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PDA Letter

Volume XLV • Issue #10

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November/December 2009

In This Issue:

PDA Parenteral Drug Association

Connecting People, Science and Regulation®

Challenges of an Industry in Transition Loom Large at Joint Conferences

Walter Morris, PDA

It would be an overstatement to say the pharmaceutical industry is in retreat, but saying the industry needs a safe and effective treatment for what ails it is not. The challenges it faces are driven by external political pressures for low-cost medicines and internal product development slowdowns and are hastening the movement of resources from high-cost to low-cost labor markets, divestments and mergers.

Such rearguard activity to protect bottom lines places pressure on organizations across the board, from the research and development groups to the marketing and sales teams. For those in manufacturing and quality control/assurance, the challenges are not unlike those faced in other manufacturing industries in similar circumstances—drive down costs via outsourcing and off-shoring and maintain high quality standards. Unlike other manufacturing and industries, these actions have exposed the industry to a new phenomenon which everyone is just beginning to fully grasp—economically motivated adulteration (EMA)—and failure to prevent it can be fatal to consumers and damaging to an already battered industry.

EMA was the unwelcomed backdrop to both of PDA's large joint regulatory conferences this fall—one with the U.S. FDA in Washington, D.C. and the other with the European Medicines Agency (EMEA) in Berlin. The overarching theme of each meeting was that the authorities are focused squarely on patient safety and guarding against EMA is one of their top priorities.

Rarely does a meeting delve so comprehensively into all of the pertinent issues facing the pharmaceutical industry as the *2009 PDA/FDA Joint Regulatory Conference* did. Expert presentations covered the present and future industry challenges posed by health care economics, EMA, evolving regulatory enforcement policies, the never-ending daily challenges of producing the highest quality medicines possible, and the impact the industry has on patients.

The *2009 PDA/EMEA Joint Conference* tackled the tough regulatory issues facing the European Union's top health agency as it too grapples with a global marketplace and continued efforts to harmonize within the Union itself. Sessions provided intimate settings to discuss: • Europe's complicated regulatory framework and efforts to make it more accessible • harmonized regulations • the latest quality standards. The success of the conference prompted EMEA not only to commit to the next meeting, scheduled 18 months apart, but to propose going to an annual schedule starting in 2012.

In this issue, the *PDA Letter* is pleased to bring you a number of reports from the two meetings (see p. 11, pp. 22, p. 52–53). We hope you enjoy them, and hope they inspire you to attend next time if you didn't get a chance this year.

SAVE THE DATE FOR THE

2010 PDA/FDA Joint Regulatory Conference

September 13-15, 2010 | Renaissance Hotel | Washington, D.C.

The date is set and the planning is well underway for the ***2010 PDA/FDA Joint Regulatory Conference***. To get you ready we have set up an "Advanced Notification System." This notification system is quick and easy. Just visit http://tiny.cc/kFDxx, give us some basic information and we will send you a quick e-mail letting you know when the 2010 agenda is posted and the conference website is open.

Year after year, your colleagues at FDA provide updates on the current state of affairs impacting the development of global regulatory strategies, while industry professionals from today's leading pharmaceutical companies present case studies on how they employ global strategies in their daily processes.

Immediately following the conference, the PDA Training and Research (PDA TRI) will host a course series.

Here are the courses that we have confirmed for 2010:

- A Former FDA Investigator's Perspective on Conducting Effective Deviation Investigations, Root Cause Investigations, Corrective and Preventive Actions (CAPA) – *new course!*
  Instructor: **Jeff Yuen**, President and CEO, *Jeff Yuen & Associates Inc.*
- Establishing and Operating and Effective GMP Auditing Program
  Instructor: **Robert Dana,** Sr. Vice President of Regulatory Affairs and Training Research Institute, *PDA*
- Essentials of US and EU GMPs for Manufacturers of Active Pharmaceutical Ingredients
  Instructor: **Michael Anisfeld,** President, *Globepharm Consulting Inc.*
- Making the Grade with the FDA
  Instructor: **Barbara van der Schalie**, Clinical Training Manager, *SAIC-Frederick, Inc.*
- The Quality System: Design, Implementation, Evaluation and Management of Processes
  Instructor: **Robert Kieffer,** *RGK Consulting*

So, we are getting ready and we hope that you are as well. Again, visit **http://tiny.cc/kFDxx** to receive an Advanced Notification on *the* premiere event of 2010!

If you have any questions we would like to hear from you.

PLEASE CONTACT:

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Regulatory Compliance
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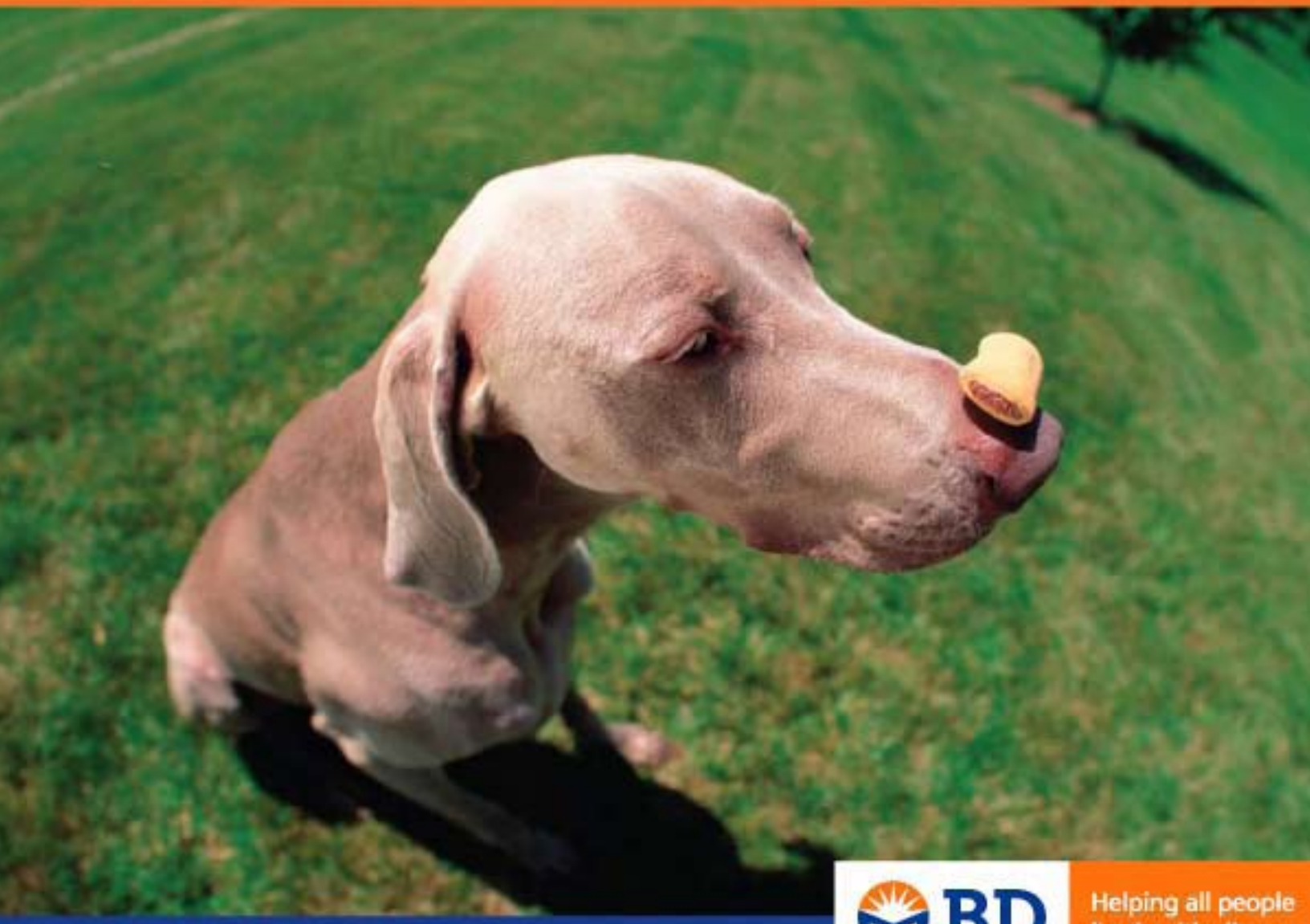

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Cover art:
PDA is dedicated to connecting industry and regulators to advance regulatory science to ensure the safety of patients.

Coming Next Issue:
Pharmaceutical Microbiology: A report from PDA's 4th Annual Microbiology Meeting

A Call for Volunteers: Editorial Committee Openings

The November/December issue of the *PDA Letter* is a perfect example of how members can participate in the Association and contribute to our membership publication.

Each issue, PDA members contribute to the *PDA Letter* in ways both seen and unseen. Nearly every issue published contains an update from a chapter or a program planning committee. Several times a year we receive reports from members regarding past meetings. TRI course instructors contribute advice on training and write about upcoming courses. Advisory Board and Board of Director members check in a few times a year to keep the membership abreast of the latest leadership decisions. These are, of course, the visible contributions.

Behind the scenes, the Letter's editorial staff works with the *PDA Letter* Editorial Committee (PLEC), listed on this page. This group helps set the annual editorial calendar of topics, which we post online and in the Letter. The box on page 28 has next year's topics, and we are looking for authors (always!). The committee also helps the editorial staff review feature articles for relevancy to the membership and for technical merit. This process helps us work with authors to refine their articles so that they bring the greatest value to the membership. Additionally, PLEC helps us identify good authors for articles, and some of the members have written for us. The level of commitment for the committee is not as high as serving on an Advisory Board, Chapter or Task Force, but it keeps the volunteers quite busy throughout the year and requires participation in teleconferences periodically.

We thank the members of the current committee for their participation. Many of them are "charter" members of the group, which was founded in 2005. After four years for some, we've decided to reshuffle and give other members an opportunity to participate in the *PDA Letter*. Of course, current PLEC members are welcome to reapply for the committee this time and in the future—all applications will be considered! So if you are interested in helping PDA continue to produce a high-quality membership magazine, please email me at morris@pda.org and include in the subject line PLEC. We hope to fill the eight existing spots and possibly expand the committee to ten.

Your Name Here?

Volunteer for the PDA Letter Editorial Committee. Send an email to morris@pda.org. Go to www.pda.org/PDALetter for more information

PDA Letter

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Remarks of Dr. Joshua M. Sharfstein

Principal Deputy Commissioner • U.S. Food and Drug Association

September 14, 2009
2009 PDA/FDA Joint Regulatory Conference

Thank you very much for inviting me to this conference, which I understand is entitled, *Securing the Future of Medical Product Quality, a 2020 Vision.*

I have to tell you that I am impressed with your conference already…because it takes a little courage in the world of medical product technology to look a decade ahead.

I read online that the Parenteral Drug Association was founded in 1946 as an organization to share technical information among pharmaceutical manufacturers.

It is humbling to think about how much has changed over the past 60 years…and that makes it hard to imagine what is coming next.

Yet I accept the premise of this conference…that it is so important to look forward to the next stage in innovation and science for product quality.

This is a topic that greatly interests the new FDA Commissioner, Dr. Margaret Hamburg and myself. Helping to shape this future of product regulation is one important reason why we accepted these positions.

As you may know, both Dr. Hamburg and I bring public health experience to FDA. She served as the Commissioner of Health in New York City for six years and as Assistant Secretary for Planning and Evaluation at HHS. I served as the Commissioner of Health in Baltimore.

As we wrote recently in the New England Journal of Medicine, we see FDA as a public health agency…and our goal is revitalize FDA's historic public health mission.

A fair question for you to ask is the following: In the context of this conference, what does a public health approach mean?

Let me share four thoughts on this question with you today.

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First, a primary principle of public health is prevention. In a city health department, whether the topic is drug addiction, HIV, infant mortality or tuberculosis, our goal is to prevent a problem rather than deal with its consequences.

This is also true at FDA.

For example, in the area of food, FDA has presided over a series of increasingly large recalls over the last few years—including tomatoes, lettuce peanuts, alfalfa sprouts and other products.

But only now is FDA getting the resources and working with Congress on the authority to shift to a preventive approach—putting in place basic manufacturing controls across the food industry to identify weaknesses and make plans to avoid problems.

The medical product industry is far ahead of the food industry in establishing these basic controls, and yet problems still can occur.

That's why thinking of the key problems together, in settings like this conference, is so important. When one company falters because of a quality problem, it's their problem to fix and then prevent.

But when a problem recurs across an industry, it's the industry's problem, and it's FDA's job to help think about solutions.

As one example, Dr. Hamburg and I have been impressed by efforts involving the International Conference on Harmonisation, global regulators and industry. The goal of these efforts is to understand from the start what makes a product of high quality…rather than waiting to discover that after the fact. We would like to foster more such productive collaborations that lead to concrete results in preventing problems.

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Second, a public health approach requires the best available science. When we faced the issue of infant mortality in Baltimore, we started by seeking data—why were babies

dying? Where were they dying? What did those caring for them perceive to the problems and solutions?

At FDA, Dr. Hamburg and I understand that product quality issues also rest on a base of regulatory science.

That's why internally, Dr. Hamburg is encouraging Dr. Jesse Goodman and other leading scientists at the agency to identify key projects that, if supported, can improve product quality and streamline approval pathways—making them at once quicker and more reliable. Dr. Hamburg is also supportive of efforts to improve scientific training and quality at the agency.

We would like to see more guidance documents emerge out of these scientific efforts, to provide a clear and transparent process to address longstanding quality issues and to help developers seeking to bring important products to the market.

Externally, Dr. Hamburg has a key message—that product development to save lives requires both basic science and regulatory science. Investing billions in the former while starving the latter is unbalanced, like a rower with a massive right arm and a puny left arm. It's no surprise that the result is not the forward movement we all are hoping for.

The good news is that we have found many receptive to and understanding of the need for investments in regulatory science at all levels—from consumer advocates to companies to the investment community.

Industry has an important responsibility for moving regulatory science forward—one that you can meet through efforts like this conference.

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Third, a public health approach…by definition…involves the public. Transparency is a key priority now at FDA. We have launched a Transparency Initiative to understand how the agency can better explain the bases for its decisions to the public and regulated industry.

In the next decade, with the speed of information only accelerating, it is a good assumption that product quality problems will eventually come to light.

It is better for companies to develop effective communication systems now…rather than stumble when others are providing key messages about your products for you.

Recently, I have been asking FDA's centers about the challenges of handling product quality issues. Some of these challenges are internal, and Dr. Hamburg recently outlined a series of steps we are taking to streamline public notification and enforcement when serious product quality issues are identified.

Other challenges are external to the agency. Companies are naturally reluctant to issue press releases or conduct recalls. However, when the public health really is at stake, FDA is going to take a basic position—you can explain the problem to the public, or we will. Either way, the public needs to know.

Risk communication about product quality issues is a very important topic, and could be the subject of an entire conference.

One reason that companies may be reluctant to share information on product quality problems is that they fear patient and consumer overreaction. I know from my experience as Health Commissioner that the public is best able to understand two messages—either something is totally safe or totally unsafe.

We need to work together to establish a couple other messages, so that we can explain some of the nuances—such as there are both risks and benefits, and the benefits outweigh the risks. Alongside transparency, better risk communication will be a priority at FDA.

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Fourth, and finally, the premise of public health is that what matters is the health of the public. It's sort of the public health version of Francis Peabody's famous statement in 1925 that the "secret of the care of the patient is in caring for the patient."

Looking at the topics for this conference, I wish I had retained more of my organic chemistry and biology. If only I could offer some original insights into "sterilizing filtration of liquids and gases, depth filtration of process streams and process systems and viral removal and purification."

In evaluating product quality issues for 2020, I would imagine there are many potential ways to resolve key challenges—I urge you to consider the health of the public as the North Pole for your compasses.

This is where a partnership with FDA is so important. Both Dr. Hamburg and I have been so impressed by the expertise and knowledge of FDA staff. I am sure there are some at the agency who do know a lot about sterilizing filtration of liquids and gases, for example. We have also been impressed that the staff have an innate public health compass—knowing, for example, that rules serve a purpose and when they no longer do, we have to look to change the rules.

We hope to see many productive and creative efforts where the agency can share its knowledge and expectations, and we can foster a new generation of safe and effective medical products for the American people.

ATTENTION ALL ACTIVE PDA MEMBERS–YOUR VOTE MATTERS!

Go to www.pda.org/2010ballot and Vote for Directors and Officers

Now is your chance to cast your vote for the 2010 PDA Board of Directors and Officers. We have a fantastic selection to present to you and all nominees have the expertise, experience and capability to make a significant contribution as a member of PDA's governing body, but ultimately only you can make that decision.

We encourage you to take a couple of minutes and exercise your "member right" to vote! Just go to www.pda.org/2010ballot.

All PDA members in good standing as of noon on October 29, 2009 are eligible to vote. Voting for this election will close at 11:59 p.m. EST on December 4, 2009. All votes cast after this date and time will not be accepted.

If you need assistance, please contact the PDA Membership Service Department at +1 (301) 656-5900 ext. 119 or howe@pda.org.

Thank you for being a valued PDA member and voting!

Bill Paulson to Mange Publishing Responsibilities for IPQ

Over the past two years, PDA has been proud to work with Bill Paulson, a widely known and respected journalist in the field, to launch and support his publication, International Pharmaceutical Quality (IPQ) and provide it to our members. During this time, IPQ has developed a worldwide reputation for its in-depth analysis of key pharmaceutical quality regulatory issues and its contribution to the industry/regulator dialogue.

In mid-November, PDA is turning over the publishing responsibilities for IPQ to Bill, who will continue to provide IPQ to PDA members on a complimentary basis for an interim period while subscription, site licensing and sponsorship opportunities are being pursued. We strongly encourage you and your organizations to contact Bill regarding subscription, licensing and sponsorship opportunities to ensure that you continue to receive this valuable resource.

IPQ will continue to report on key meetings and developments worldwide in which PDA and its members are involved.

Bill can be reached through the IPQpubs.com website (paulson@IPQpubs.com) and at 202-841-5027.

USP Unveils Chapter on EM for Nonsterile Drugs

USP Representative Previews Chapter at PDA's 4th Annual Micro-Meeting

Walter Morris and Emily Hough, PDA

The United States Pharmacopeia (USP) used the *4th Annual PDA Global Conference on Pharmaceutical Microbiology* to generate discussion about its draft chapter on environmental monitoring and control in nonsterile drug product manufacturing areas among the approximately 200 microbiologists and sterile product experts gathered at the 2-1/2 day event.

Environmental monitoring in critical areas for sterile drug manufacturing is a well-established, involved practice in pharmaceutical manufacturing, but monitoring and control practices for nonsterile manufacturing areas, particularly for nonsterile drug products, vary widely in the industry.

Leonard Mestrandrea, PhD, an industry consultant who sits on the USP Microbiology and Sterility Assurance Expert Committee writing the chapter, discussed the details at the conference. As the draft stands now, monitoring frequency is risk-based and depends on, for one, the dosage form manufactured. Nonsterile processes for product that is ultimately sterile obviously warrant more frequent monitoring than the same sort of processes for nonsterile products. Mestrandrea noted that a 2006 PDA survey helped shape the document.

According to Mestrandrea, one method to apply microbial control in the manufacture of nonsterile products is to use a risk-based approach to understand the process, define where microbial contamination could occur and effectively determine the best control and monitoring method. When performing a risk assessment, it is important to consider the route of administration of the drug product, the synthesis, isolation and final purification of the drug substance, the microbiological attributes of the pharmaceutical excipients, the formulation, chemical and physical attributes of the drug product, the manufacturing process and the dosage regime. It is also important to consider the age and medical status of the intended recipients of the drug product, the administration of immunosuppressive agents and the presence of disease, wounds, organism damage and invasive medical devices associated with the recipient.

USP is seeking extensive comment on the draft chapter even prior to publishing it in the USP Pharmaceutical Forum early next year.

USP is seeking extensive comment on the draft chapter even prior to publishing it in the USP Pharmaceutical Forum early next year.

A U.S. FDA official pointed out during a Q&A that followed the Mestrandrea's talk that a company just recently entered into a consent decree with the Agency following findings by investigators that their environmental control program was not satisfactory for the nonsterile products involved. Nevertheless, other participants worried that the standards promulgated in the draft USP chapter will be too tight for products that often contain preservatives or are administered through the human GI tract.

The Parenteral Drug Association is forming a Task Force to comment extensively on the chapter.

To get more information about this draft chapter, please contact **Radhakrishna Tirumalai**, Senior Scientist, Standard Development, USP, at rst@usp.org.

Suggesting Sampling Frequency for Different Dosage Forms

Dosage Form	Frequency of Environmental Monitoring
Oral solid dosage forms, i.e., compressed tablets, powder and liquid filled capsules	Quarterly
Liquid oral dosage forms	Monthly
Topicals, i.e., lotions, ointments and creams	Monthly
Rectal suppositories	Monthly
Vaginal suppositories	Weekly
Nasal sprays	Weekly
Inhalation aerosols and solutions	Daily

Environmental Monitoring frequencies per draft USP Chapter "Environmental Monitoring and Control in Non-sterile Drug Product Manufacturing Areas"

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Last year, exhibitors of this conference represented the following:

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European Health Authorities Eye Patient Safety as They Seek Global Alliances

Third PDA/EMEA Joint Conference facilitates dialogue on drug supply security

Walter Morris, PDA

The European Medicines Agency (EMEA) told industry manufacturing, control and regulatory professionals gathered at the *2009 PDA/EMEA Joint Conference* that complicated supply chains, while necessary, are a weak link in quality control.

Opening plenary session speakers from the EMEA and the UK's Medicines & Healthcare products Regulatory Agency (MHRA) outlined a number of interconnected challenges that are applying increasing pressure on the ability of both manufacturers and health authorities globally to safeguard the quality of pharmaceutical products.

Katrin Nodop, an EMEA Inspections Section representative, noted that the European Agency is working earnestly on partnerships with regulatory agencies in other regions to get a better grip on the growing challenges. One tool the EMEA uses is confidentiality arrangements, currently in effect with the U.S., Japanese and Canadian authorities. Nodop said, "Slowly, slowly our own priorities shift from the European perspective to the global one."

To be effective in the future, the EMEA will seek "proper arrangements" to facilitate communication, collaboration and cooperation with industry and other health authorities. "We need to have proper arrangements so we can rely on the local regulators to do their work," Nodop said in reference to countries like China and India which are now major suppliers of both active and inactive ingredients to drug manufacturers in Europe. The EMEA will "try to contribute to assist them through training and the exchange of staff to improve their regulatory capacity."

Gerald Heddell, Director of Inspections, Enforcement & Standards, MHRA, UK, noted that changes in the economic environment and the escalating cost of R&D will only accelerate the trend towards outsourcing to India, China and other developing economies. "I believe that many third country suppliers are responsible, well-managed companies, but recent experience reminds us that we need to be vigilant. And the further away, the more remote our sources of supply are, the more that vigilance is necessary," he said.

The European Commission recognizes that strong legislation is the centerpiece to combating an influx of falsified medicines and ingredients into the legal distribution chains throughout Europe. Last year, the Commission introduced COM (2008) 668 (Dec. 10, 2008) to amend Directive 2001/83/EC on pharmaceuticals by introducing new tools to target illicit products. The Council of Europe and the European Parliament currently are discussing the proposal through their respective legislative processes.

COM (2008) 668 targets falsification of medicines in relation to their identity, history and source. European Commission, Enterprise and Industry representative **Sabine Atzor** explained at the PDA/EMEA Joint Conference that the amendment is intended to make the "legal supply chain watertight against the entry of illegal products."

The proposal recognizes three "pillars" to combat the problem:

- Product Characteristics to authenticate
- Actors and Good Distribution Practices (GDP)
- Active Pharmaceutical Ingredients (API)

The first pillar, according to Atzor, would mandate the use of specific safety features (such as a serialization number or a seal) which allow the verification of product identity and safety. It would also prohibit the removal, tampering or covering (over-labeling) of safety features on packaging by actors along the distribution chain between the manufacturer and the last handler (pharmacist) or end user. The safety features should allow verification of authenticity, pack-identification and pack-tampering, she explained.

Current EU legislation does not provide the basis for such safety features. The amendment offers a Community-wide, harmonized legal basis for prescription drugs. Details of the proposal, if adopted, would be ironed out in the implementation phases. Another aspect of the first pillar is the requirement that manufacturers notify the authorities when there is suspicion of falsified medicines. Under the current Directive, notification is not an obligation and liability is unclear. The proposal would hold manufacturing authorization holders liable for damages caused by falsified medicines in terms of their identity.

Regarding GDP, the proposed amendment delineates responsibilities of the various actors in the supply chain. An important element in this area is the definition of trading, inserted to ensure coverage of entities that are virtual in nature. The legislation reads: *All activities consisting of negotiating independently on behalf of another person the sale or the purchase of medicinal products, or billing or brokering medicinal products, apart from supply medicinal products to the*

public, and not falling under the definition of wholesale distribution (proposed 17A of Article 1). The legislation spells out the expectations for each entity that trades drugs.

Atzor explained that the role of manufacturers, wholesalers and other entities involved in pharmaceutical trade is crucial to the system. The authorization of manufacturers, importers and wholesale distributors by the competent authorities.

To strengthen this area, the proposal will make it mandatory for drug firms to audit API suppliers and for wholesale distributors to audit their suppliers. In addition, wholesalers and those involved in trading will have to adhere to GDP and maintain a quality system. "We consider this to be a very important tool for all companies to ensure that the products they use are safe and of high quality," said Atzor.

Atzor also updated the audience on the status of several other legislative initiatives, including the Commission's proposal for GMPs for "certain" excipients. She used the *2008 PDA/EMEA Joint Conference* to discuss an impact assessment conducted on the excipients proposal (see "Are GMPs on the Horizon for Pharmaceutical Suppliers?", March 2008 *PDA Letter*, p. 16). This year, she announced that the proposal has moved forward and that the Council of Europe and the European Parliament are currently considering the proposal.

One Community initiative intended to help all players in the anti-falsification effort is the EudraGMP database, which recently went public and was updated with additional information. **Francisco Peñaranda**, EMEA Inspections Sector, presented the essentials of the system at the PDA/EMEA Joint Conference.

First, Peñaranda outlined the following reasons the EudraGMP database was launched:

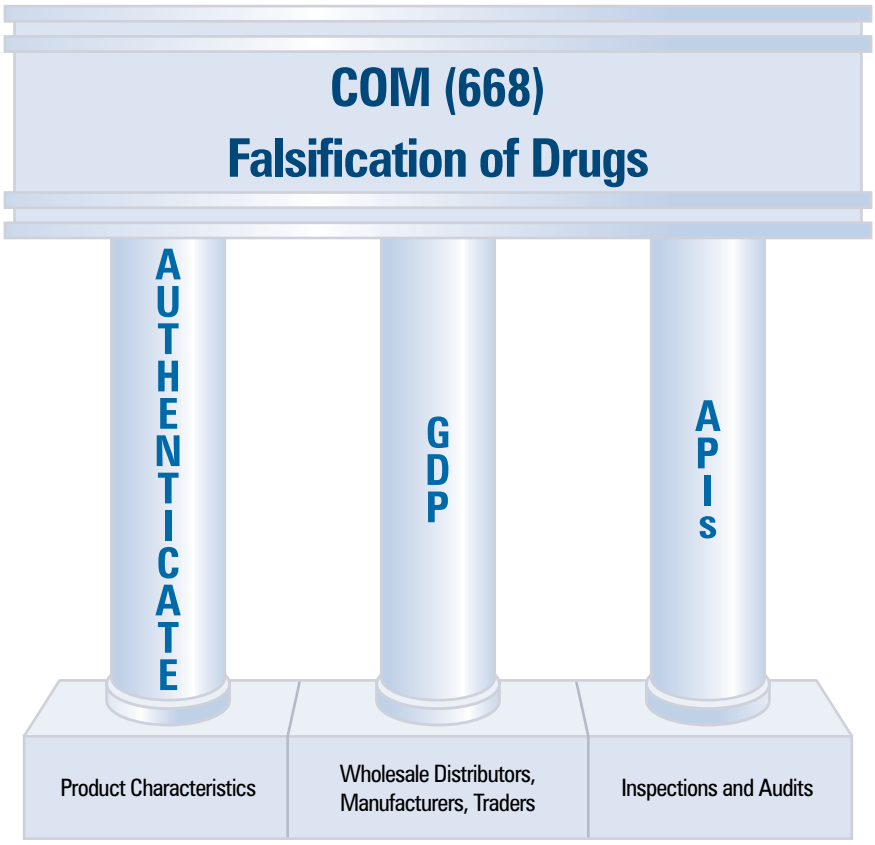
- No single pan European source of information on European manufacturers or on inspections performed by European Competent authorities was available online
- Procedure for paper exchange of information exists but not used effectively due to administrative burden and delays
- Inspectors and assessors were not aware if information provided by applicants was the latest update
- Resulting planning difficulties and duplication of inspections, particularly for 3rd country inspections
- Non-GMP compliant information difficult to find and follow-up difficult to coordinate
- Transparency: Access to general public

The database has both a government and public face, with Competent Authorities having access to much more information than the public. The database had included GMP certificate and Manufacturing/Importing authorization information since 2007, but in 2009, noncompliance information was added and public access was turned on. In its third and fourth phases, EudraGMP will include inspection planning in 3rd countries and information for faulty manufacture.

Full read and write access is available to all EEA and MRA Inspectorates. Full unrestricted read access is available to all EEA national competent authorities, the EMEA and European Commission and some non-EEA authorities, including the U.S. FDA. Public access is restricted and does not include access to noncompliance information.

A number of other health authorities were represented at the two-day conference, including the Laboratoire National de Santé (Luxembourg), the Irish Medicines Board, the States Agency of Medicines (Latvia), the Agence Française de Sécurite Sanitaire des Produits de Santé (France) and the conference host country's Regierungspräsidium Darmstadt.

The EMEA and PDA agreed to hold a fourth joint conference in 2011, following the 18-month schedule established at the first conference in 2006. The two organizations mentioned the possibility that the conference would become an annual event after 2011.



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Rick Friedman's Welcoming Remarks from the PDA/FDA Meeting

Good morning. This year's conference comes at a time when the essential role of daily adherence to GMP in assuring product safety has never been clearer. In particular, I think most will agree that raw material sourcing, including both active ingredients and excipients, is a huge and complex issue requiring a systemic solution beyond traditional implementation of CGMP. The greed that leads to Economically Motivated Adulteration has affected countries all over the world, both with immature and mature regulatory systems. The vulnerability of the global distribution system to ingredient safety risks remains very worrisome. This slide (see below) shows that the latest DEG contamination last month brings the global death toll to 788. In the last twenty years alone, DEG contamination has affected 7 countries, resulting in the deaths of approximately 660 worldwide consumers, many of them children. And the DEG adulteration of excipients like glycerin and propylene glycol is just one example of ingredients at risk. Heparin was a new ingredient that we found last year to be vulnerable to intentional contamination. We have all learned together in recent years that as unknowns in your supply chain increase so does cumulative uncertainty and risk. And we have also certainly learned that integrity can be compromised, not only by those lacking understanding of proper procedures for manufacturing or handling drugs, but also by those with bad intentions. So the question we all have to collectively deal with is, "how do we improve the system to prevent these grave risks?"

That background is why the 2009 PDA/FDA Conference committee has made outsourcing and related issues such as contracting, quality agreements, lifecycle knowledge management and supply chain security as key topics for this year's conference. On a higher level, the committee also wanted to do a few other things:

1) We wanted to create plenary sessions with compelling speakers who will have the latest news on these and other issues you are concerned about.

2) We hoped to make each breakout and even breakfast session so interesting and attractive, that it would be excruciatingly difficult for you to choose which one you should go to. As you look over the agenda, I predict you will have this quandary many times during the conference.

3) We've placed unprecedented focus this year on the impact of drugs on the lives of patients, including the great benefits of breakthrough drugs as well as the dangers of drug diversion and counterfeiting. Author Katherine Eban will join us for tomorrow's plenary session and will tell you a true story of drug diversion that is remarkable, and should not be missed.

4) Another idea by the committee was to include not only conceptual speeches, but also practical industrial case studies. So we've made sure the breakout sessions include either root causes of failures or continual improvement success stories.

5) And, as usual, we've included top thinkers from the industry and FDA to provide insights and discuss policy evolutions. Our great

788 Deaths due to DEG Contamination 1937–2009

Year	Country	Product	No. of Deaths
1937	USA	Sulfanilimide	107
1969	South Africa	Sedative	7
1986	India	Medicinal Glycerin	14
1990	Nigeria	Acetaminophen Syrup	47
1990/2	Bangladesh	Acetaminophen Syrup	339
1995/6	Haiti	Cough Medicine	85
1998	India	Cough Medicine	33
2006	Panama	Cough and Anti-Allergy Syrup	46
2008	Nigeria	Teething Formula	84
2009	Bangladesh	Acetaminophen Syrup	26

list of speakers includes our Principle Deputy Commissioner (Dr. Sharfstein) in a few moments in the opening plenary, and folks from all medical product Centers including CDER Center Director Dr. Woodcock on Wednesday.

The presentations and discussions address how we can collectively improve the system. So sit back and enjoy the ride for the next two-and-a-half days.

"We expect that you will hear a lot of insights and thought provoking ideas to help to all of us harness the complexity of our daily work and adopt practices to meet today's global challenges"

We expect that you will hear a lot of insights and thought provoking ideas to help to all of us harness the complexity of our daily work and adopt practices to meet today's global challenges.

Hopefully you will bring back many good ideas to your organization for possible quality system enhancements. So thanks for attending this year's joint conference, and we hope you thoroughly enjoy it.

Recall Study Results Unveiled at the PDA/FDA Meeting

Emily Hough, PDA

Lynn Torbeck, President, Torbeck and Associates, discussed at the *2009 PDA/FDA Joint Regulatory Conference* a study of drug product recalls he has been working on with the U.S. FDA since 2007. The study involves recalls occurring because of quality defects that have the greatest potential impact on patient safety. **[Editor's Note:** Torbeck provided a preliminary overview of the work at the 2008 PDA/FDA conference; see the October 2008 *PDA Letter*, p. 22.**]**

Torbeck found that out of 105 Class 1 recalls examined, 49 involved prescription (Rx) drugs and 56 were of over-the–counter (OTC) therapies. There is an "increasing trend in Class 1 recalls from 2000-2008, and it increases in both prescription and in over-the-counter [products]," he said. Of the problems discovered in Class 1, 32% were for undeclared new drugs, 26% were for microbial contamination, 9% were for lack of content uniformity, 7% associated with Heparin, 6% for an incorrect label and 5% because of tableting issues. The remaining 15% were associated with other issues.

"Of the voluntary recalls prompted by FDA's suggestion, 61% of those were over-the-counter undeclared new drugs." Torbeck said in this case, an increase of recalls was actually a good thing.

Torbeck found recalls that were initiated because of product contamination that either caused serious illness or death or posed a serious risk of such outcomes to people with compromised immune systems, the elderly or the very young. Items containing Burkholderia cepacia, however, can be found in ordinary products like "mouthwash, eyewash, nasal spray, adult and baby wipes, surgical prep cloths, skin cream and electrolyte solutions." Part of the problem with the bacteria is complacency, since that product contamination is generally not considered not to be a real problem as there is generally a lower risk for normally healthy people.

Another issue that was found was subpotency; 121 recalls for this issue were found from November 2000 to October 2008, 80% were for prescription and 20% were for over-the-counter products. Of that, Class II recalls made up 38% and Class III made up 58%.

Torbeck reported that 75% of recalls were associated with stability failure. He said that development and stability are done with a minimum of studies and data resulting in poor estimates and a lack of product and process knowledge and that this supports the FDA promotion of designing quality into the product at the beginning of the product life cycle.

Category of Recalls

Recalls are actions taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority.

Class I Recall: A situation in which there is a reasonable probability that the use of or exposure to a volatile product will cause serious adverse health consequences or death.

Class II Recall: A situation in which use of or exposure to a volatile product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Class III Recall: A situation in which use of or exposure to a volatile product is not likely to cause adverse health consequences.

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PDA/FDA Sessions Highlight Regulatory Changes, Quality

Barbara Zinck, Zinck Consulting

Quality Agreement Session Brings High Attendance

Even though quality agreements have been used by pharmaceutical and biopharmaceutical companies for more than ten years, the topic is still of interest based on the full attendance at the *2009 PDA/FDA Joint Regulatory Conference* session on quality agreements/technical agreements/cooperative agreements.

The U.S. FDA, industry and contractor perspectives on presented quality agreements were provided by **John Eltermann**, Jr., Director, Division of Manufacturing and Product Quality, CBER, U.S. FDA; **Barbara Zinck**, President, Zinck Consulting and **James Shirey**, Director/Team Leader, Contract Operations Quality Assurance, Pfizer.

There was consensus by all presenters that quality agreements are beneficial to clarify and document responsibilities and expectations between the applicant and the contract manufacturing organization regarding quality aspects of outsourced activities for manufacturing, laboratory testing and vendors. Even though quality agreements are not in a U.S. FDA regulatory requirement, and thus quality agreement issues may not result in a regulatory citation, the consequences of a bad agreement may result in a FDA 483 observation. It is necessary to have the quality roles and responsibilities defined.

A quality agreement is an effective mechanism to document the FDA required quality roles and responsibilities and also satisfies European regulatory requirements for quality agreements. This continues to be an important topic as evidenced by quality agreement issues and questions raised not only during this session but also in subsequent sessions.

Presenters Emphasize More Agile, Consistent Regulatory Change Needed

Change is a continuum and the complexity of the change affects implementation strategies, tactics, approval time, regulatory impact, product quality (revalidation and stability) and training. Multi-market regulatory changes present challenges for implementing a change since some regulatory approvals are rapid and some regulatory approvals are extensive. A more agile and consistent global regulatory change management system would benefit industry, regulators and patients.

The U.S. FDA desired state for change management and applying quality risk management to change controls is for FDA to perform an initial verification and subsequent inspection and only require regulatory filings for formulation changes. Quality by Design and enhanced science during development is leading to better understanding of the product's design space which may lead to lower filing categories in the future.

Change Management presentations at the *2009 PDA/FDA Joint Regulatory Conference* were made by **Sue Schniepp**, Vice President, Quality Systems, Javelin Pharmaceuticals; **Richard Norgard**, Executive Director, Global Manufacturing Compliance, Pfizer and **Rick Friedman**, Director, Division of Manufacturing and Product Quality, CDER, U.S. FDA.

Attention Drawn to the Importance of CAPA

Corrective actions and preventive actions are important elements of any organization's quality system. These activities impact the drug product manufacturer's ability to eliminate or reduce the risk of failure to meet customer's expectations and established product requirements. **Kim Trautman**, Medical Device GMP/Quality Systems Expert, CDRH, U.S. FDA, at the CAPA session at the PDA/FDA Joint Regulatory meeting emphasized in her presentation not only regulatory requirements but also the importance of corrective and preventive actions (CAPA) as evidenced by 98 Warning Letters that were issued for CAPA deficiencies. Data analysis and statistical rationale is necessary for trigger points but should not be used to justify not acting. The U.S. FDA is not looking for set time frames for CAPA completion but is instead looking for uniformity and consistency with set goals, prescribed actions and follow-up steps. Simply changing a procedure as a corrective action is inadequate since it does not get to the systemic root cause. The Global Harmonization Task Force (GHTF) Study Group 3 will be publishing tentatively in December 2009 a quality management system (QMS) medical device guidance on CAPAs related to QMS processes.

Marsha Major, Director, Quality and Compliance, Johnson & Johnson, emphasized the importance of senior management support up to the president, and having a formalized escalation process across the organization is critical for success of CAPA programs. J&J's new process generates minor, major or critical incidents which determine the level of investigation. Effectiveness checks are performed for critical incidents and evaluated for major incidents and ineffective CAPAs go back into the CAPA system.

Martin VanTrieste, Vice President of Quality, Commercial Operations, Amgen, demonstrated that the key to identifying preventive actions is to have good trending with a holistic review of data. Amgen's CAPA system is patient focused, risk-based with effort, resources and timelines proportional to patient risk. Faster root cause identification leading to more effective CAPAs with fewer significant and repetitive deviations in conjunction with management support and review results in a CAPA system that makes good business sense that can improve business processes and prevent problems in addition to detecting problems.

REPORT FROM THE 2009 PDA/FDA JOINT REGULATORY CONFERENCE

Assessing Risks of Changing Sterile Drug Manufacturing Sites at PDA/FDA Workshop

Cliff Campbell, Campbell Informatics

The meeting was organized as an afternoon workshop and was held in conjunction with the *2009 PDA/FDA Joint Regulatory Conference* at the Renaissance Hotel in Washington D.C. on September 16. The session drew an audience of 36 participants from the U.S. FDA, industry and the consultancy community. A total of 21 manufacturing companies were represented.

Jon Clark, Associate Director for Policy, OPS, CDER, U.S. FDA, opened proceedings by welcoming attendees, introducing the speakers and summarizing the pre-contract dialogue that had taken place between the Office of Pharmaceutical Science (OPS) and **Cliff Campbell**, President and Founder, Campbell Informatics, in regard to process modeling and 21st Century compliance. In his subsequent presentation, he described risk assessment as an evolutionary process—with the current assignment being part of that process—and outlined the core principles underpinning successful risk assessment (commensurate, science-based, qualitative/quantitative, transparent, assumptions and uncertainties stated). He confirmed that while the current code of federal regulations (CFRs) require sterile site changes to be reviewed and approved prior to implementation, the contract has demonstrated that the use of a comparability protocol is a permissible option, satisfying the Agency's requirements for risk communication. He then itemized deliverables and timelines associated with the comparability protocol process, distinguishing between data commitment, data acquisition and data summarization aspects. He referenced a number of requirements in regard to qualitative/quantitative risk communication, including detailed description of proposed site changes, description of existing data supporting the rationale, summary of the studies to confirm risk analysis and acceptance criteria that these studies must meet. He concluded by reminding attendees that this advice amounts to "redirection to existing regulation" and that there was ample precedent for such an approach which from an Agency standpoint is not a rule change and, therefore, available to manufacturers as of now.

Campbell presented an overview of the contract scope, the emphasis being on the identification and control of sources of variability and sources impurity in relation to terminally sterilized (TS) synthetic drugs and aseptically processed (AP) biotech drugs from formulation to fill in both cases. He cited a number of source documents, including *PDA Technical Report No. 44, Quality Risk management for Aseptic Processes* but stressed that the assignment deliberately chose to operate on a first principles basis, relying on established Agency guidance (TS & AP) when developing the interview question sets. He described the interview process along with the additional case study material acquired from a subset of participants. In response to the level of subjectivity that he encountered in the course of the assignment, he highlighted the benefits of a standardized approach addressing product, process and plant profiles at both the donor and recipient site. He then summarized the post-interview discussions that took place at OPS. These again included the issue of standardization and recommended that a comparability protocol used in conjunction with U.S. FDA's MAPP 5040.1 document [a manual of policies and procedures for product quality microbiology information in the common technical document for quality] that provided a level of specificity and uniformity that reviewers require. He presented a schematic representation of the proposed comparability protocol and annual report sequence geared towards unambiguous implementation by industry. He concluded by emphasizing that, properly crafted, the comparability protocol is synonymous with the risk management plan that the Agency requires and identical (size, acceptance criteria, rationale) to traditional prior approval supplements minus the data, this item being acceptable in summary format via annual report, amendment or special report.

Ian Symonds, Director, Aseptic Quality Assurance, Global Quality Assurance, GlaxoSmithKline, provided attendees with a highly informative presentation on the technicalities and practicalities of terminal sterilization, beginning with a risk-based summarization of fluid load vs. porous load scenarios, commenting that porous loads require considerably more examination and analysis. Based on his experience, he described a number of factors that can result in poor sterilization performance, including steam valve malfunction, cooling cycle variation, fan failure and drain blockage. He then presented a process flow diagram on behalf of a typical synthetic product fill-finish operation, advocating the use of risk-based icons to highlight sources of variability and impurity and their related controls. He recommended that these diagrams be in place at each site and be used as the basis of both gap and risk analysis between donor and recipient locations and as a communication mechanism when engaging with regulatory authorities. As a sidebar, he emphasized that such diagrams are equally valid in regard to aseptic processing and other aspects of pharmaceutical manufacture and are by means specific to terminal sterilization. He also presented a cycle control chart for a typical sterilization step. In addition to its more recognized function of cycle-by-cycle monitoring and record-keeping, he

explained how atypical traces can be used as a valuable early warning system and as a diagnostic tool in regard to deteriorating equipment/utilities/instrumentation (leakage, vacuum pump, steam quality, control sensors, etc.). He concluded his presentation by responding to a number of MAPP 5040.1 terminal sterilization issues that had been raised by OPS in the course of the assignment. These included heat distribution and penetration, thermal monitors, effects of loading, microbiological efficacy of the cycle, identification and characterization of bioburden.

Terry Milby, Director, CMC Regulatory Affairs, Genentech, presented his company's perspective on expanded change protocols for drug product transfers, which he viewed primarily from a business efficiency standpoint. He explained that within Genentech, risk ranking is performed after each identified risk factor has been assigned a composite risk score and is used to sort the risks relative to each other while risk filtering uses weighting factors, cut-off values for scores or other criteria to fit the risk ranking into the company's management or policy objectives. In regard to "regulatory relief," he confirmed that risk ranking and filtering is used to determine the risks associated with drug product transfers, thereby defining the filing category and scope of the associated qualification studies. In terms of determining specific drug product transfer risks, he distinguished between licensed and unlicensed facilities, in-house and CMO transfers, approved and unapproved products and itemized a number of key aspects in regard to process differences between donor and recipient (filling systems, freeze/thaw cycles, processing times, product contact surfaces, product manipulations). From a qualification/validation perspective he distinguished between first product introductions on the one hand and subsequent product introductions on the other—where risk assessment may establish that a reduced number of studies is permissible. He concluded by emphasizing that while each drug product may behave differently during the course of a site transfer, there are common categories of risk that can be proactively managed. His recommendation was to focus on the product path, new equipment and technologies, and Quality System and personnel training differences between the sites.

Clark led an open forum discussion between attendees and speakers, **Steve Langille**, PhD, Senior Microbiology Reviewer, OPS, CDER, U.S. FDA, joined the panel for this section of the workshop and **Keith Webber**, PhD, Deputy Director, OPS, U.S. FDA, also participated from the floor. A number of topics were discussed, with key points summarized as follows:

1) Equivalence: Various views were expressed in regard to inter-site equivalence, the general consensus being that physical sameness is not a requirement. Attendees agreed that gap analysis driven by the type of process flow diagram that Symonds presented was highly beneficial and represented standard/recommended practice within their companies.

2) Complexity: A number of participants described a "sliding scale" of complexity, including basic capacity expansions using identical/similar technology within the same site, transfers to established sterile facilities within the same company, construction of a green-field facility in a new location with novel technology, new product and untrained personnel. There was general agreement that while the comparability protocol option had relevance for each of the above, the more complex scenarios are by definition more demanding and will result in more vigorous scrutiny from the Agency. As with many other aspects of compliance, applicants were advised to use logic and good science to determine what is and isn't permissible here.

3) Basis of Comparison: Campbell argued that if each site independently complies with MAPP 5040.1, then direct comparisons need not be made and sterility assurance equivalence can be inferred between the two sites. On this view, F_0 [a measure of sterilization effectiveness. See the glossary of terms for more information on page 5 in *PDA's Technical Report No. 1, Revised 2007, Validation of Moist Heat Sterilization Process Cycle Decision, Development, Qualification and Ongoing Control*] can be equally realized by independent but in locally validated autoclave cycle parameters vials can be aseptically processed via independent but locally validated fill technology, etc. As an aside, he remarked that in certain cases, operating variables of equipment are miscategorized as process parameters, resulting in unduly onerous equivalence criteria being applied.

4) Fitness for Purpose: Initial consensus was that Site B should be equal to or superior to Site A "in every respect." On reflection, however, most participants agreed that in situations where Site A has been deliberately or unintentionally overdesigned Site B should not be disqualified or penalized for being of an apparently "lesser" standard. This comment applies equally to equipment, environmental and automation design, fitness for purpose being the necessary and sufficient condition in every case. That said, a number of participants were of the view that regardless of regulation or guidance, operations conducted within Grade A (or Grade B) at the donor site cannot be downgraded to Grade B (or Grade C) at the receiving site or that operations conducted within "isolator technology" cannot be transferred to "non-isolator technology." It seemed that attendees agreed to disagree on this item.

5) Filing: Attendees presented a number of filing scenarios in regard to sterile product transfers. The majority view was that a single comparability protocol per transfer was the most realistic option with the initial site utilizing a traditional supplement inclusive of data. The possibility of developing a single protocol to accommodate multiple sites was not discounted, but this was considered to be a more challenging and impracticable scenario by the U.S. FDA who also confirmed that review cycle for comparability protocols would be similar to traditional PAS (four months for comments etc.).

6) Contract Manufacturing Organizations(CMOs): The valuable role of established, reputable CMOs was confirmed by several attendees and acknowledged by FDA. The same rules of engagement apply to CMOs as to in-house transfers (GMP compliance, established track-record with

candidate process, experienced personnel, robust quality management system). FDA's concern in this area, expressed by Langille relates to inappropriate transfer by applicants to unqualified/unaudited CMO establishments.

7) Failure Mode & Effects Analysis: The role of FMEA was discussed in some detail, the conclusion being that it is best used selectively rather than indiscriminately. The majority view was that FMEA should be applied at the unit operation level of detail, i.e., in tandem with the type of process flow diagram previously mentioned and when analyzing particularly intractable problems at the equipment/component level. It was also noted that other options exist—either as alternatives or precursors to FMEA, including preliminary hazard analysis and fish-bone diagrams, both of which have valid roles to play.

8) GMP Inspections: A discussion took place in regard to how FDA's inspection division would need to be brought into the proposed process. In summary, establishing and maintaining GMP compliance at the receiving site is an obvious prerequisite to any transfer, the sponsor being obliged to engage FDA's compliance division to inspect the facility and coordinate with review staff as appropriate.

9) Pilot Program: Reiterating a point made in his presentation, Clark confirmed that what is being proposed via the assignment is not a rule change, and there is no necessity or benefit in engaging in a pilot program prior to formal implementation. That said, some attendees seemed reticent to accept that the workflow that Campbell presented in his talk could be implemented without some form of pilot on the industry side. By way of riposte, participants were advised that relative to traditional supplements, there is nothing new in terms of studies, data, criteria, rationale, summaries—other than the revised timing and approval mechanism of some of these items.

10) Guidance: Extending the previous point, Clark confirmed that while a guidance or policy document may eventually emerge, these are by no means prerequisites to the preparation or submission of successful comparability protocols by applicants.

11) Journal Article: Clark informed attendees that an article on the assignment is currently being drafted by Campbell and Langille. The *intent* is to have this prioritized for publication in the *PDA Journal of Pharmaceutical Science and Technology*. Participants will be informed once details have been finalized.

12) CDER vs. CBER: Attendees were advised that the assignment and its findings are specific to CDER-regulated drug products and that manufacturers should liaise directly with CBER in regard to the comparability protocol option for biologics. From a CDER perspective, Webber stressed that comparability protocols are intended to be a multifunctional tool that have been successfully used in a number of change-related areas, within drug product and drug substance manufacture alike. While CBER was not officially represented at the workshop, there was strong industry consensus that the comparability protocol mechanism has equal validity for biologics.

Quality Systems IG Discusses Continual Improvement at PDA/FDA

Quality System Interest Group Leader Anders Vinther, PhD, Genentech

Once again, the Quality System Interest Group (IG) met at one of the PDA major events—this time at the September *2009 PDA/FDA Joint Regulatory Conference* in Washington, D.C. Approximately 150 engaged PDA members discussed continual improvement of the quality system, practical applications of quality risk management(QRM) and the results of a survey completed amongst the Interest Group members prior to the conference.

FDA's **Tara Gooen**, Team Leader (Acting), New and Generic Drug Manufacturing Team, Office of Compliance, CDER, U.S. FDA, discussed the Agency's expectations that companies evaluate and improve their quality systems. We often speak about continual improvement of our manufacturing processes, waste reduction, etc., but it is important also to remember improvements to the quality system itself. Although, this is currently discussed in relation to implementation of the ICH Q10 on pharmaceutical quality systems, the requirement is really not new. Gooen pointed to various sections of 21 CFR 211 including 211.180(e), which requires data to be assessed and trended and for firms to identify changes. After discussing the United States and ICH expectations to continual improvements and the benefits of implementing such she listed various recent examples of warning letters related to inadequate quality systems. Below is a list of four examples:

- 21 CFR 211.22(b), Lack of quality agreements with roles and responsibilities
- 21 CFR 211.22(d), Analytical methods are not appropriate for raw material and finished product release
- 21 CFR 211.22, Quality Control Unit approves or fails to review inadequate/incomplete records, fails to ensure appropriately maintained equipment
- 21 CFR 211.180(e), Lack of periodic review of process, including: complaints, recalls, returns and salvages

"Consumers need to be confident that drugs meet our manufacturing requirements for identity, strength, purity, and quality, and have been evaluated by the FDA for safety and efficacy"

Gooen concluded with a quote from Janet Woodcock, MD, Director, CDER, U.S. FDA: Consumers need to be confident that drugs meet our manufacturing requirements for identity, strength, purity, and quality, and have been evaluated by the FDA for safety and efficacy.

Various examples of how quality risk management (QRM) can be implemented into individual quality system elements was discussed by **John McShane**, Director of Validation, Validation, Genentech. He started out by reminding the audience that QRM can be termed as an enabler in ICH Q10, and that QRM doesn't really show the full benefit until it is fully "operationalized" into all activities that ultimately can be linked to patient risk. Because QRM is not "an exact science" but dependent on the experience of the risk management team, rigorous training is critically important to ensure consistency in risk scoring. This is particularly important because the score determines the criticality and thereby potential action needed.

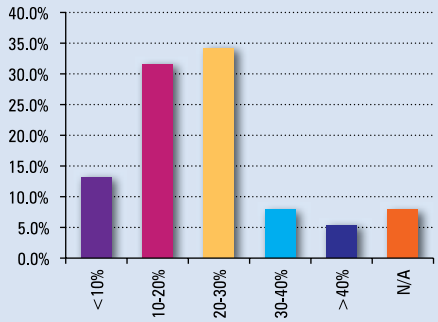
Examples of QRM applications were shown for the validation v-model with QRM incorporated at all steps from planning to qualification, for tech transfers and for deviations and changes. For the latter two examples, it was emphasized that the risk control strategy (RCS), which summarizes the risks identified and how these can be reduced and/or controlled needs to be updated when new information is identified and this very often comes from changes and deviations. One of the questions from the IG members was about where the RCS is stored. The answer from McShane was that this could be done in a number of ways—typically in the general document repository and that the most important thing is that it is available and readable to those regularly involved in the topic covered by the RCS. They need to know where the risks are, how these are mitigated/reduced and they also need to update the RCS when new relevant information is available.

The last topic on the agenda was a summary and discussion of the quality systems survey, which was sent out to all Quality System IG members prior to the conference. There were 36 questions and 38 IG members responded to the survey. The survey and its results

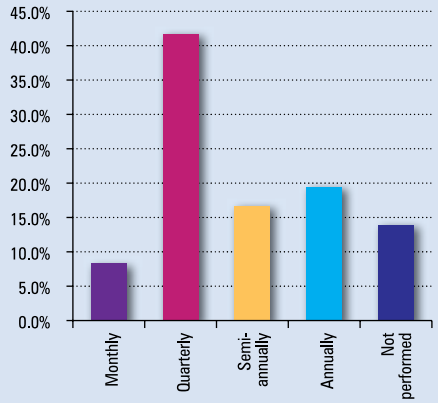
do not necessarily reflect "state of the industry," but rather a "sample" showing quality system implementation amongst responding Quality System IG members, some of the results are shown graphically in this article. The following are key findings:

- A majority of the organizations have a 10-30 % quality to total headcount ratio.

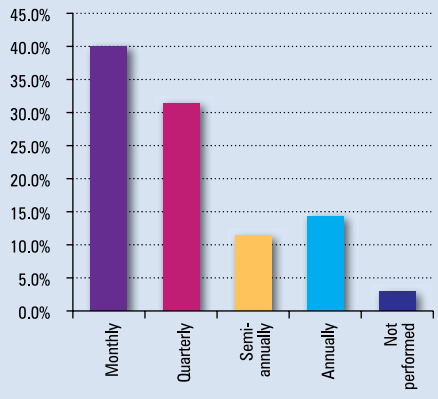
What is the percentage of Quality to Total (Manufacturing & Quality) Headcount?



How often does your company perform Corporate-level Quality System Management Reviews



How often does your company perform Site-level Quality System Management Reviews

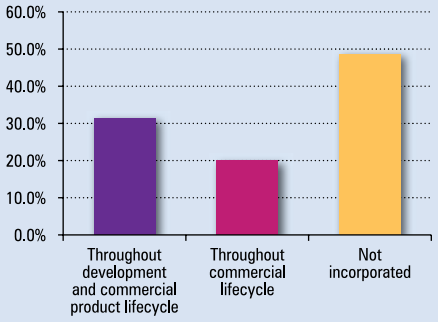


- In terms of quality system management reviews, these are generally implemented and are performed on a regular basis covering most key processes. However, less than 50 % include continual improvement activities on the agenda.

The survey and its results do not necessarily reflect "state of the industry," but rather a "sample" showing quality system implementation

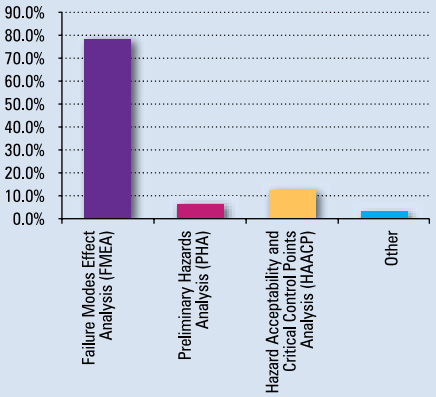
- Design space principles are being used by ~65 % of the respondents.
- Knowledge management is being discussed by many companies, incorporated into the general work by ~50 %, but very few are yet applying IT tools.

Knowledge Management is systematically incorporated into the Quality System (Manufacturing & Quality) Headcount?



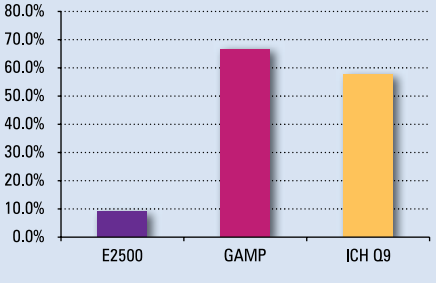
- Risk management is, in general, integrated into the quality system now but in terms of tools, almost exclusively, only FMEA is used.
- ~15 % have converted equipment, utilities, facilities validation to risk-based systems, ~50 % will do so when modified and ~15 % plan not to transition.

The typical Equipment, Utility and Facility risk assessment method used is



- One topic that would be interesting to discuss in a future meeting is the fact that there was an approximately 50:50 split of respondents that have/have not QA approved commissioning plans and system drawings for Engineering and IT.
- In terms of a validation approach, a majority of respondents use GAMP and ICH Q9 as basis for their program and less than 10% use E2500.

The basis for the Validation program is



Out of the Ashes—Pharmaceutical Companies Survive the Recession and Expand!

Emily Hough and Walter Morris, PDA

Emily Hough has monitored the pharmaceutical financial news throughout 2009, and in this report, she concludes that not everything is bleak. Mergers and acquisitions are creating new opportunities; generics manufacturers are healthy and expanding; skilled workers in Asia are finding new opportunities because of the transfer of research and manufacturing jobs to their countries, and in some cases, new economic life is sprouting in big pharma's wake.

The global recession is the latest blow to an already beleaguered pharmaceutical industry, which faces scrutiny from politicians who want cheaper medicines for constituents and investors who want research investments to produce the next generation of blockbuster drugs. Following a decade in which the industry saw all boats rise, the last decade has been one of flagging success. The recession only adds to the uncertainty and has hastened plant closures, consolidations and the transfer of research and manufacturing capacity from North America and Europe to emerging markets in Asia.

Confirming the bad news was *2009 PDA/FDA Joint Regulatory Conference* keynote speaker **Barbara Ryan**, Managing Director, Deutsche Bank Securities. "First and foremost," she told the audience, "I think it's important to start off by saying that there is no question that the economics within the pharmaceutical industry have been and are under assault. They're under assault from a lot of different directions, and that is the reason that we see so much drama and change within each of your organizations. The likelihood is great that that will continue to be the case. The good news is the industry is in fact evolving to a changing world.

On top of the uncertainty surrounding imminent health care reform in the world's largest market for pharmaceuticals—the United States—most of the large research pharmaceutical interests face a "patent cliff" between 2010-2012, when about $30 billion (USD) in revenue will begin to evaporate, Ryan reported. "As a result pharma company growth has been slowed, earnings stability and improvement have been driven by the obvious cost-cutting," she said. Generics companies, on the other hand, stand to gain market share as the patents fade away.

> ***"The lifeblood of the industry is R&D and innovation, but returns have to be substantially improved"***

The ultimate solution for big pharma is to improve the returns on R&D investments, money for which has been in decline. "The lifeblood of the industry is R&D and innovation, but returns have to be substantially improved," said Ryan. However, she predicts R&D budgets to drop in the coming years, which could be a good thing. "I don't think this is all bad, because I don't think there is any data that says spending more gets you more. In fact, the data might suggest the reverse—that there's been an inverse correlation between R&D budgets and productively."

Mega-Mergers

Besides the cost-cutting that most large companies have undertaken in recent years, mergers and off-shoring have become the two biggest weapons in big pharma's arsenal to combat the financial siege. Companies are utilizing mergers to soak up overcapacity that is resulting from blockbusters going off patent and a dearth of prospects in the pipeline.

"The mergers are happening now because those senior managements have [looked at the cost-cutting] strategy, and they have to assess how it's working out, and it isn't working out very well," Ryan said. In spite of the measures to right-size sales forces, research ➤

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organizations and manufacturing operations, "the stocks have continued to go down."

Consolidation, therefore, is the next best strategy, and consolidation is what is happening…big time. In the last year, the business wire buzzed with news of mergers and acquisitions throughout the industry, with several mega-mergers taking place: Merck and Schering-Plough, Pfizer and Wyeth and Roche and Genentech. ***(1)*** Industry analysts like Ryan wonder openly if Eli Lilly, GlaxoSmithKline and AstraZeneca themselves won't soon be involved in merger activity.

Momentum behind pipeline acquisition and shared drug development has grown in recent years.***(1)*** This allows a big pharma company to utilize its massive resources to complete the final stages of clinical development after smaller companies provide the initial leg work.***(2)*** Oftentimes, these strategic mergers and acquisitions are in areas complementary to the purchasing firm's existing business. For example, GlaxoSmithKline acquired Stiefel Laboratories in order to "grow and diversify [its] business through targeted acquisitions." With this deal, GSK strengthens its dermatological businesse by receiving 15 projects in late-stage development and a number of brand products on the market.***(3,4)*** Likewise, Abbott Laboratories is in the process of absorbing the prescription drug unit of Solvay, giving Abbott "sole possession" of a "shared cholesterol drug venture."***(5)***

Other times, the mergers and acquisitions move a company into a new area, such as biotech or niche therapies. Ryan pointed to the Pfizer–Wyeth merger as a prime example. "Not only does Pfizer–Wyeth create an opportunity to reduce costs, but it also creates an organization that has much more diversity and less dependence upon a single product…So Pfizer now is much more substantial in biologics, which they needed to be, and is obviously a player in vaccines, which was necessary. And so we see this occurring across the industry as well. Acquisitions of biotech will continue."

Abbott's purchase of the Solvay drug unit also places the U.S.-based drug giant in charge of Solvay's Dutch cell-based flu vaccine plant, a €137 mil. business in 2008.***(6)*** Johnson & Johnson also recently jumped into the flu vaccine market, purchasing the Dutch firm Crucell.***(6)***

It will be equally important to small biotech as it is to big pharma for this kind of consolidation to continue, as capital from outside the industry dries up

"I think what is interesting to know today is that the capital that pharma has is actually more valuable than it has been in a long, long time, because money is scarce today. Five years ago it wasn't so. Biotech companies would go out and get money from just about anybody, except from pharma, so that they could pursue something to a late-stage, and then sell it to pharma for a lot of money. Today I think those opportunities are few and far between, so the venture capital funds are basically shut down for many of these companies."

The Downside of M&As

Companies also merge business units to form new ventures to help share cost and risk. For example, Pfizer and GlaxoSmithKline combined their HIV drug businesses into a "jointly owned company" earlier this year.***(7)*** The new company's portfolio boasts eleven existing drugs, with six more in development. In June, Merck and AstraZeneca announced a similar arrangement, agreeing to jointly develop two cancer drugs that would be used as a combination treatment. Working jointly on a combination therapy prior to the marketing authorization is an unusual step, but one the two firms feel will accelerate approvals.***(8)***

Cost-cutting remains a reality, however, and mergers are only going to accelerate plant closures, off-shoring and reduction of research capacity. Ryan elaborated on the impact on research organizations: "I think if you take Pfizer, they are spending $7 billion on R&D. They will acquire Wyeth, and they are spending $4 billion on R&D. There is no way on the planet Earth, that that combined organization is going to spend $11 billon/year on R&D."

Indeed, Pfizer announced reductions to the R&D function not even two months following Ryan's talk. The firm plans to close six R&D facilities in New Jersey, New York, North Carolina and the United Kingdom and release 39,000 employees.***(9)***

In an effort to cut costs, Johnson and Johnson and Merck have announced layoffs of about 8,200 and 16,000 employees, respectively.***(9)*** Both Genentech and Roche have shed employees since the merger.

A state like New Jersey is particularly vulnerable to the new jobs calculus in the industry, due to the heavy concentration of firms located there. Known as "the capital of pharmaceutical research, manufacturing and marketing," New Jersey saw an 11% reduction in pharmaceutical-related jobs (42,000 to 37,800) between 1990 and 2007, a period when overall employment in the industry grew by 40%.***(10)***

Though the closing of research and manufacturing sites in Europe and the United States is painful in those regions, the concomitant opening of facilities in India and China is helping those economies grow. A prime example of this dichotomy is a recent decision by Sanofi-Aventis to close or divest eight of its research sites in high-cost regions and increase investment in Asia. It has closed four locations and divested one in France and plans to either close or divest three additional sites in the United Kingdom, Japan and Spain.***(11)*** On the flip side, it has opened a biometrics center in Beijing and will increase its investment in research and development in China.***(12)***

It is estimated that the pharmaceutical industry has doubled the amount spent outsourcing from $11.4 billion in 2001 to about $24.9 billion in 2007.***(13)*** In July 2009, India ranked first as the top destination for pharma outsourcing, followed closely by China which jumped ahead of Ireland.***(14)***

Traditionally, Ireland has held a strong stake in the pharmaceutical sector, but it too has suffered during the recent recession as companies turn to India and China.***(15)***

Not all jobs lost in the United States and Europe go to Asia. For example, some of the lost jobs in New Jersey are reappearing in California (via the Roche/Genentech merger) or in places like Florida (Stiefel/Barrier Therapeutics merger). In some instances, the mergers are sending jobs back to New Jersey, as is the case with Roche's decision to its global oncology research facilities in California to New Jersey.***(10)***

Out of the Ashes

While the industry's activity to reinvent itself unsettles employees and local economies, the highly skilled workforce left behind is not totally helpless. Examples of entrepreneurial activity sparking in the wake of a plant closure exist and are encouraging. In some cases, the divesting company plays an active role in transforming the facility from a corporate outpost to a hub of entrepreneurial growth.

For example, new life was found for Wyeth's Rouses Point, New York facility when the company worked out a plan with Akrimax Pharmaceuticals, a New Jersey-based contract manufacturer. Under a deal struck in 2008 with the help of then Sens. Hillary Clinton (D-NY) and Charles Schumer (D-NY), Akrimax agreed to purchase the facility and then lease a portion back to Wyeth for two years while Akrimax transferred its own products into the plant.***(16)*** Earlier this year, Akrimax's founders launched a new venture, Rouses Point Pharmaceuticals, to operate the manufacturing facility. The president of Rouses Point Pharmaceuticals Ben Maizel, said that he estimates $100 million coming into the facility within the next three years.***(17)*** Wyeth continued research operations at the Rouses Point facility, but this was ended following Wyeth's merger with Pfizer.***(18)***

Ann Arbor, Michigan also has seen new life come in the wake of a large pharma plant closure. Following Pfizer's decision to shutter a research facility in the city, the University of Michigan stepped in and purchased the 30-buidling 173.5 acre campus facility for $108 million.***(19)*** In this case, the poor economy and sinking real estate market in the United States served as allies, because the deteriorating value of the property convinced the cash-flush University to make the deal, some say at an 85% discount to what the site normally would have demanded.***(19)*** With plans to expand the facility by 33% ***(20)***, it is believed that around 2,000 jobs will be created over the next 10 years.***(21)*** The mayor of Ann Arbor and leaders from the university believe that this purchase will enable the formation of offshoots and/or startup companies in the area.

In Plymouth, Michigan, a former Pfizer facility is now the home of the Michigan Life Science and Innovation Center. A combination of state, local and private foundation organizations purchased the site.***(22)*** Some of the firms operating in the facility demonstrate the entrepreneurialism of Pfizer's former employees, including Velesco Pharmaceutical Services, Next Generation, Lycera, and Esperion Therapeutics.

Respond to Change

In closing, Ryan acknowledged industry's resilience. "We've been in this place before, the industry has had it's ups and downs in terms of R&D productivity and I think that we're probably just in a lull. However, the industry, the leading companies, as a consequence of the survival mode methods are going to be bigger and therefore are going to be slower growing and more mature companies. But below them, there will be tremendous headroom for innovation and

Signs of Life

Pharmaceutical companies are still opening and acquiring sites, even in light of the recession. The following is a sampling of new economic development in the pharma industry:

- Abbott Laboratories has opened up a new pharmaceutical R&D facility in Singapore in March.
- GATC Biotech will invest more than five million euros into its headquarters unit in 2010 to create offices and labs for 100 additional employees.
- The Johns Hopkins University has launched twelve startup companies to fund early stage biomedical inventions.
- Medis has opened a drug packaging plant in the Czech Republic in mid-August.
- GlaxoSmithKline is planning to expand in India, China and Russia within five years.
- Hisamitsu Pharmaceutical Co., a Japanese company, has bought Noven Pharmaceuticals so it can boost its presence in the United States.
- Proctor & Gamble sold its prescription drug unit to Irish drug maker Warner Chilcott, this move will expanded the company's reach into 14 new countries.
- Chromecell has opened a new research center in New Jersey.
- Pfizer will develop drugs and medical technology over the next five years in South Korea.
- Merck Sharpe and Dohme is constructing a new vaccines and biologics facility in Carlow, Ireland.
- Hovione, a Portuguese pharmaceutical company, has taken over a former Pfizer manufacturing plant in Ringaskiddy, Ireland, and is set to create up to 80 jobs over the next two years.
- Eli Lilly opened a state-of-the-art biotechnology center in California

companies and individuals to prosper."

She reminded audience members of a quote by Charles Darwin, *It is not the strongest of the species that survive, nor even the most intelligent, but the one most responsive to change.*

References

1. Henske, Preston and Tim van Biesen. "Mega Mergers Can't Cure the Pharmaceutical Industry." *BusinessWeek*, July 26, 2009, http://www.businessweek.com/technology/content/jul2009/tc20090724_243995.htm?campaign_id=rss_daily
2. Gryta, Thomas. "Biotech Deals Lose Luster." *Wall Street Journal*, April 15, 2009, page B5.
3. GlaxoSmithKline Completes Acquisition of Stiefel, July 22, 2009, GlaxoSmithKline, *http://www.gsk.com/media/pressreleases/2009/2009_pressrelease_10078.htm*
4. De La Merced, Michael J. and Andrew Ross Sorkin. "Glaxo to Acquire Lab for $2.9 Billion." *The New York Times*, April 20, 2009, http://www.nytimes.com/2009/04/21/business/global/21glaxo.html
5. Wilson, Duff. "Abbott in $6.6 billion deal for Drug Unit." The New York Times. September 28,2009, *http://www.nytimes.com/2009/09/28/business/28drug.html?em*
6. Gray-Block, Aaron and Ransdell Pierson. "Abbott, J&J strike deals, boost vaccines." Reuters, September 28, 2008, http://www.reuters.com/article/newsOne/idUSLS28347420090928
7. "GlaxoSmithKline and Pfizer's HIV Drug Business Merger: An Industry Shift?" *Seeking Alpha*. April 21, 2009, http://seekingalpha.com/article/132000-glaxosmithkline-and-pfizer-s-hiv-drug-business-merger-an-industry-shift
8. Winslow, Ron. "AstraZeneca, Merck to Test Cancer Drugs in 'Cocktail.'" *The Wall Street Journal*. June 1, 2009, http://online.wsj.com/article/SB124380640803770139.html
9. "Pfizer Streamlines R&D Activities; Plans Job Cuts," *Wall Street Journal*, November 9, 2009, http://online.wsj.com/article/BT-CO-20091109-712931.html
10. Peterson, Iver. "Smaller Firms Gain Foothold as Big Drug Makers Shrink." *New York Times*. May 15, 2009, http://www.nytimes.com/2009/05/17/nyregion/new-jersey/17pharmanj.html
11. Whalen, Jeanne. "Sanofi Overhauls R&D to Help Costs, Pipeline." *The Wall Street Journal*. July 1, 2009, http://online.wsj.com/article/SB124637623883773925.html
12. "Sanofi-Aventis SA," *Gale Group*. March 9, 2009
13. Chaturvedi, Swati. "Outsourcing in Pharmaceutical Industry." *Bionity.com*, http://www.bionity.com/articles/e/49803/
14. Taylor, Nick. "India vs China: Outsource What to Where." *Outsourcing-Pharma.com*. July 7, 2009, http://www.outsourcing-pharma.com/Preclinical-Research/India-vs-China-outsource-what-to-where
15. Van Egeraat, Chris and Frank Berry "The Irish Pharmaceutical Industry Over the Boom Period and Beyond." Trinity College Dublin Institute for International Integration Studies. December 2, 2008, http://ideas.repec.org/p/iis/dispap/iiisdp271.html
16. "Senator Clinton Visits Akrimax Pharmaceutical Manufacturing Facility in Rouses Point, New York." August 5, 2008, http://www.votesmart.org/speech_detail.php?sc_id=401162&keyword=&phrase=&contain=
17. "More Manufacturing Business Coming to Akrimax Facility." Akrimax Pharmaceuticals. February 18, 2009, http://www.akrimax.com/media-room/item/7
18. "Pfizer Slashing Hundreds of Jobs in New York's North Country." WCAX.com November 9, 2009, http://www.wcax.com/global/story.asp?s=11471157
19. "University of Michigan's Ex-Pfizer Site Acquisition is 'Watershed Moment,'" Ann Arbor.com, September 6, 2009, http://www.annarbor.com/business-review/university-of-michigans-ex-pfizer-site-acquisition-is-watershed-moment/
20. Gardner, Paula. "University of Michigan Expansion to Ex-Pfizer Site May Not Harm Ann Arbor Landlords," Ann Arbor.com, September 6, 2009, http://www.annarbor.com/business-review/university-of-michigan-expansion-to-ex-pfizer-site-may-not-harm-ann-arbor-landlords/index.php
21. Gavin, Kara. "University to Buy Pfizer's former Ann Arbor Property." *The University Record Online*. January 16. 2009, http://www.ur.umich.edu/0809/Jan12_09/10.php
22. "Ex-Pfizer Lab Becomes Michigan Life Science and Innovation Center." *Great lakes IT Report*. September 24, 2009, http://www.wwj.com/Ex-Pfizer-Lab-Becomes-Michigan-Life-Science-and-In/5294107

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Impact and Use of ASTM Standards in the Pharmaceutical Industry	February 2, 2010
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Sterile Drug Manufacturing and Aseptic Processing	April 27, 2010
Preparing for a Regulatory Inspection	June 23, 2010
PDA Training	July 28, 2010
Top Stories from the PDA/FDA Meeting	October 1, 2010

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

Regulatory Briefs

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

North America

Revised Draft Guidance on Structured Product Labeling Standard Available

The U.S. FDA has made a revised draft guidance available for industry and reviewers entitled, *SPL Standard for Content of Labeling, Technical Q and A's.*

It is intended to assist sponsors who submit labeling content to FDA's Centers for Biologics Evaluation and Research (CBER) and Drug Evaluation and Research (CDER) using the structured product labeling (SPL) standard in extensible markup language (XML) and provides information to the Agency staff who review and manage that information using electronic systems.

Comments are due by December 28, 2009.

Agency Pilot Program to Evaluate Proprietary Name Submissions, Procedures Underway

A pilot program evaluating proposed proprietary name submissions and procedures to register for participation and submit data is available. This is an opportunity for pharmaceutical firms to participate in a two-year voluntary program for the evaluation of proposed proprietary names.

The pilot program will be conducted by the U.S. FDA's CDER and CBER and will enable participating pharmaceutical firms to evaluate proposed proprietary names and submit the data from those evaluations to the Agency for review, as outlined in the FDA concept paper "PDUFA Pilot Project Proprietary Name Review."

FDA began accepting requests to participate in the pilot program October 1, 2009.

U.S. FDA Draft Guidance Available on Risk Evaluation, Mitigation Strategies

A draft guidance is available on format and content of proposed risk evaluation and mitigation strategies (REMS), REMS assessments and proposed REMS modifications.

The draft guidance describes the format and content of a proposed risk evaluation and mitigation strategy, including REMS supporting documentation; the content of assessments and proposed modifications of approved REMS; what identifiers to use on REMS documents and how to communicate with the U.S. FDA about a REMS.

Comments should be submitted by December 30, 2009.

International Harmonization

ICH Steering Committee Meeting Brings Five Annexes Closer to Harmonization

The International Conference on Harmonisation (ICH) Steering Committee and its expert working groups met in St. Louis, Missouri from October 24-29, 2009.

At the meeting, three Annexes to the Q4B guideline (Annex 7: Dissolution, Annex 9: Tablet Friability and Annex 10: Polyacrylamide Gel Electrophoresis) reached Step 4 and another two (Annex 11: Capillary Electrophoresis and Annex 12: Analytical Sieving) reached Step 2.

The next ICH Steering Committee will be held in Europe from June 5-10, 2010

The ICH Quality Implementation Working Group is also developing a training program for workshops that will be held in the three ICH regions that will cover the ICH Guidelines Q8, Q9 and Q10 with the aim of achieving globally consistent implementation of ICH guidelines Q8, Q9 and Q10. This training will consist of case studies representing the four phases of the life cycle of a pharmaceutical product. The workshops will be held in Brussels in June 2010, in Washington, D.C. in October 2010 and in Tokyo in November 2010.

Key Regulatory Dates

Comments Due:

Dec. 28
U.S. Guidance, SPL Standard for Content of Labeling, Technical Q and A's

Dec. 16
U.S. FDA draft guidance on REMS assesments and proposed modifications.

Workshops:

ICH and IWG training for Q8, Q9, Q10:

June 2010, Brussels
October 2010, Washington, D.C
November 2010, Tokyo

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The Hunt for Opportunities

Jay Forte

Ours is an unpredictable world. Many times, regardless of how effectively we plan, some things just fail. The dinner party that should have been great based on the planning, but the meal was a disaster. The meeting's presentation that was well prepared but then the equipment failed. Or, a disciplined and diligent savings plan that lost nearly half of its value in today's recession. These challenging situations define our days. Some curse and yell; others see them for the opportunities they present. Inaugural Poet Maya Angelou writes, "I've learned that you can tell a lot about a person by the way he or she handles these three things: a rainy day, lost luggage and tangled Christmas tree lights." Failures, changes and unexpected events have the ability to either destroy or advance; it is in our outlook and response that allows us to turn these failures into opportunities.

Thomas Alva Edison experienced repeated failures. His true success was not his invention of the light bulb but rather his tenacity and outlook that believed failures were a means to gain new information and new perspectives. Our most successful employees are not those who land on their feet after every project or event; instead, they are those who have the persistence and optimism to learn from difficulty and use what they learn to re-imagine, recreate and re-experiment. They are the ones who have learned to be positive and to constantly hunt for opportunities.

Organizations that constantly hunt for opportunities, perform better, innovate more and succeed in tough times because they possess the following qualities:

1 They create, support and live a culture that teaches, inspires and encourages employees to look for the opportunity in every event.

Failures are unparalleled opportunities to reinvent success. These organizations "celebrate extraordinary failures and punish average successes." Effort, innovation and intent are celebrated; unusual, non-conventional and non-conformist perspectives are applauded. Occasional failures show that employees are pushing performance to the edge. As Tom Peters states, "A day without a screw-up is a day without enough reach." These workplaces encourage their employees to focus on the positive; they create a culture that is open, free-thinking, and believes "yes we can."

2 They commit the time and effort to help employees learn their strengths and use them to develop opportunity-thinking.

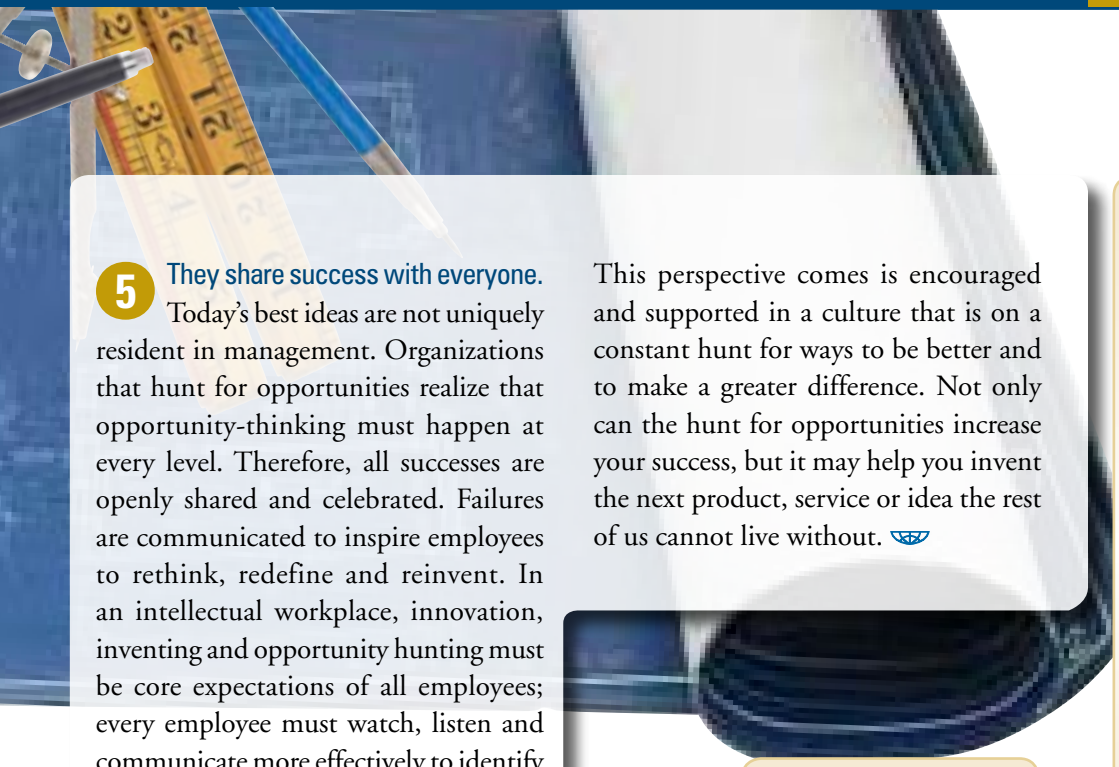
Each of us has the potential to be great at certain things; we each have intrinsic talents and strengths. Successful employees know their talents and understand that these talents help them to be naturally perceptive in certain areas; they commit to deliberative practice in develop these areas. They focus their hunt for opportunities in their talent and strengths areas, areas in which they have the greatest insight.

3 They focus on learning and actively solicit input from everyone.

Organizations that hunt for opportunities are always learning, asking great questions and are exceptional listeners. They listen to new perspectives, facts, ideas and dreams. They listen to customers, employees, vendors and strangers. They read books, blogs, periodicals and newspapers. They read and listen to topics that may appear to be unrelated. They regularly ask, "how about," or, "what if." They assess what they hear; they consider everything. They then share what they hear with their teams to expand their hunt for opportunities.

4 They focus on exponential, not incremental, opportunities.

All discussions of opportunities are directed to significant, not average, results; performance "lite" is unacceptable. They use the information they glean about the market, customer, strengths and trends to consider opportunities that have the potential to be significant. Successful organizations know nothing lasts forever and they must continually reinvent themselves—each time more significantly than the last. These organizations constantly review what they do; they focus on the exponential in their hunt for exponential opportunities.



5 They share success with everyone. Today's best ideas are not uniquely resident in management. Organizations that hunt for opportunities realize that opportunity-thinking must happen at every level. Therefore, all successes are openly shared and celebrated. Failures are communicated to inspire employees to rethink, redefine and reinvent. In an intellectual workplace, innovation, inventing and opportunity hunting must be core expectations of all employees; every employee must watch, listen and communicate more effectively to identify improvements and opportunities. The more successes are shared with everyone, and failures are seen as a way to improve, the more performance- and idea-risks employees will take—all in the hunt for opportunities.

In today's uncertain recessionary period—where the regular, average or incremental approaches are not sufficient—successful organizations have mobilized their teams to be on the hunt for opportunities. It may be in a retail store that creates a new and more "hip" line of products that are less expensive to match today's reductions in consumer spending. It may be a restaurant that now opens at lunch, creates a mobile delivery van or a special take-out section to appeal to a changed demographic. It may be a financial services firm that sponsors savings, investing and retirement education to create more savvy and loyal investors who better appreciate and value the firm's conservative and pragmatic approach.

Some people are distracted or discouraged by failure and change. Others see these as opportunities for greater success. This perspective comes is encouraged and supported in a culture that is on a constant hunt for ways to be better and to make a greater difference. Not only can the hunt for opportunities increase your success, but it may help you invent the next product, service or idea the rest of us cannot live without.

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

About the Author:

Jay Forte is a speaker, consultant and nationally ranked thought leader. He applies years of research, along with his training as a CPA, working with organizations that want to successfully activate and inspire exceptional employee performance. Renowned for producing results, Jay's first book, *Fire Up Your Employees and Smoke Your Competition* was published in March 2009. For information on keynotes, speaking, consulting or to see the daily "BLOGucation," visit: www.humanetricsllc.com or www.FireUpYourEmployees.com or call: (401) 338-3505

Volunteer Spotlights

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Christopher J. Smalley, PhD, Director, Global Quality, Pfizer

Education: BSc, Pharmacy, Philadelphia College of Pharmacy; MS, Pharmaceutical Chemistry, Temple University College of Pharmacy; MBA, Temple University Fox School of Business; PhD, Healthcare Administration, LaSalle University

PDA Join Date: 1984

Areas of PDA Volunteerism: PDA Training Committee Chairman(1991-1995); PDA Science Advisory Board member (2006-present); PDA 2010 Annual Meeting Program Committee co-Chair; PDA Board of Directors member(2009-present); Facilities and Engineering Interest Group Leader (2006- present); Task Force for the Technical Report on Moist Heat Steam Sterilization co-Leader; Task Force for the Technical Report on Single Use Systems member

Professional Awards Won: 1994–Navy Achievement Medal; 1995–Sterling Winthrop President's Champion Award; 1996–Sanofi Pharmaceutical Preapproval Inspection Award; 1999–Wyeth Computer Compliance Recognition Award; 2007–Air Force Humanitarian Service Award

Which PDA event/training course is your favorite? Wow, do I have to chose only one?! I enjoy so many of the training courses because they are being taught by professionals who are doing the job on a daily basis–they are current on the issues and techniques. But I enjoy the PDA/FDA Joint Regulatory Conference because the U.S. FDA is truly an active partner in the program, not only contributing speakers and expressing the current thinking at the agency but sharing where they see us going into the future. Although when forced to chose, I would say the Annual Meeting. It is at the Annual Meeting that there is so much to chose from that I struggle with which session to attend during the concurrent sessions!

How has volunteering with PDA benefited you professionally? I consider myself a pharmacist above all. I continue to work part-time as a hospital pharmacist to insure that I maintain my perspective of all the pharmaceutical products that are out there and how they are being used. As a pharmaceutical scientist, I need to stay active in PDA so that I know all of the technology and techniques that are out there, because the world is changing very rapidly, and PDA is a key tool in my toolkit to keep up with the changes.

Renaud Janssen, PhD, Technical Support Director, Sales, Marketing & Technical Support, Helvoet Pharma

Education: MS, Chemical Engineer, Catholic University of Leuven, Belgium,1980; PhD, Applied Sciences, Catholic University of Leuven, Belgium,1984

PDA Join Date: 1993

Areas of PDA Volunteerism: Speaker at several PDA conferences on various topics related to elastomeric components for parenteral use,topics include Pre-Filled Syringe components, Extractables and Leachables, coated rubber products and Visual Inspection; Program Planning Committee for PDA's Universe of Pre-filled Syringe and Injection Devices Conference Member and Moderator (2009)

Interesting Fact about Yourself: Good novels are written at all places on the globe!

Why did you join PDA and start to volunteer? PDA is the reference organization to join for anybody who is interested in parenteral sciences. PDA offers numerous possibilities to learn, discuss, exchange ideas, network, etc. PDA's activities in Europe have considerably grown in the last years and to the best of my capacities and possibilities I want to support that growth. Eventually better health by better health care is in the interest of every individual.

Of your PDA volunteer experiences, which stand out the most? Serving for the first time on a program planning committee and moderating a conference session.

How has volunteering through PDA benefited you professionally? Volunteering through PDA has offered me the possibility to get more involved, to meet with people and to know them and the concerns they have in their professional lives better. Formal meetings are one way of doing this, but informal meetings often are another way of digging out things in more detail.

Which member benefit do you most look forward to? Hard to say which is the most valuable one. Having online access to the electronic archive of presentations is extremely helpful; while on the other hand, the *PDA Journal of Parenteral Science and Technology* offers very interesting publications.

Which PDA event/training course is your favorite? *The Universe of Pre-filled Syringes and Injection Devices*. It is an extremely well-attended conference with good quality presentations. It offers the possibility to update oneself on all aspects of this very fast growing part of parenteral packaging. The best presentations related to pre-filled syringes can be attended at this conference. The way of organizing this conference alternatively in the United States and in Europe makes this truly a global event.

What would you say to somebody considering PDA membership? Enjoy! Enjoy the opportunities to learn either from behind your desk, by attending conferences and workshops and by making active contributions to events and publications. Enjoy becoming a better professional by interacting with peers!

Recipients of the 2008 Honor Awards

www.pda.org/2008honorawards

The honor awards have been bestowed to esteemed PDA members since the first award was given in 1958. It is our intention to highlight the 2008 Honor Award Winners who were recognized at PDA's Annual Meeting banquet. Be sure to look at this section in future issues for additional winners or online at www.pda.org/2008honorawards.

Frederick D. Simon Award

This award is presented annually for the best research paper published in the *PDA Journal of Pharmaceutical Science and Technology*. The paper that was picked was entitled, "Qualification of High-Recovery, Flocked Swabs for Microbiological Environmental Monitoring of Surfaces." The 2008 Frederick D. Simon Award Recipients are:

Manuela Bini

Gilberto Dalmaso, PhD

Michela Ferrari

Roberto Paroni

2010 PDA Upcoming

For an updated PDA calendar of events please visit www.pda.org/calendar

JANUARY

25-29 **2010 Aseptic Training Program—Session 1**
(Week 2: Feb. 22-26)
Location: Bethesda, Maryland
Website: www.pda.org/aseptic

26-27 **PDA Conference on Investigational Medicinal Products: A Science and Risk Based Approach in Product Development**
Location: Paris, France
Website: www.pda.org/IMP2010

FEBRUARY

10-11 **Choosing the "Right" Microbial Identification Program for your Biopharmaceutical/Pharmaceutical Quality Control Laboratory**
Location: Bethesda, Maryland
Website: www.pdatraining.org

22-24 **San Diego Course Series**
Location: San Diego
Website: www.pda.org/sandiego2010

23-24 **PDA Europe Conference on Pharmaceutical Microbiology**
Location: Berlin, Germany
Website: www.pda.org/europe

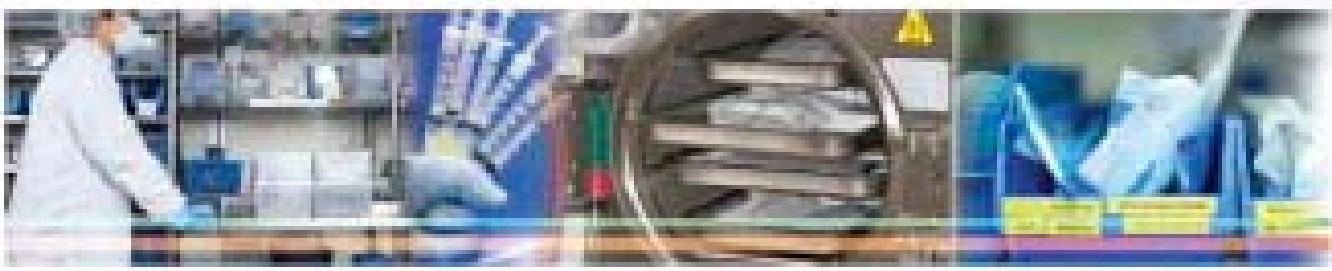
23-24 **PDA Workshop on Small Batch Production**
Location: Berlin, Germany
Website: www.pda.org/europe

25 **PDA Workshop on Technical Report 22: Process Simulation Testing for Aseptically Filled Products**
Location: Berlin, Germany
Website: www.pda.org/europe

Web Seminars

January 14
Software Implementation in One Third of the Time and Cost
Time: 1:00 – 2:30 p.m. EST

For a full list of upcoming PDA Web Seminars please visit: www.pda.org/webseminars



Events

Save These Dates

MARCH

2-3 **PDA Conference on Endotoxins**
Location: Milan, Italy
Website: www.pda.org/europe

3-5 **Pharmaceutical Water System – Microbiology Lab Course**
Location: Bethesda, Maryland
Website: www.pdatraining.org

10-12 **Developing an Environmental Monitoring Program**
Location: Bethesda, Maryland
Website: www.pda.org/EMP

15-19 **2010 PDA Annual Meeting**
Location: Orlando, Florida
Website: www.pda.org/annual2010

16-17 **PDA Workshop on Stoppers & Elastomers**
Location: Cologne, Germany
Website: www.pda.org/europe

18 **PDA Workshop on Siliconisation**
Location: Cologne, Germany
Website: www.pda.org/europe

22-26 **2010 Aseptic Training Program – Session 2**
(Week 2: April 19-23)
Location: Bethesda, Maryland
Website: www.pda.org/aseptic

23-24 **PCMO Conference**
Location: Frankfurt, Germany
Website: www.pda.org/europe

25 **Interest Group Meeting: Technology Transfer**
Location: Frankfurt, Germany
Website: www.pda.org/europe

APRIL

6-8 **2010 St. Louis Course Series**
Location: St. Louis, Missouri
Website: www.pdatraining.org

7-9 **Cleaning Validation**
Location: Bethesda, Maryland
Website: www.pda.org/cleaning

12-15 **2010 PDA Pharmaceutical Cold Chain Management Conference**
Location: Bethesda, Maryland
Website: www.pda.org/coldchain2010

13-14 **PDA Workshop on Filtration**
Location: Berlin, Germany
Website: www.pda.org/europe

15 **Interest Group Meeting: Pre-filled Syringes**
Location: Berlin, Germany
Website: www.pda.org/europe

20-21 **PDA Workshop on Bio-films**
Location: Frankfurt, Germany
Website: www.pda.org/europe

22 **Interest Group Meeting: Biotech and Interest Group Meeting: Visual Inspection**
Location: Frankfurt, Germany
Website: www.pda.org/europe

27-28 **Workshop on Container Closure Systems + Annex 1**
Location: Berlin, Germany
Website: www.pda.org/europe

28-30 **Development of Pre-Filled Syringes**
Location: Bethesda, Maryland
Website: www.pda.org/prefilledsyringes

2010 PDA Annual Meeting

Manufacturing Excellence

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

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

PDA

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*.

PDA New England Chapter Holds Meeting, Facility Tour

NEPDA Planning Committee member Myron F. Dittmer, Jr., MFD & Associates

On September 9, the New England chapter of PDA (NEPDA) held its first meeting of the season at the Best Western Executive Court Inn & Conference Center in Manchester, N.H. with over 115 people in attendance, as well as 12 vendor sponsors. This was a record number for a meeting, which provided financial support and a variety of services and products for attendees to view.

The dinner was preceded by a facility tour of Lyophilization Services. This New England state-of-the-art contract fill/finish facility is located in Bedford, N.H. It features large scale commercial-size lyophilizers and represents a significant investment for future growth and expansion planned by the company. The tour consisted of a walk-thru of medical devices suites and support areas, as well as the aseptic fill and formulation drug suites. Also viewed were support areas such as glassware processing, material sterilization processing, clean staging, as well as labeling/packaging and inspection areas. A mezzanine area containing all the clean utility systems which supply all the suites was viewed. These included WFI, USP Purified Water, Clean Compressed Air, Clean Steam, chilled water, HVACs and other systems.

Prior to the main speaker presentation, chapter president **Jerry Boudreault**, President, Drug Developement Resources, updated us on upcoming events planned for later this year. He also presented **Dianne Moustafa**, a NEPDA Student Chapter Member-at-Large, with a $5,000 transfer scholarship. Dianne recently graduated from Middlesex Community College with an overall GPA of 3.77. She has been an active member of the NEPDA Student Chapter since its inception in 2008. Currently working at the Genzyme Corporation as a manufacturing technician, she is pursuing a degree in engineering at Boston University. [**Editor's Note:** See related article on page 39 of this issue.]

Members of PDA's New England Chapter took a facility tour of Lyophilization Services Fill/Finish Facility

(l-r) Jerry Boudreault, Drug Development Resources; Russell Morrison, Commissioning Agents; Maryellen Brown, The Chisholm Corporation; Louis Zaczkiewicz, Genzyme

The keynote speaker of the evening was **Jeanne Moldenhauer**, PhD, Vice President, Excellent Pharma Consulting and current leader of the PDA's Microbiology/Environmental Monitoring Interest Group. Jeanne is also on the Science Advisory Board and is the author of numerous books and articles on the topic. Jeanne's talk centered around environmental monitoring in clean environments. She described some of the major differences between the major regulatory documents such ISO, European Union, U.S. FDA, Japanese, WHO and compendial requirements. While noting the required elements of an acceptable good environmental monitoring program, she cautioned that if not properly developed warning letters are often issued to address deficiencies.

Jeanne then discussed progress on the task force working on a revision of *PDA Technical Report No. 13 (revised), Fundamentals of an Environmental Monitoring Program*, which will include new features that are being planned for this revision. Some of these include an update on regulatory documents, more emphasis on risk assessments, new sciences and technologies available, information about analytical variability, updated bibliography and updated validation requirements for support systems such as utilities. The revision of TR-13 is expected to be approved by PDA by the end of this year.

Jeanne also provided an update on the latest technologies including rapid micro biosystems; airborne microbial samplers; IMD-A system, which enumerates both viable and non-viables; flocked swabs with ScanRDI that counts microbial colonies after 90 minutes; REBS system, which collects, enumerates and identifies microbes in 15 minutes; PallCheck for surface monitoring and ATP biolumescence methods for water monitoring.

Following the presentation, an expert panel was assembled for a question and answer period consisting of Jeanne Moldenhauer, **Edward Balkovic**, PhD, QC Microbiologist, QC Micro. Tech Support, Genzyme and **Joseph Potvin**, Senior Supervisor, QC, Wyeth Pharmaceuticals. The panelists took questions from the audience on environmental monitoring and related issues for a lively discussion.

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PDA's New England Chapter Supports Students

Emily Hough, PDA

Since starting its student chapter in 2008, PDA's New England Chapter (NEPDA) has been making strides to educate students at Middlesex Community College (MCC) and other area schools about the opportunities that PDA members enjoy.

NEPDA officers have gone one step further this year by awarding a student of MCC $5,000 to transfer to a four year school to continue her education. PDA's New England Chapter Officers, have unanimously awarded **Diane Moustafa** the NEPDA $5,000 Student Transfer Scholarship. This scholarship will allow her to continue her education in the biotechnology field at Boston University.

Diane has been involved with the New England PDA Student Chapter since its inception in 2008. She has attended several dinner meetings and has even helped present work that she did in class to members. Her story is one of determination and achievement. Diane, a mother of four, with only a few classes to go to complete her Business Management degree, took a biology class and developed a "hunger" for the material. She quickly changed her major to Biotechnology. As one of her final requirements before graduating Middlesex Community College, Diane needed to complete an internship so she became a temporary employee with the Genzyme Corporation for three months. After her short time there, she was notified that Genzyme was creating a position for her.

Diane's accomplishments have come in part due to the knowledge she has attained as a member of PDA. During her time at Genzyme, Diane attended PDA New England Chapter dinner meetings. She went to one meeting that addressed the importance of glass inspection. A couple of weeks after the meeting, a shipment of glassware was delivered to Genzyme. Diane inspected the glassware and found some of it to be defective. She explained to her supervisors what was wrong and where she had learned her knowledge. Diane said she received recognition for her findings and received a Spot Award and Employee of the Month Award. "Without the knowledge of the glassware inspection for impurities, this glassware could have ended up on the production floor. It is needless to say how important I find the knowledge I receive from PDA."

Diane will now attend Boston University, after graduating MCC a member of the Phi Theta Kappa Honor Society with a 3.77 GPA.

As one NEPDA officer said, "[Diane's] story is proof of the benefit of the student chapter to PDA and the wisdom of starting the scholarship program."

To become a member of PDA's New England Student Chapter, email **Jerry Boudreault**, New England Chapter President at boudreault@ddres.com. To learn more about the NEPDA $5,000 Scholarship, visit www.pda.org/newengland.

Faces and Places: 2009 PDA/FDA Conference Sessions

Welcoming Remarks


Rick Friedman, FDA


Martin Van Trieste, Amgen

P1: Opening Plenary Session

(l-r) Barbara Ryan, Deutsche Bank Securities; Jacqueline Scott, National Academy for State Health Policy; Michael Bonney, Cubist Pharmaceuticals

P2: Effective Pharmaceutical Quality Systems

(l-r) Steve Mahoney, Hogan and Hartson; Stephan Roenninger,F. Hoffmann – La Roche; Swroop Sahota, Schering-Plough; Joseph Famulare, FDA

P3: Pharmaceutical Safety and Good Distribution Practices

(l-r) Kathleen Greene, Novartis; Edwin Rivera-Martinez, FDA; Marc Payne, Novartis; Katherine Eban, Journalist; Eric Berg, Amgen

P5: PDA Center Initiatives Going Forward

(l-r) Bob Dana, PDA; Dennis Bensley, Jr., FDA; Chris Joneckis, FDA; Janet Woodcock, FDA; Jonathan Sackner-Berstein, FDA; Doug Stearn, FDA

P7: FDA Compliance Expectations Going Forward

(l-r) Joseph Famulare, FDA; Rick Friedman, FDA; Martine Hartogensis, FDA; Mary Anne Malarkey, FDA; Tim Ulatowski, FDA; Doug Stearn, FDA

A1: Management Reviews


Kirk Huber, Novartis


Shane Killian, Johnson & Johnson

C1: Product Containment

(l-r) Edwin Melendez, FDA; Nigel Hamilton, Sanofi-Aventis; James Skrine, Amgen; Nancy Waites, FDA; Louise Johnson, Aptuit

P6: A Patient's Perspective


Amy Giertych, Baxter

B1: Quality Agreements/Technical Agreements/Cooperative Agreements

Barbara Zinck, Zinck Consulting; John Eltermann, Jr., FDA; James Shirey, Pfizer


Martyn Becker, Martyn Becker Associates

A2: CAPA


Kimberly Trautman, FDA


Laurie Norwood, FDA


Marsha Major, Johnson & Johnson; Martin Van Trieste, Amgen

B2: Technology Transfer


Anurag Rathore, Indian Institute of Technology


Mai Huynh, FDA

A4: Knowledge Management


Stephan Roenninger, F. Hoffmann – La Roche; Joseph Famulare, FDA; Lothar Hartmann, F. Hoffmann – La Roche

C2: Continual Improvement


(l-r) Victor Yamauchi, Amgen; Peggy Rooks, Abbott; Robert Sausville, FDA; Ian See, MedImmune

A3: Change Management


(l-r) Sue Schniepp, Javelin Pharmaceuticals; Maria Guazzaroni Jacobs, Pfizer; Rick Friedman, FDA; Richard Norgard, Pfizer

C4: Standard Development

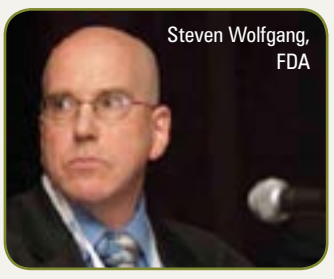

Dave Schoneker, Colorcon


Betsy Fritschel, Johnson & Johnson


Paul Balcer, FDA; Jon Clark, FDA

B3: Supplier Qualification: Auditing/Products and Services


Gerard Pearce, SQA Services


Steven Wolfgang, FDA

Breakfast V: "Ask CDER Compliance"


Tara Gooen, FDA; Grace McNally, FDA; Vibhakar Shah, FDA

Faces and Places: 2009 PDA/FDA Conference Sessions

IG1: Biotechnology Interest Group

Duncan Low, Amgen

Jill Myers, BioPro Consulting

Stephen Notarnicola, Biogen Idec

IG3: Filtration and Pharmaceutical Water Interest Group

(Clockwise starting at back left) Russell Madsen, The Williamsburg Group; Gary Zoccolante, Siemens Water Technologies; Theodore Meltzer, Capitola Consulting; Sei-ichi Manabe, Sepa-Sigma

Breakfast IV: Ask the FDA about Regulated Products and Standards

David Cummings, FDA

IG2: Packaging Science Interest Group

Desmond Hunt, USP; Edward Smith, Packaging Science Resources

Deborah Thomas, West Pharmaceutical Services

IG 10: Process Validation & Quality Risk Management Interest Group

(l-r) Jeffery Hartman, Merck; Wallace Torres, F. Hoffmann – La Roche; Mike Long, KPM International Associates; Scott Bozzone, Pfizer; Michael Popek, FDA; Chris Joneckis, FDA

IG8: Pre-Filled Syringes Interest Group

Thomas Schoenknecht, Amgen

Eric Berg, Amgen

Klaus Wuttke Gerresheimer, Bünde

IG6: Quality Systems Interest Group

(l-r) Tara Gooen, FDA; Anders Vinther, Genentech; John McShane, Genentech

Breakfast VI: Knowledge Management and PAT

Wallace Torres, F. Hoffman – La Roche; Paolomi Mukherji, Clarkston Consulting; Vince Mathews, Eli Lilly

Faces and Places: 2009 PDA/FDA Exhibits and Networking


FDA


DBA


BioBall


Empiristat


PHARMA-BIOSERV


CAPE COD

Faces and Places: 2009 PDA/FDA Exhibits and Networking

Passport Raffle

Marianne Feyas, AstraZeneca; Gene Fuchs, American Stelmi

Daniel Poulin, Afton Scientific; Alison Caballero, PDA

Thomas Peither, Mass & Peither AG GMP Publishing; Linda Mikulan-Maxfield, Baxter

Patricia Stancati, Sartorius Stedim Biotech

Aldelberto Cordova, Baxter; Peter Pratt, BioScience International

Book Signing

Thomas Peither, Mass & Peither AG GMP Publishing; Lizzie Leininger, Elizabeth Leininger Consulting

Peter Pratt, BioScience International; Maria Guazzaroni Jacobs, Pfizer

Faces and Places: 2009 PDA/EMEA Joint Conference

Session 1: Welcome and Conference Overview

(l-r) Véronique Davoust, Pfizer; Katrin Nodop, EMEA; Gerald Heddell, MHRA; Peter Boeken, F. Hoffmann-La Roche

S1: Counterfeiting & Supply Chain: European Legislation

(l-r) Andrew Bonser, Pfizer; Sabine Atzor, European Commission; Véronique Davoust, Pfizer

Session 2: Survey of Current and Pending European Legislation and Guidance on GMP and Supply Chain

Véronique Davoust, Pfizer; Sabine Atzor, European Commission; David Cockburn, EMEA; Francisco Peñaranda, EMEA

(l-r) John Shabushnig, Pfizer; Maik Jornitz, Sartorius Stedim Biotech and Richard Johnson, PDA, listen intently at the PDA/EMEA conference

Faces and Places: 2009 PDA/EMEA Joint Conference

M2: GMP Annex 2 and Challenges in Advanced Therapy Products

Ian Thrussell, MHRA; Ian Rees, MHRA; Annie Rietveld, Health Care Inspectorate; Hiltrud Horn, Horn Pharmaceutical Consulting

Q4: Implications of Q10 for Industry and Inspectorate

Lothar Hartmann, F. Hoffmann-La Roche; Liam Murphy, Amgen; Jacques Morénas, AFSSAPS

M3: Dedicated Facilities

David Cockburn, EMEA; Catherine Lefebvre, AFSSAPS; Stephen Brown, Vivalis

Conference Co-chairs, Véronique Davoust, Pfizer and Katrin Nodop, EMEA, receive flowers and thanks from PDA's Georg Roessling and Jim Lyda

Meet the Regulator: RAQC Meets with David Cockburn

(l-r backrow) Alan Burns, Sartorius Stedim Biotech; Michael Vanderwerf, GlaxoSmithKline; David Cockburn, EMEA; Stephan Roenninger, F. Hofmann–La Roche; Steve Mendivil, Amgen; Junko Sasaki, Dainippon, Sumitomo Pharma

(l-r frontrow) Jeff Broadfoot, Cangene; Karen Ginsbury, PCI Pharmaceutical Consulting; Louise Johnson, Aptuit; Bob Dana, PDA

Q1: Translating Design Space into CMC Section of Dossier and Managing Variations

Jean-Louis Robert, Laboratoire National de Santé and EMEA Quality Working Party

S3: Inspection of Importers and How They Manage Supply Chain Issues

Karl-Heinz Menges, Regierungspräsidium Darmstadt; Ester Helfrich, Mylan dura

Faces and Places: Friends — Old and New

(l-r) Georg Roessling, PDA; Maik Jornitz, Sartorius Stedim Biotech; Stefan Köhler, AstraZeneca

Richard Johnson, PDA; Joshua Sharfstein, FDA

John Shabushnig, Pfizer; Bob Myers, Beacon Pointe Group; Richard Johnson, PDA, pose following Bob's reception honoring his service to PDA

Past Chair, Vince Anicetti, sitting next to Chair-elect Maik Jornitz

John Shabushnig, Pfizer; Joshua Sharfstein, FDA

(l-r) Joyce Bloomfield, Merck; Zena Kaufman, Abbott

Faces and Places: 2009 PDA/EMEA Joint Conference

The meeting was a great place to network

Jacques Morénas, AFSSAPS, makes a comment during the meeting

Members Join in PDA's Supply of Fun

Conference goers enjoy dinner and Berlin on a guided boat tour

Exhibitors

Operational Excellence and Interaction Drive 2010 Annual Meeting

Orlando, Fla. • March 15-17, 2010 • www.pda.org/annual2010

Christopher Smalley, PhD, Pfizer

How many times have you heard that something was new, improved or different? In reality, things are always changing, but there have been times when the change has been major. In the 1950s, manufacturing and marketing of pharmaceuticals made a major change. Similarly, the advent of biopharmaceuticals marked a major change. We are now in the midst of another major change once again in manufacturing.

Like another industry recently in the news, we are moving to a model where **manufacturing excellence and quality** are linked to provide optimal productivity and customer benefits. Are you interested in being on the leading edge of that change? If your company is moving in this direction, then you need to be a part of it. But in these days of limited resources and tight budgets—where can get the most information value for your buck?

So with apologies to those dedicated sales people in that other industry—here comes our big pitch, if you're looking for manufacturing excellence knowledge, industry trends and interactive networking opportunities the *2010 PDA Annual Meeting in Orlando* March 15-17 has several "models" to choose from.

Here's a "test drive" of what we have to offer …if you are interested in **manufacturing process science**, then we have a track to choose here. It is a sleek, sporty model that features process automation, blow-fill-seal technology, excellence in facility design, information management and optimization of compliance and efficiency to improve your knowledge of what is new and exciting in manufacturing science.

And if you're interested in **quality by design**, then we have a track to choose here as well. It is a luxury model designed to put you in the forefront of this concept with presentation like implementing QbD for cost efficient control, creating a design space and QbD for a price competitive product.

You say you want to know more about process analytical technology or develop an understanding of rapid microbiological testing, on-line endotoxin testing, real time release, laser absorption or mycoplasma detection and inactivation? Well we have a sophisticated model here that will address the latest advancements in rapid and real time microbiological and analytical quality control methods.

Time to upgrade to the forefront of **developmental science**? We have a track that includes presentation on technology transfer, statistical analysis in process validation life cycles and creating a chromatography design space.

This is only a sampling of what awaits you if you join us in investigating what is truly new and different.

And when you need a break from the impressive selection of papers and presentations, we have an outstanding array of exhibitors eager to discuss and demonstrate the products that will launch you into the 21st century. Not to mention our informative **poster presentations**. Learn about other examples of the great models we have whether you are involved with **QbD, PAT, manufacturing process science, development science or quality**, come meet, see and hear what our presenters have to share.

And while you're in Orlando for the meeting, join us for our Lean Manufacturing Workshop on March 17 and our selection of exceptional **TRI training courses on March 18 and 19.**

And remember, this is Orlando, Fla. so bring the family and be prepared to be entertained by that other magic. They will not want to miss it.

The *PDA 2010 Annual Meeting* in Orlando March 15-17 is the place to network, interact, discuss, challenge and learn about the major changes taking place in our industry. You don't want to miss it!

Visit www.pda.org/annual2010 for details and to register.

Winners at PDA/FDA Joint Regulatory Conference

The PDA Training and Research Institute (TRI) released it 2010 Course Catalog, the first ever to be available solely electronically, in conjunction with the *2009 PDA/FDA Joint Regulatory Conference.*

To promote awareness of the catalog's availability, a postcard was sent to all PDA members and a kiosk was set up at the PDA/FDA Conference. At the kiosk, members could scroll through the catalog pages which were displayed on the TV monitor. When viewing the catalog at the meeting, conference attendees had the opportunity to discuss their training needs, PDA's course offerings and capabilities with members of the PDA and TRI staffs and to enter their names in a raffle drawing for a 50 inch TV.

The drawing was held at the beginning of the closing plenary sessions on Wednesday morning, and PDA President **Richard Johnson** drew **Jim Skrine's** name.

Winners at the PDA/FDA Meeting

Aldelberto Cordova, Sr. Principal Engineer, Baxter BioScience, won two silk ties from Bioscience International

Marianne Feyas, Director of Compliance and Quality, Quality Assurance, AstraZeneca, won a Sony Noise Canceling Headphones from American Stelmi Corporation

Maria Guazzaroni Jacobs, PhD, Director/Team Leader QRP/CMC, Pfizer Global Research, Pfizer, won two silk ties from Bioscience International

Lizzie Leininger, PhD, Principal Consultant, Elizabeth Leininger Consulting, won an IPod Shuffle and a risk management instruction book from Maas & Peither AG GMP Publishing

Linda Mikulan-Maxfield, Senior Manager Corporate Compliance, Supplier Quality, Baxter, won an IPod Shuffle and a Maas and Peither book from Maas & Peither AG GMP Publishing

Daniel Poulin, Production Manager, Production, Afton Scientific, won an IPod Shuffle from PDA

Jim Skrine, Executive Director, Quality, Amgen, won a 50 inch TV from PDA TRI

Report from the 2009 PDA/FDA Joint Regulatory Conference

TRI Scores a Record-Breaker at the 2009 PDA/FDA Conference

Stephanie Ko, PDA

The Training & Research Institute is proud to announce a record-breaking success at the PDA/FDA Joint Regulatory Conference, which took place September 2009 in Washington, D.C. Despite the growing number of companies facing budget cuts in the weakened economy, we received the highest number of participants of any course series we've ever held—over 170 registrations. While we are extremely pleased that we were able to respond to industry needs with a targeted selection of course topics, we are even more pleased to see that companies recognize the importance of training and education in any economy.

Of particular interest were the top three most sought after courses. The first was **"Preparing for Regulatory Inspections for the FDA and EMEA,"** taught by **Dave Chesney**, Vice President, Strategic Compliance Services, Strategic Compliance, Parexel Consulting. This course prepared participants for hosting an inspection, primarily focusing on EMEA GMP or pre-approval site inspections. The course was designed along several principles, two of which emphasized to attendees the importance of understanding the law governing their operations and understanding legal basis for FDA inspects.

Second in line was **"Quality by Design for Biopharmaceuticals: Concepts and Implementation,"** taught by two instructors: **Anurag Rathore**, PhD, Director, Department of Chemical Engineering, Indian Institute of Technology, and **Patrick Swann**, PhD, Deputy Director, Division of Monoclonal Antibodies, CDER, OPS, U.S. FDA. The course allowed participants to better understand how their job responsibilities will evolve in the QbD paradigm and the role they play in ensuring successful implementation of QbD. Topics included critical quality attributes; design space; risk assessment and management; regulatory aspects; PAT; establishing control strategy and life cycle management of design space.

And finally, the third was **"Role of the Quality Professional in the 21st Century,"** taught by **Robert Kieffer**, President, RGK Consulting. This course was designed in response to the continuous challenges of improving quality, compliance and customer service while reducing costs. It was also created in response to relatively recent regulatory emphasis on systems and risk management from documents such as "Pharmaceutical cGMPs for the 21st Century—A Risk-based Approach," "Quality Systems Approach to Pharmaceutical CGMP Regulations," and Q10 "Pharmaceutical Quality Systems." Course participants learned new skills in order to improve and redefine the role of the quality professional.

Popularity in these courses may signal a desire on the part of the attendees to better understand what the current thinking is along these topics and to determine the next steps to ensure they are "up-to-date" in their approach. It may also be renewed interest in quality due to the publication of the ISO "Q" documents which reflect a change in quality thinking.

If you are interested in any of the top three courses mentioned, I encourage you to scroll through our 2010 catalog at www.pdatraining.org to find when these courses or similar course topics will be offered again.

It's important to mention that almost all courses at PDA are only offered once a year, if not once every two years, so don't wait to register when you see a training opportunity that could benefit you.

PDA Training and Research Institute Courses

I wish to thank the other instructors who contributed their valuable time and efforts to our record success with the following courses:

"Qualification and Validation of API Manufacturing Operations"
Daniel H. Gold, PhD, President, D.H. Gold Associates

"Developing a Robust Supplier Management Process"
Lisa Hornback, Principal Consultant, Hornback Consulting

"GMP for Clinical Trial Materials: Regulations and Applications"
Robert Dana, Senior Vice President, Quality and Regulatory Affairs &Training and Research Institute, PDA
Vince Mathews, QA Consultant, Eli Lilly

"Process Validation for Pharmaceuticals: Current and Future Trends"
Scott Bozzone, PhD, Senior Manager, Global Quality Operations Validation, Pfizer

"Risk Management in Aseptic Processing"
Harold Baseman, Chief Operating Officer and Principal, ValSource

TRI's Review of 2009

Bob Dana, PDA

As I sit in my hotel room in Berlin, Germany, where I am attending the *2009 PDA/EMEA Joint Conference*, I think back to January of this year and my assumption of the responsibility for PDA's Training and Research Institute (TRI). In a way, it seems like a long time ago, yet in another way it seems almost like yesterday. To paraphrase a song from the Grateful Dead, *what a long strange ride it's been*. This year-end reflection provides me an opportunity to look back at my first year in this position.

Since TRI was founded twelve years ago in 1997, I had been a believer in the value of education for our members and the value of TRI as a contributor to PDA's efforts and business model. I actually had the good fortune to see the original TRI facility at the University of Maryland Baltimore County Technology Center when it was just a shell and construction on the facility had just gotten underway. Later, as a member of PDA's Board of Directors, I had the opportunity to learn a bit more about TRI and some of the challenges and opportunities it was addressing. When I joined PDA's staff in 2005 as Vice President of Quality and Regulatory Affairs, I became even more involved in TRI and its operations sometimes helping to identify potential course topics and faculty and working as part of the team in developing and presenting training for representatives of the government of Kazakhstan. I even participated as a faculty member, teaching as part of TRI's flagship Aseptic Processing Program, as well as a couple of other TRI courses in the United States and in Japan.

I have a great deal of respect and admiration for those who came before me as heads of TRI: The founder, the late **Mike Korczynski**, without whose vision and tireless efforts there would have been no TRI, subsequent directors, **Rick Rogers** and **Bob Mello** and my immediate predecessor, **Gail Sherman**. Gail's vision and dedication to growing TRI and keeping it running and successful during the construction of and move to a new facility rivaled Mike's in getting TRI up and running. I'm glad to join that group.

So what was 2009 like for TRI and me? As the year began to unfold, a new phenomenon began to develop—the global economy had tanked and companies were forced to look at their budgets and expenses. Unfortunately, when money becomes tight, travel and training are among the first things to be reduced. Course enrollment was

off and we were even forced to cancel some offerings entirely due to low enrollment. It didn't take me long to realize that "I'm new here—give me some time!" wasn't going to get it done for long. So we took a look at what we could do differently.

We needed to find a way to replace some of the lost revenue arising from the fall off in enrollment. I had long believed in the value of doing in-house training and education and had done some of that myself earlier in my career. TRI had done some in-house training in the past, but it didn't seem to be a focus. We set out to change that. We developed a fairly aggressive approach to developing and publicizing our in-house training capabilities and have had a lot of support from PDA staff and other PDA members, including some of our faculty and Board members. I'm proud to say that those efforts are bearing fruit and our in-house training program is growing and becoming more successful every day. In 2009, we were able to provide in-house training to several companies on a variety of topics, including basic GMP, CAPA and Root Cause Analysis, Process Validation, Aseptic Processing Technology and Environmental Monitoring.

Besides in-house courses, we took our training to Asia, the Middle East and Russia. In Shanghai, we held training courses on Process Validation, *PDA Technical Report No. 1, Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Qualification and Ongoing Control and PDA Technical Report No. 26, Sterilizing Filtration of Liquids.*

Our venture into the Middle East was in response to a request from PDA's Israel Chapter for training. **Hal Baseman**, COO and Principal, ValSource, developed and presented two courses on quality risk management and process validation. Hal was assisted by **Raphy Bar**, consultant, BR Consulting and **Karen Ginsbury**, President, PCI Pharmaceutical Consulting of the Israel Chapter. One of the gentleman from the Israel Chapter we worked with was named Gad, and I can tell you from personal experience when you are in Israel and someone introduces himself by saying "Hi Bob, I'm God (Gad)," you sit up and take notice! We hope to continue this program with the Israel Chapter in 2010 and would welcome the opportunity to partner with other PDA Chapters in a similar manner.

PDA developed a unique opportunity in 2009 to provide training to representatives of the Russian Ministry of Health (Roszdravnadzor). Partnering with Eli Lilly and Purdue University, four weeks of "home and away" training were provided in Moscow, Bethesda, Md., Indianapolis, Ind. and West Lafayette, Ind. Between travel to Shanghai, Tel Aviv and Moscow, I was kept very busy this summer.

We've already done a couple of lab courses in-house. We can also tailor many of our courses to your specific needs and can even develop new course offerings to meet those needs.

So at this point, I'll put in a plug—if you need training in your company but don't have the budget to send your employees to us—call me. We'll bring our lecture courses to you, and we may even be able to bring some of our lab courses to your facility as well. We've already done a couple of lab courses in-house. We can also tailor many of our courses to your specific needs and can even develop new course offerings to meet those needs. Give us a call—I promise you won't be disappointed.

Our staff in Bethesda was busy as well this year managing over 60 courses at our Bethesda facility, as well as in San Diego, Calif., Silver Spring, Md., St. Louis, Mo., New Brunswick, N.J. and San Francisco, Calif. In addition, we conducted training courses in conjunction with major PDA Conferences such as the 2009 Annual Meeting, the Microbiology Conference, the Visual Inspection Forum and the PDA/FDA Conference. We established an attendance record during our courses at the 2009 PDA/FDA Conference. None of this would have been possible without the dedication and hard work of the TRI staff: **Amber Andrews**, **Rachel Davis**, **Stephanie Ko** and **James Wamsley**.

Our cadre of instructors have also been great. They continue to show up, teach their courses, offer suggestions, ideas for improvement and words of encouragement. That we have continued to be successful is in large measure due to all their efforts, and I am grateful to them all.

Although I am writing this in October, by the time you will read this the year-end holidays will be here. Let me take this opportunity, on behalf of all of us here in TRI, to wish everyone the very best for the holiday season and a happy and prosperous 2010; one in which you all have the opportunity to experience a TRI course and continue your career long learning.

So, in closing, let me say thanks to everyone who has helped me this year: My staff, our instructors, the PDA staff and my wife and her business partner who took a weekend out of their own time to help me move out of my old office and get quasi-organized in my new one. Last, but by no means least, I'd like to thank our students. Like Mike Korczynski, without them there would be no TRI!

A Science and Risk-Based Approach For Investigational Medicinal Products

Paris, France • January 26-27 • www.pda.org/IMP2010

Karen Ginsbury, PCI Pharmaceutical Consulting and Volker Eck, PhD, PDA

PDA is holding its next conference on Investigational Medicinal Products (IMPs) in Paris, France, on January 26-27, 2010. The conference will certainly touch on hot topics under discussion. To underline the value of the lectures, it is worth recalling what happened, for example, last time in Rome, Italy. **Carlo Pini**, PhD, Head of Biotechnology, Istituto Superiore della Sanità, opened the conference with a keynote address providing a concise overview of EU regulations and guidances for IMPs and their national implementation. As a regulator, Pini is well-placed to give an overview based on his experiences which he shared with the audience. The outcome of the 2001/20EC directive is that the European Union now has common rules for clinical trials ensuring subject protection via ethical committees. There is a European database for clinical trials and the role of the QP is defined. Labeling practices are defined and there is assurance of GMP and GCP compliance. Pini emphasized that the Investigational Medicinal Product Document (IMPD) is essentially equivalent to the marketing authorization and is used as such during inspection of manufacturers of IMPs. Where biotechnology derived materials are concerned, Annex 2 of the GMPs applies to IMPs and this annex is presently being updated and is about to published. Biological clinical trials applications are still authorized at the national level with each member state in the European Union having specific procedures linked to the European Union directives but there is no overall harmonization particularly with respect to the level of detail needed in an application for a biological/biotech product. Pini mentioned that the EMEA guideline on mitigating risk in first-in-human trials focuses on using risk assessment and addressing initial and escalating doses. The use of science applied on a case-by-case basis should address quality issues and provide solutions. Risk assessment should be seen as an ongoing process that must be revisited as development progress and knowledge is gained of product and process capability. The EMEA defines a "comparability exercise" at the production/process level for a comparative process evaluation. Pini closed his keynote presentation with a mention of the quality guidance for biological IMPs that is under preparation at EMEA and is currently a finalized concept paper. A draft guidance should be available by the end of the year. Additional presentations addressed United States regulations: FDA's GMPs for phase 1, the draft process validation guidance issued in November 2008 and FDA's GCP *Guidance for Clinical Investigators, Sponsors and IRBs–Adverse Events Reporting—Improving Human Subject Protection*, which particularly focuses on the sponsor responsibility in coordinating the reporting and assessing of the effect of isolated reports from sites in the context of pre-clinical toxicity data and data from other sites involved in the study.

A case study of how a reduced viral validation package could be developed as appropriate for the different phases of development provided practical tips on how to substantially reduce the amount of work performed in early phases of trials. Where it is not feasible to perform worst case challenges, it would be acceptable to demonstrate that the actual process parameters work when run at the set points provided that the process is then run at those conditions. In order to show reproducibility, at least two independent experiments should be performed. The take-home from this presentation was that for viral safety the mechanism of viral clearance must be understood on a per product basis and that you cannot extrapolate from one product to another, although in-house data may be used where a documented rationale is presented.

Several case studies presented project management from drug substance manufacture at early/late phase through commercialization with emphasis on operating efficiency, speed and cost considerations. The message was that a multi-stage project plan needs to be managed and a coordinated effort made to balance the correct activities at the right time and avoid costly delays once patients have been recruited. GMP, regulatory and quality considerations must be integrated with clinical timelines. Impurity profiles may change during scale-up which could require comparability studies which entail delays. Regulatory considerations such as time for change approval at different regulatory agencies throughout Europe or in different areas of the world can cause substantial delays or cause a company to run out of approved stock for a particular site which could compromise a site.

Several presentations by qualified persons provided useful tips based on hands-on experience as to problems that have been encountered during batch certification, audits and oversight of release of clinical trials material particularly with respect to the revised Annex 13 to the European Union GMP Guide where the actual release of clinical trials material is performed by the sponsor and not by the QP who only certifies compliance with pertinent GMPs.

Attendees heard that MHRA (United Kingdom) GCP regulations require rapid notification if the scientific value of the trial is brought into question e.g., if a site in a multi-center trial is not complying and their data might be ruled out, this could invalidate the trial. It would not be ethical to continue with the trial once this is known; therefore, MHRA wants to be involved in the decision-making process as early as possible. This is not a requirement of EU GCPs, but it is certainly a valid and appropriate ethical procedure that sponsors might want to adopt.

Sourcing of materials from India and China was discussed in the light of recent supply chain concerns, and a session was devoted to supply chain issues related to labeling and managing hospital pharmacy supplies. The latter presentation allowed industry to gain insight into one of their customers, the hospital pharmacies that often manage numerous trials running in parallel. Issues with regulatory filings for IMPDs were discussed.

The conference closed with a short but lively Q&A panel discussion triggered by a proposed requirement of the Italian regulators for dedicated facilities for phase 1 studies for biologics. The thinking behind this requirement is that the toxicological profile of the products (especially biological and new

chemical entities) may be poorly understood at this stage of development and, therefore, it is preferable to separate between commercial production lines and those used for these types of product. The discussion focused on the meaning of the term "dedicated facility," and it was clarified that the facility would be dedicated to phase 1 material and not to a single product (which would not be feasible from industry's perspective). Additional points of discussion were about what constitutes comparability between material from pre-clinical through commercial batches, where process validation begins and what exactly do companies mean if they claim to perform filter validation before phase 1 when the product may be hard to come by and prohibitively expensive. This was the PDA's third European Union conference on IMPs and as usual provided a lively forum for QP, regulatory, quality, operations and R&D personnel to mingle and exchange experiences—good and bad. The number of questions and discussions, not just during formal sessions but at breaks, lunch and networking activities showed the animation and overall level of interest in the subject matter. The next conference deals with very practical issues presented and discussed, such as:

- Formulation development in early phases
- Process and product development
- Facility and microbiology aspects for development projects
- Clinical trial material supply

This setting concentrates on practical challenges in early and late stage development like how to render a drug substance of low solubility into an injectable drug product and other features specific and particular to parenterals.

We hope to see you next time in Paris.

PDA Europe Conference on Pharmaceutical Microbiology Planned

Berlin, Germany • February 23–24 • www.pda.org/calendar

Francesco Antonetti, PhD, Merck-Serono and Volker Eck, PhD, PDA

PDA has held a very successful global conference on Pharmaceutical Microbiology in Bethesda, Md. in October. Just before that, PDA Europe held a discussion forum on implementing rapid microbiology methods with representatives from the European Health Authorities including the European Medicines Agency (EMEA). Both events saw intense exchange of positions and expectations between industry, suppliers and regulators on hot topics for industrial microbiologists. During the debate in Frankfurt-Offenbach, Germany, on rapid microbiology methods, for example, Health Authority representatives revealed ongoing discussions within EMEA working groups on procedures to better enable continual improvement.

In view of the changes to the European Union guide on variations to marketing authorizations (MAs) as a result to the legislation passed by the European Parliament and in cooperation with the European Commission, the EMEA is discussing how to better enable continual improvement. One option under evaluation was introducing pre-authorized post-approval change management plans and protocols.

"The purpose of the changes that will be introduced with the implementation of the revised variation regulation is to simplify the variations procedure and at the same time assure patient safety and product quality," said **Riccardo Luigetti**, PhD, Scientific Administrator, CHMP/CVMP Quality Working Party, EMEA. "Changes within the approved design space will be allowed without further regulatory review and groups of variations to the same MA, as well as variations (or group of variations) that affects multiple MAs of the same MA holder will undergo a common assessment. All this should help to implement technologies like rapid microbiology methods faster, thus reducing the risk of failure during sterile manufacturing, for example."

Gustavo Marco, PharmD, Pharmaceutical Assessor, MHRA, said that sometimes data from suppliers to the pharmaceutical industry like equipment manufacturers is needed to assess the appropriateness of claims made in MA applications. "When data from suppliers is required, we may need the applicant to put us in direct contact with suppliers so we have access to such crucial data. I cannot emphasize enough the role of the Expert Summary Report of the CTD written by the quality expert to clarify such interdependence and to justify the supporting data provided. In case of doubt or before embarking into a resource consuming endeavor like developing alternative rapid microbiology methods, I recommend applicants to ask for a scientific advice meeting with the competent authorities to avoid misinterpretations," Marco said.

"Rapid microbiology methods have reached a mature state as technology. They can be essential to build and maintain appropriate sterility assurance levels in sterile manufacturing processes," said **Paul Hargreaves**, Principal Medicines Inspector, MHRA. "It is disappointing to see how few sites in Europe have actually implemented such technologies, although they are relatively easy to establish in a GMP environment. Having inspected many sterile manufacturing premises, it is safe to say that several critical observations could have been avoided if such methods had been in place. They actually help to understand better the root cause of problems and save money in avoiding reworking or even worse recalls."

The European conference on pharmaceutical microbiology issues will continue this dialog. In particular, challenges in manufacturing from a microbiology standpoint will be presented. Topics presented will include:

- Microbiology—myths, legends and fantasies
- Statistics in microbiology and their correct application
- Developing specifications for microbiological characteristics
- Environmental monitoring and Annex 1 to the EU GMP Guide
- Viral contamination testing: How and what
- Issues around biological indicators and efficacy testing
- Impact of house strains, baseline changes on e.g., bioburden testing and validation
- Identification of contaminants

The PDA Europe Conference on Pharmaceutical Microbiology will be held in Berlin, Germany, February 23-24, 2010. In preparation of this event, the organizing committee is inviting interested individuals to submit papers on these or other topics. Please send abstract of those to Volker Eck at *eck@pda.org*. We look forward to welcoming you.

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