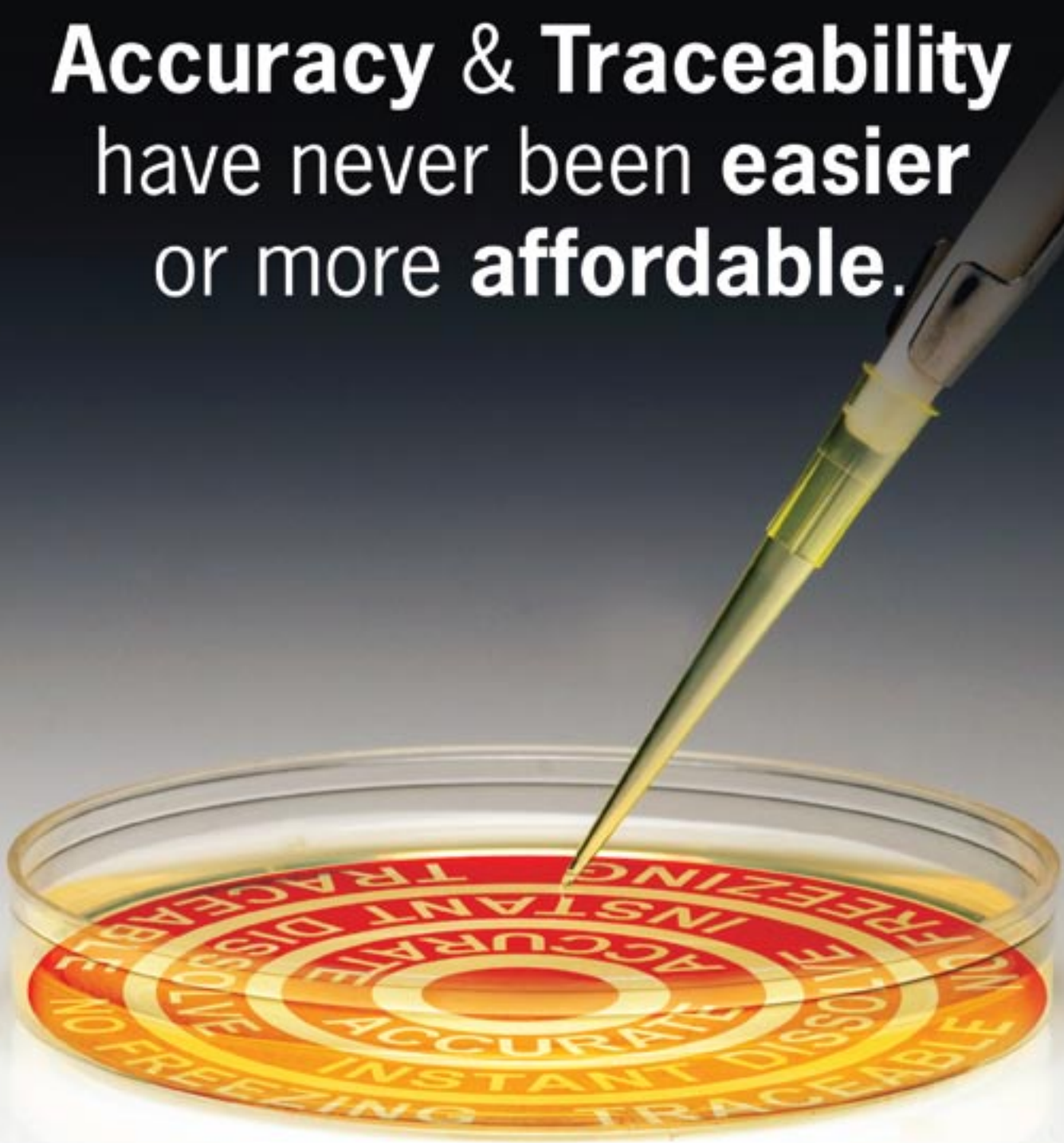

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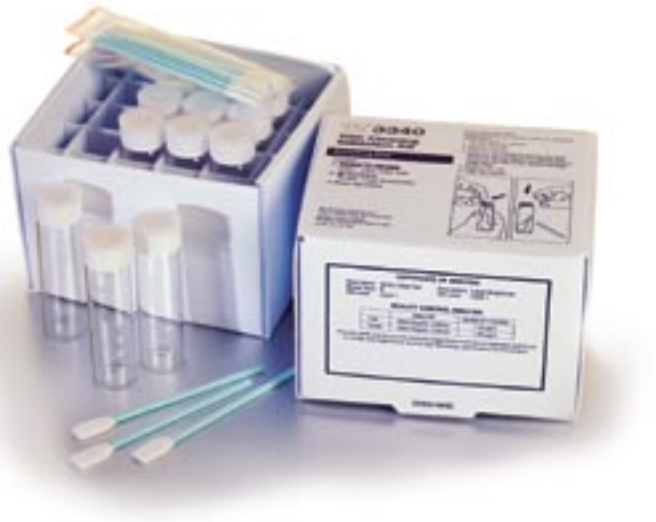

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2010 PDA Annual Meeting

Manufacturing Excellence

March 15-19, 2010
Gaylord Palms Resort & Convention Center
Orlando, Florida

Conference	|	March 15 - 17, 2010
Exhibition	|	March 15 - 16, 2010
Career Fair	|	March 15 - 16, 2010
Courses	|	March 18 - 19, 2010

www.pda.org/annual2010

The *2010 PDA Annual Meeting* will explore an area of immense importance to the global bio/pharmaceutical industry – ***Manufacturing Excellence***. Join your industry and regulatory peers at this meeting to examine manufacturing best practices and strategies that can maximize your company's efficiency and productivity, while delivering safe and reliable drugs to patients. The program will address creating an environment of quality and operational excellence through properly planned and performed process design, validation, contamination control, testing, handling, product and supply chain security, and much more.

Complementing the conference are PDA Training and Research Institute (PDA TRI) courses, an exhibition featuring today's leading bio/pharmaceutical companies and service providers, PDA's 6th Annual Career Fair and enhanced networking opportunities that take advantage of all that Orlando and the exciting Gaylord Palms Resort and Convention Center have to offer.

Take your career to the next level with the knowledge, best practices and valuable contacts you will gain at the *2010 PDA Annual Meeting*.