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PDA Letter

Volume XLIV • Issue #5

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May 2008

In This Issue…

EMEA Opens Door to Dialogue on Proposed Annex 2 Revisions

Stephen Brown, Vivalis, and Jim Lyda, PDA

February 19 in Budapest saw a superb example of industry-regulator information exchange to the benefit of all. The occasion was the open meeting to discuss the draft revision of Annex 2 of the European GMP.[1] About 50 delegates took part in the discussion on the proposed draft, including the regulator delegation consisting of **Emer Cooke**, Head of Inspections Sector, EMEA; **Ian Rees**, Inspector and rapporteur of the Annex 2 drafting group, MHRA; and **Paul Hargreaves**, Senior Inspector, MHRA.

The open meeting and the discussion and exchange of views it fostered was an adjunct to the overall consultation process and was intended to help stakeholders better focus on key issues when submitting their comments. There will be no official report on the open meeting.

The current version of Annex 2, written in the 1990's, was meant to provide supplementary guidance to the EU GMP Guide, now known as Part I, *GMP for Medicinal Products.* Following a review of the GMP Guide, GMP Annex 18 (consisting of the harmonized ICH Q7A standard) became GMP Part II,[2] covering active pharmaceutical ingredients (APIs). In 2005, a concept paper was published giving notice on the intent to revise Annex 2.[3] The draft revision was published for public consultation in November 2007, with a consultation deadline of March 14, 2008. **[Editor's Note:** PDA submitted comments on the draft revision on March 14, and the comments can be found at www.pda.org/regulatorycomments. The cover letter was published in the April *PDA Letter*, p. 28.**]**

The open meeting was facilitated by **Hannelore Willkommen**, and opened with a presentation by Cooke describing the structure of European GMP, how guidance is developed, and how Annex 2 fits within that context. The EMEA considers Parts I and II of the GMP guide to be wholly compatible and applicable to biologicals manufacture. Annex 2 is intended to provide supplementary guidance to both Parts I and II of the GMP Guide, modifying certain details as appropriate.

Next, Rees reviewed the development of draft Annex 2 within the Inspectors Working Group (IWG). Since the original Annex 2 was published, there have been many advances in science, manufacturing and testing technologies. In addition, the range of product types today is significantly greater than in the

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Conference	September 8-10
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The US Food and Drug Administration (FDA) announced the Good Manufacturing Practices (GMPs) for the 21st Century initiative in 2002, giving the industry its first glimpse of the future of regulatory oversight for pharmaceutical production. The intent of the original initiative was to offer the industry the necessary tools to provide more post-approval flexibility, making continual improvement less of a regulatory burden, and to promote better self-regulation to improve regulatory compliance status.

In the five years that have passed since the announcement, regulatory health authorities and industry have partnered by harmonizing requirements and implementing new systems for assuring and maintaining pharmaceutical quality. The 2008 PDA/FDA Joint Regulatory Conference will provide examples of how these new approaches have been successfully implemented. In addition, the conference will examine what is working well and where the industry and regulatory health authorities still need to work to achieve modernized quality systems.

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Great presentations and a great city make for a fantastic second PDA/EMEA conference

The Snapshots will return next issue with info from the 2008 Annual Meeting

Coming Next Issue:
European Regulatory Update Novel Technologies for Drug Delivery

Editor's Message

The *PDA Letter* had the good fortune of attending the 2nd PDA/EMEA Joint Conference in Budapest this past February, which turned out to be the perfect follow-up to the first one in London. PDA's **Jim Lyda** and **Volker Eck,** PhD, provide timely and informative summaries to two popular workshops that preceded the conference—the workshop on Annex 2 revised (see cover story) and the one on cleaning and disinfection (see p. 18). **Walt Morris** provides a small summary of the conference itself and the momentum it generated for a potential third PDA/EMEA meeting (p. 20). **Emily Hough** summarizes a presentation on European GMP inspection findings (p. 22). The Faces & Places returns with four pages of photos from the event; we hope you enjoy them. Finally on the meeting, **Astrid Guenther** summarizes the New Member Breakfast which took place the first day of the conference (p. 32).

Because of the little time between the PDA/EMEA conference, the PDA Annual Meeting and the Quality Systems workshops in China, the Science & Technology Snapshot and the Quality & Regulatory Snapshot are on holiday this issue, but will return in June with a complete rundown of activities at the 2008 Annual Meeting in Colorado Spring.

Correction

In our overzealous attempt to release an article in the April Letter from the March PDA conference on cold chain distribution, the editorial staff failed to properly check and edit a quote from Rosa Motta. In the article, entitled "Regulators Focus on Cold Chain Practices," FDA's Motta actually said: "For example, manufacturers are expected to know the [effects of] temperature excursions on the drug. This is an important element of stability testing. Also we expect manufacturers to gather knowledge regarding the stability characteristics of the drugs they manufacture as part of drug development and also as part of cGMP requirements. This knowledge of this particular characterization of drugs will help manufacturers in selecting adequate containment closure systems and shipping methods. Information about the stability characteristics of drugs can be useful in developing plans for procedures for disposition of drugs exposed to adverse conditions and to conduct those investigations related to these events." We apologize to her and our readers for the error.

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A New Strategy for Programs

PRESIDENT'S MESSAGE

Bob Myers

With PDA's Annual Meeting recently past and this issue of the PDA Letter dedicated to the events of February's PDA/EMEA Joint Conference, it is a good time to talk about PDA's strategy for our meetings and programs.

Our Annual Meeting has become our largest scientific meeting of the year. Our members will see a clear distinction between the content of the Annual Meeting versus our strong regulatory conferences that we hold with the U.S. FDA and EMEA.

The Annual Meeting now addresses cutting-edge scientific topics related to PDA's core competencies, among which are: sterilization science, innovative drug products, filling methods and manufacturing equipment.

The Annual Meeting also will allow us to fulfill another strategic goal of locating events in convenient venues for all our members. With our membership growing strong all over the world, we have to carefully select venues to be fair to everyone's budgets. With the PDA/FDA Joint Regulatory Conference already established as PDA's premiere event on the U.S. East Coast, and the PDA/EMEA Joint Conference becoming a standard event in Europe, we have decided that the Annual Meeting will normally be held in the western United States. In 2009, the Annual Meeting will return to the highly popular Red Rock Resort in Las Vegas and in 2010, we are looking at venues in northern California. I advise all of our exhibitors interested in supporting the 2009 Annual Meeting to commit early because space in the exhibits area will fill up quickly.

Of course, PDA offers a number of targeted scientific conferences important to smaller segments of our membership. Our annual microbiology conference will be held October 20–23 in Chicago, a city that is home to many of our members. We are working with our New England Chapter to develop a conference which might be held routinely in Boston.

PDA sponsors other meetings that crisscross the Atlantic every other year. For one, our *The Universe of Pre-Filled Syringes and Injection Devices* franchise, which returns to the United States in '08, and will be held in San Diego October 6–7. The *PDA Pharmaceutical Cold Chain Management* meeting goes the other way in 2008, taking place in Berlin November 4–7.

Check the PDA calendar of events on our website and in the center of each *PDA Letter* to learn about all of the meetings, workshops and TRI courses we are sponsoring.

Finally, I want to thank all of our volunteers who made our first two big meetings of the year a huge success. For the PDA/EMEA Joint Conference, Program Co-Chairs **David Cockburn, Stephen Bellis** and **Lothar Hartmann,** PhD, led a dedicated program committee. The EMEA and its representatives on the committee deserve praise for their tireless work to make the meeting happen.

For the Annual Meeting, program Chair **Maik Jornitz** and Vice Chair **Ian Elvins** did a fantastic job leading a large planning committee that delivered one of PDA's best science meetings to date. The success of the large Annual Meeting Exhibition is a credit to the hard work of the Exhibit Advisory Committee, led by **Art Vellutato.**

I hope to see you at one of our upcoming events!

2009 PDA Annual Meeting

The Microchip: Impact on the Pharmaceutical/Biopharmaceutical Industry

Friends and Colleagues:

The PDA 2009 Annual Meeting will explore an area of immense importance to our industry - the current and future impact of computerization and automation. Few would disagree that the microchip has and will continue to revolutionize the pharmaceutical and biopharmaceutical industry. There is virtually no area of the industry that is not affected, from the discovery process to the management of clinical trials; from process development and design, plant control systems to automated batch records; from analytical technology to the management of Change Control and deviation handling - the list is endless.

Have you or someone you know in the bio/pharmaceutical community done something cutting edge or revolutionary in the past year that has involved the use of computerized systems, something that would be of particular interest to the global industry? Such as:

- Solved an unusually difficult technical problem
- Developed an efficiency or quality improvement idea
- Introduced a novel way of using computers and automation to improve process reliability or consistency
- Managed process development data with unique software applications
- Introduced new ways to automate Quality Assurance processes

PDA encourages you to submit a scientific abstract for presentation at the PDA 2009 Annual Meeting, which will be held on April 20-24, 2009, at The Red Rock Casino and Resort in Las Vegas, Nevada. Abstracts must be noncommercial in nature, describe new developments or work and significantly contribute to the body of knowledge relating to pharmaceutical manufacturing, quality management and technology. Industry case studies demonstrating advanced technologies, manufacturing efficiencies or solutions to regulatory compliance issues are preferable and will receive the highest consideration. All abstracts will be reviewed by the Program Planning Committee for consideration of inclusion in the meeting as a podium or poster presentation.

PDA is seeking presentations of 30 minutes in length, which present novel solutions and practical approaches. The following list is a guide of the suitable topics for papers. It is not exhaustive and any paper which fits the overall topic of the conference is welcome.

Development Science

- Advances in Aseptic Filling/Processing
- Advances in Dosage Form Delivery Systems
- Automated Sterilization Technologies
- Contamination Control/Facility Manufacturing Control
- Cell Culture/Line development
- Implication and application of ICH Q8 and the Q8 Annex to process design and development
- Implication and application of ICH Q9, Risk Management to process design and development
- Knowledge and Information Management
- Process Analytical Technologies (PAT)
- Process Modeling and Creation of a Design Space During Product Development

Manufacturing/ Process Science

- Aseptic Processing
- Automated Manufacturing Systems
- Barrier/Isolators/RABs
- Blow-Fill-Seal Automation
- Building Management and Control
- CIP/SIP and Multi-product Manufacturing
- Design/Management of Multi-product Facilities
- Electronic Documentation
- Innovative Manufacturing Approaches
- Knowledge and Information Management
- Online In-process Testing (e.g. Container Closure/Filter Integrity, etc.)
- Production Strategies for a Global Market
- Robotics
- Tracking and Tracing Technologies
- Visual Inspections
- Warehouse Control Systems

Quality Science

- Application of ICH, Q9, Risk Management to Quality Systems and GMP Compliance
- Compliance Monitoring and Trending
- Data Spreadsheet Qualification Case Studies
- Designing Pharmaceutical Quality Systems Across the Product Lifecycle, ICH Q10
- Environmental Monitoring
- Knowledge and Information Management
- LIMS and Lab Management Systems
- Microbiological Methods and Trends
- Quality Management Systems
- Supplier Quality Management Systems including Contract Manufacturing
- Tracking and Tracing Systems
- Training and Education Systems
- Validation of Pharmaceutical and Biopharmaceutical Processes

Photo courtesy of Bayer Healthcare

Call for Papers

April 20-24, 2009 | Las Vegas, Nevada

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- 2-3 paragraph abstract, summarizing your topic and the appropriate forum (case study, discussion, traditional, panel, etc.)
- Take-home benefits
- Session objectives
- Rationale

Recent Sci-Tech Discussions: Cleaning Validation of Coating Tank and Storing Wet Equipment

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

Cleaning Validation of Coating Tank

We have got tanks (2 no.) for manufacturing of sugar syrup for liquid preparations & coating solutions for coating. In sugar syrup tank, we manufacture only sugar syrup with or without color whereas in coating solution tanks contains materials like Opadry, solvent (methylene chloride etc.) & some other additives (not an API). In both the cases no API is added into the tanks.

Is it required to do cleaning validation of such tanks, spray guns (coating) & stirrer used, even though it has no API? If yes…what needs to be tested? Visual cleanliness during line clearance is current criteria we are following.

Respondent 1: If processing of API is not done with the equipments as you mentioned then Cleaning Validation is not required. Visual line clearance is sufficient.

But risk assessment of degradation products of excipients will be required.

Respondent 2: Cleaning validation is required for the equipments, which are part of your manufacturing process. However details of validation changes from equipments coming in direct contact with product vs all other ancillary equipments.

Respondent 3: What needs to be tested depends on the materials and the processes involved. But in answer to the question, "Is cleaning validation required?" I would ask the question, "Why do you think it is not required?"

Integrity and quality of a product does not reside with the API alone. I could argue that it was this sort of thinking that got Roche into trouble recently where they had not adequately cleaned and validated the cleaning of a reagent holding tank-eventually leading to recalls and withdrawal of a license [now reinstated].

Respondent 4: I too agree with this. There will be some materials that have a great impact if not studied. For example, in formulations where HPMC 100 nonactive is used for sustained release in some formulations—if the vessel used for this is not cleaned properly then there are chances that this will hamper your other products which are immediate release. Thus the type of ingredients should be given due consideration.

And coming to the MACO I would be thankful if anyone could provide me the details of how to proceed regarding my doubt. We had a MACO of 0.007ppm as our worst case matrix but this value is very difficult to achieve in routine. In such cases how do we substantiate for the cleaning process? Can anyone throw some light on this?

Respondent 5: Yes cleaning validation is certainly required, be it solid dosage equipment. In case you are using the vessel for multi products, then certainly you need to validate it after cleaning the vessel. In case you are running the same product in the next batch then you may get away with just cleaning and reusing it for the next batch. Still, if the gap between the two batches of the same product allows sufficient time for the residues to dry/form cake film, it would be advisable to clean the vessel using CIP/SIP (Steam - Water combined mixing Jets). In fact, CIP/SIP is really not product/area specific. What we want to ensure is that contamination/cross contamination are avoided.

Respondent 6: Also consider that "sugar" is food for bacteria. Warm, damp climates are breeding grounds.

Storing Wet Equipment

Can anyone provide an example of a warning letter, or a specific guidance document reference, that states that equipment should not be stored wet?

What are people's thoughts on the storage of wet equipment (even if you do validate a clean hold time)?

Respondent 1: Warning letters or not this quite clearly contravenes GMP requirements in that equipment should be protected from contamination & storing an item of equipment wet increases the risk of micro proliferation.

Respondent 2: Equipments should not be stored wet as it may result in microbial proliferation. Here are the references:

- 21 CFR 210, 211, Subpart D–Equipment 211.67 - Equipment cleaning and maintenance.
- USFDA 1993 GUIDE
- Point No. 7, PIC/S recommendations on validation master plan installation and operational qualification non-sterile process validation cleaning validation, PI 006 - 02, 1 July 2004
- Health Canada document entitled "Cleaning Validation Guidelines" (GUI-0028)

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PDA
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Recent Sci-Tech Discussions: Storing Wet Equipment, continued from page 8

- WHO TRS 937, Annex 4 Supplementary guidelines on good manufacturing practices: validation, Appendix 3 Cleaning validation
- ICH Q7, 12.7 (12.70 TO 12.76)
- Schedule M, Equipment Design, Size and Location, 4.1 to 4.6

Respondent 3: Storage of wet equipment is generally a bad idea, even for a non-sterile process. It allows for microbial growth, build up of endotoxin, etc. This would be a direct violation of 21 CFR 211.67:

Sec. 211.67 Equipment cleaning and maintenance:

(a) Equipment and utensils shall be cleaned, maintained, and sanitized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.

(b) Written procedures shall be established and followed for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a drug product. These procedures shall include, but are not necessarily limited to, the following: (1) Assignment of responsibility for cleaning and maintaining equipment; (2) Maintenance and cleaning schedules, including, where appropriate, sanitizing schedules; (3) A description in sufficient detail of the methods, equipment, and materials used in cleaning and maintenance operations, and the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance; (4) Removal or obliteration of previous batch identification; (5) Protection of clean equipment from contamination prior to use; (6) Inspection of equipment for cleanliness immediately before use.

(c) Records shall be kept of maintenance, cleaning, sanitizing, and inspection as specified in 211.180 and 211.182.

PDA Interest Groups & Leaders

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

SECTION TITLE

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

SECTION LEADER

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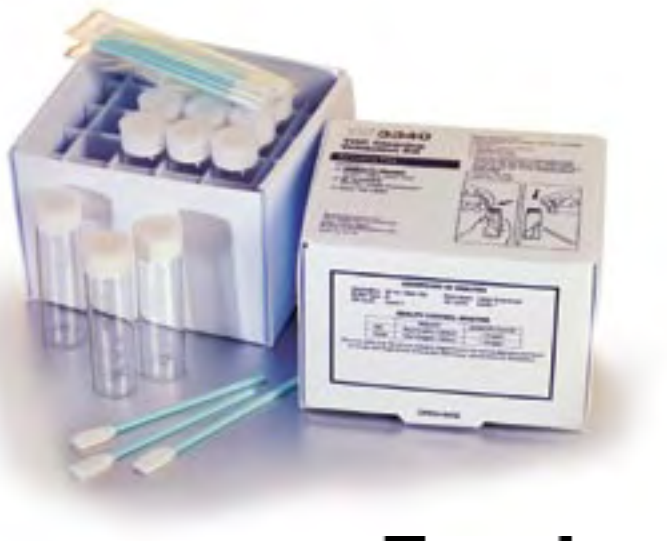

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EMEA Opens Door to Dialogue on Proposed Annex 2 Revisions, continued from cover

1990's. Draft Annex 2 has been reformatted into Part A (General Guidance) and Part B (Specific Guidance on Selected Product Types). A key purpose of the revised Annex is to take into account legislative changes for Advanced Therapy Medicinal Products,[4] the Tissue and Cells Directive,[5] the advent of quality risk management (QRM), and new guidance on somatic cellular therapy and gene therapy. Additional input on tissue engineered products (TEPs) is being sought. There is possibility of another public consultation on the TEPs section or the whole annex before the end of 2008. A publication date for the final version of Annex 2 has yet to be set.

Following the introduction by Cooke and Rees, the program shifted to the industry views, with presentations from representatives of four European industry and professional associations. **Anita Derks,** Global Qaulity Manager, Biotechnology, F. Hoffmann-La Roche, presented the positions of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the European Vaccine Manufacturers (EVM). The European Biopharmaceutical Enterprises (EBE) was represented by Roche's **Lothar Hartmann,** PhD, Head–External Relations, Global Quality Department. PDA's position was presented by **Jim Lyda.** Representatives from three major pharmaceutical companies also presented: **Volker Lenz,** PhD, Manager, QA & Compliance, Roche; **Brigitte Holst,** Manager, Novo Nordisk, and **Mary Sliwkowski,** PhD, Vice President, Genentech.

Status of the Revision

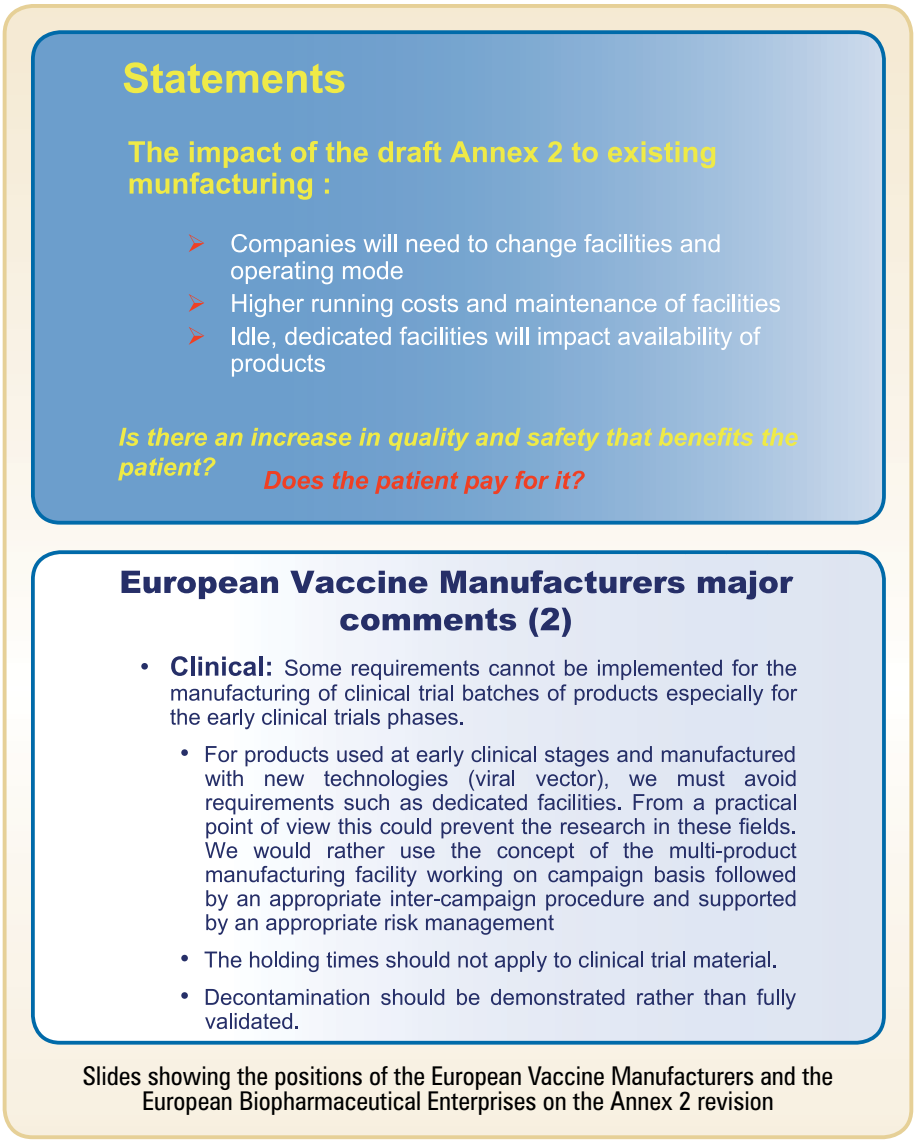
- A draft text was released for public consultation in November 2007
- Deadline for Comments is 15 April 2008
- The consultation requests input on requirements specific to Tissue Engineered products (TEPs)
- Additional expertise in the field of TEPs will be added to the drafting group
- A further public consultation may be necessary towards the end of 2008, either on the section for TEPs alone or possibly for the whole annex

Cooke presented the status of the Annex 2 revision

There were a number of common themes developed by the industry representatives. Frequently, comments were made with respect to the scope of the Annex. Presenters pointed to some overlap and some inconsistency between draft Annex 2 and GMP Part II (originally ICH Q7A), and recommended that GMP Part II should be regarded as the reference GMP guidance for API/drug substance for the vast majority of marketed products. Similarly, GMP Part I should be limited to finished medicinal products. Annex 2 would then only address GMP issues that are not yet defined, associated with new technologies, or relate to special products, e.g., tissue engineered products.

There was some feeling that Annex 2 contains prescriptive guidance regarding process controls and risk issues (environmental, biohazard, biosafety) and that the Annex should not address non-GMP issues such as environmental and personal safety, and registration. The industry representatives also suggested that draft Annex 2 is not "forward looking" and does not fully embrace current international manufacturing quality concepts (e.g., ICH Q8, Q9 and Q10, QbD, PAT, etc.). As a result, the Annex could stifle innovation, for example, by interpretations requiring dedicated equipment for certain product types. If this interpretation is indeed correct, it would counter a recent industry trend towards multiproduct facilities. The potential consequences to industry, in terms of dedicated equipment and facilities, could be much higher operating costs and significant capital costs. In this

(l-r) Anita Derks, F. Hoffmann-La Roche; Mary Sliwkowski, Genentech; Volker Lenz, Roche Diagnostics; Brigitte Holst, Novo Nordisk; Ian Rees, MHRA; Emer Cooke, EMEA; Paul Hargreaves, Medicines and Healthcare Products Regulatory Agency; Hannelore Willkommen, RBS Consulting



Slides showing the positions of the European Vaccine Manufacturers and the European Biopharmaceutical Enterprises on the Annex 2 revision

context, a number of presenters raised concerns that draft Annex 2 should not be applicable to clinical supply/investigational medicinal product (IMP) development and manufacturing.

Requirement or Interpretation?

There was discussion about possible industry "over-interpretation" of the text contained in Annex 2. For example, while there are references to dedicated equipment, the text usually suggests that the use of such equipment should be "considered" by the manufacturer. In very few cases does the text mandate a particular activity or requirement. There was a comment that the industry is frequently inferring a "most prescriptive" requirement from text that clearly allows room for discretion. In other words, requirements are being read into the text in a manner that is not stated or intended.

Several participants countered that, based on experience, there is an expectation that some inspectors will interpret the discretionary wording of the Annex in its most rigorous interpretation as the GMP standard. In other words, while the manufacturer may see a range of choices in a GMP decision when reading the Annex, the inspectors frequently start at the extreme (prescriptive) end of that range. This may require manufacturers to justify process decisions during inspections multiple times, depending on each new inspection situation.

All agreed that while European GMPs can be complex, there is no intention to be over prescriptive or to stifle innovation.

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Other Discussion Highlights

The regulatory and industry representatives agreed that redundancy between Annex 2, GMP Part I and Part II is an area that needs to be looked at again. All also concurred that the great diversity in biotechnology products and technologies today makes it difficult to cover them all in one document, giving rise to problems of interpretation.

There was discussion regarding low bioburden production of APIs with some industry representatives citing difficulties with European inspectors on this subject. The regulators advise that nothing in draft Annex 2 forbids low bioburden API processes. None of the participants disputed the necessity of achieving consistent interpretation of Annex 2 between inspectors and the industry.

Further consensus was reached on the need to define requirements for tissue engineered products, a sector of the industry not represented at the open meeting and to better define the scope of Annex 2 with respect to clinical/IMP manufacturing—Annex 2 is not specifically aimed at early stage clinical trials.

In summing-up, EMEA's Cooke called the meeting a valuable exercise that sensitized everyone to the issues that will be addressed as a result of the consultation process. There was a plea from the regulators that comments on Annex 2 be submitted in a manner useful for the redrafting process. For example, it is important to supply technical justifications and concise alternative text where changes are recommended.

Finally, there were expressions of appreciation from the attendees for the willingness of the EMEA and inspectors to discuss this important topic. As one observer said, "We asked the regulators to listen, and this is what they did. They asked us to listen, and we did as well. The meeting was worth every minute!" **[Editor's Note:** See "Industry Welcomes Annex 2 Workshop," for one participant's perspective of the Open Meeting.**]**

1. EudraLex Volume 4, Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use, Draft Annex 2: Manufacture of Biological Medicinal Products for Human Use, 03 September 2007/rev.
2. EudraLex, Volume 4, Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use, Part II: Basic Requirements for Active Substances Used As Starting Materials.
3. Concept Paper On The Revision Of Some Annexes To The European GMP Guide In The Context Of GMP For Active Substances, EMEA/INS/GMP/147444/2005.
4. Regulation No. 1394/2007/EC of the European Parliament and of the council of 13 November 2007 on Advanced Therapy Medicinal Products.
5. Regulation No. 2004/23/EC of the European Parliament and of the council of 8 February 2006 as regards certain technical requirements for the donation, procurement and testing of human tissues and cells.

Note to readers: *The preceding PDA report is not an official record or transcript. Rather, it reflects the tone and substance of the open meeting as interpreted by the authors. Readers should use caution making any regulatory or compliance interpretations based on this information.*

Industry Welcomes Annex 2 Workshop

Walter Morris, PDA

The day after the workshop on Annex 2 at the *2008 PDA/EMEA Joint Conference,* Genentech's **Mary Sliwkowski,** PhD, sat down with the *PDA Letter* to tell us how she felt the workshop went. Sliwkowski heads regulatory affairs for CMC issues for Genentech and is responsible for all interactions with regulatory authorities worldwide, both for GMP and CMC topics.

Sliwkowski originally signed up to attend the Joint Conference because her firm is "trying to reach out more into the European space than we have in the past." When they learned of the Annex 2 workshop, announced just prior to the conference, the firm "jumped at the chance to have an opportunity to be involved." Sliwkowski already had been a member of PDA's Task Force formulating comments on the draft revision of Annex 2.

When asked about how unique it was to participate in an open dialogue with EMEA, Sliwkowski acknowledged that it "is very unique, particularly for us as an American-based company." Not being in Europe, it is not always "transparent" how to interact with the EMEA. "So we really appreciate these kinds of opportunities. We did participate, about a year ago, there was a discussion around virus regulations—viral validation and some of those aspects—that was maybe one of the first ones that was biotech related." While EMEA has had open dialogues regarding other initiatives, those were not biotech focused. "So it was really unique," Sliwkowski said, "and a wonderful opportunity for us."

Overall, the EMEA was receptive to industry comments and willing to work through disagreements about interpretation. Sliwkowski explained: "There was definitely initially disagreement over the interpretation. And I think it was clear that the EMEA had one thing in mind when they put it together and had a certain perspective about it. But it was also clear that across the board, everyone of the companies that reviewed it had a very different interpretation. And so you have to say there is some kind of disconnect here. I think that did become clear to them as we discussed it, and Emer commented on that at the end."

Although EMEA didn't agree with all the presenters' interpretation of Annex 2, Sliwkowski said it was important to discuss the divergent opinions. "And even if it is a perception that we have that is maybe a misperception from their perspective, perception is reality in a lot of circumstances and you have to deal with it. I think they are recognizing that. I'm comfortably confident that they will do something about this. Modify the draft revision to some extent." The dialogue, she continued, "helps us understand where they are coming from, and I think we can use that knowledge and the discussion that we got out of this. Even if they wouldn't make a change, just having had the conversation and understanding their perspective will be helpful to us."

The workshop's format effectively facilitated dialogue between the regulators and the industry, raising awareness of each side's challenges. "It is listening on both sides," explained Sliwkowski. "It is a two-way thing, we are all in this

continued on next page

Industry Welcomes Annex 2 Workshop, continued from previous page

together, and we need to understand each other's perspectives. They have a very difficult job just trying to corral the 27 member states to come to some statement about where they are going to go with these kind of regulations and to try to modernize things. It was extremely helpful to hear today the structure that they have to deal with and how complex the regulatory structure is. And that helps you understand in the particular annex we were talking about yesterday, they don't want to revisit everything; they want to take a small slice, and some of the things we had concerns about are captured someplace else. And until you put all of that together, you don't appreciate that."

EMEA stressed the position that the EMEA GMP equals the whole of Parts I and II and all of the annexes. To industry, "that was very useful to realize that that is the perspective they are approaching it with. We can use that knowledge and take it into our next inspections and if we are being brought into a discussion about one particular thing, we can actually say, 'Well in this meeting, we had this discussion with the designers of these guidance documents and this is what their intent was.' So that helps us a lot for the future."

Industry values the relationship-building aspects of meetings like the PDA/EMEA Joint Conference and the workshops "very, very highly," said Sliwkowski. When asked to explained further, she mentioned that the neutral setting is more conducive to productive dialogue. "It is so much better to have conversations not in the heat of a particular issue at your company but in this kind of neutral setting where you can get a better understanding of where somebody is coming from." Having open discussions during an inspection, for example, is difficult because "there is a lot of pressures on both sides."

Industry values the relationship-building aspects of meetings like the PDA/EMEA Joint Conference

Regarding the specific draft revision of Annex 2, which came about from the need to apply the GMPs to advanced therapies (cell and tissue, somatic cell and gene), Sliwkoski noted industry's concern that "in the area where we've been doing this under the current regulations, this feels like we are adding a lot of things on top of it. They stated that that was not the intention at all, so that is the part we have to struggle with."

At Genentech, for instance, none of the firm's products fall into the advance therapy category. "We don't do anything in that context. All of our products are what are called at this point traditional biotech—recombinant proteins, etc. We felt like we were already dealing with what we thought was an adequate system."

EMEA stated that another driver behind the revision was ICH Q8, Q9 and Q10. While the draft includes Q9 concepts on risk management, industry asked about the Q8 concepts of quality by design and design space. "We were worried that it wasn't thinking as much about those concepts as we would have like to have seen. But what I learned here today that there are other pieces of the 'holistic GMP' that are going to deal with that."

Asked if Genentech would welcome future opportunities to participate in open dialogues with the EMEA, Sliwkowski state, "I think we would all be very pleased if that was the case. It would be good to have continued open discussions about any types of guidance that are being developed. [These workshops] add complexity, but I think we all can agree that you come away with much stronger guidances and much stronger adherence and understanding so that the implementation is easier because people who have been involved in the consultation know what the intent is and it can be grasped that much quicker than otherwise."

PDA wishes to thank Sliwkowski for taking the time to speak with the *PDA Letter* and the EMEA for supporting the Annex 2 workshop.

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Industry Comes Clean at Workshop

Volker Eck, PhD, PDA

PDA held a second edition of its cleaning and disinfection workshop in Budapest, Hungary on February 18–19, preceding the *2008 PDA/EMEA Joint Conference*. The workshop received much attention, especially from the 11 European Inspectorates present. The interaction between the inspectors and the other delegates, mostly from European pharmaceutical industry, was stimulating.

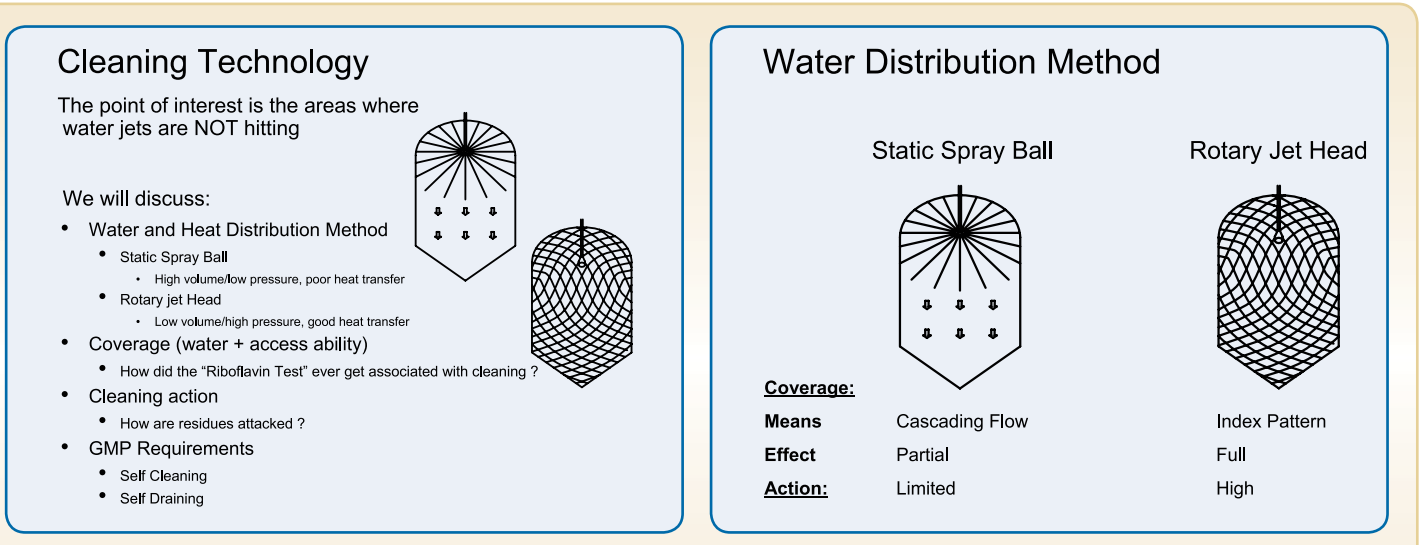
The workshop covered crucial questions on cleaning chemistry, cleaning physics and cleaning targets. A paper on "Designing an Effective Cleaning Cycle" was presented by **Dusko Filipovic**, Key-Account Manager, PMT Partikel-Messtechnik. **Esmaeil Ektefaie**, PhD, Quality Supervisor, QA, Baxter BioScience, presented a lecture entitled, "Cleaning Validation Compliance." He elaborated on regulatory requirements, documentation issues, sampling techniques and analytical methods/residues and limit setting. These two introductory presentations generated much discussion, especially the topic of suitable methodologies, recovery problems, limit setting and cleaning validation concepts in the development environment.

The use of total organic carbon measurements as a surrogate for residual contaminants, and the different calculation approaches to define an acceptable cleaning limit, were some of the specific topics aiding delegates to achieve a satisfactory cleaning strategy.

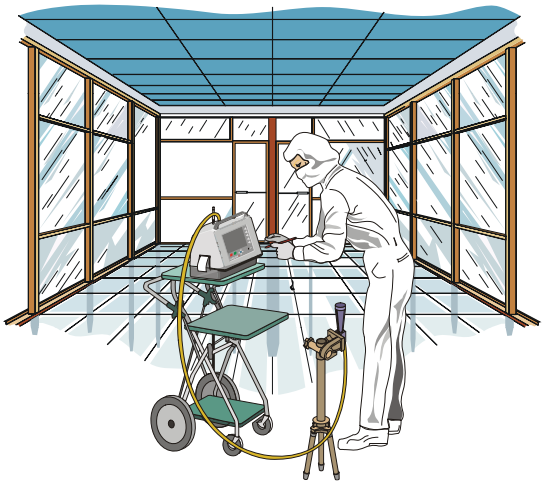
The workshop covered crucial questions on cleaning chemistry, cleaning physics and cleaning targets.

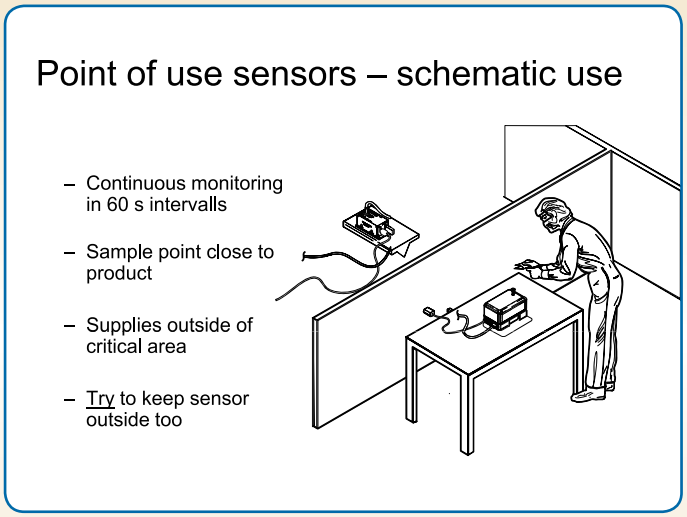
The two presentations also covered risk assessment/risk evaluation and recent additions to the EU GMP Guide. It was stressed by the lecturers that the information gathered during this exercise may have imminent effect on the limits set for residual contaminants, for example, those that have been established before without taking these results into consideration as well as those collected for new products, equipment or facilities using this important piece of information. Discussions during the workshop suggested to inspectors and industry representatives that it was most important what information was gathered in a risk assessment and risk evaluation exercise to decide whether such solutions and limits were justified or not.

Filipovic and Ektefaie's presentations were followed by exquisite lectures on advanced techniques of clean-in-place (CIP) technology by **Stephen Trombetta**, Manager, Technical Operations, Veltek, and spray applications by **Kent Milton**, Portfolio Manager, Engineering Sciences, Alfa-Laval. It was important to the delegates to learn and understand the implications of those techniques, as well as the advantages and limitations of their usage. A lively discussion followed on the design of a successful validation strategy. This took into account the impact of the characteristics of the product and the equipment on these applications. The lectures were supported by video documentation making them not only interesting, but also illustrative. The last topic handled during the first day was

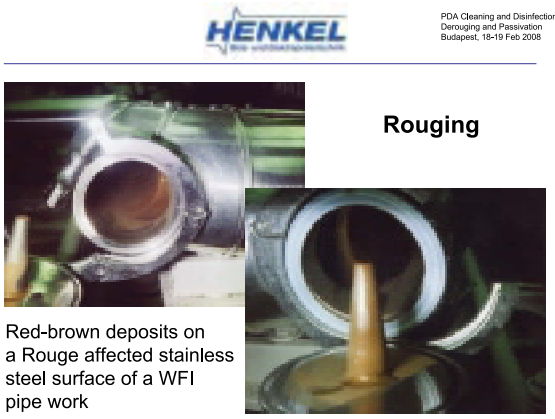


The effectiveness of static spray balls was demonstrated by Kent Milton





Joerg Dressler addressed topics like sensor placement during his presentation on environmental monitoring



Florian Andre shows an example of rouging

"Derouging and Passivation" by **Florian Andre**, Pickling & Electropolishing, Henkel Beiz-und Elektropoliertechnik. This generally accepted problem was of vast interest, as the lecture added some important aspects to maintaining, ie., water loops and manufacturing equipment in a perfect state of control. One feature that might be added to a chain of control for maintenance was a device made commercially available by several providers that could indicate the best point in time to run a passivation cycle.

By doing so, any user could prolong the frequency necessary to invest in an electropolishing procedure at a later point in time.

The second day started with directives and guidelines in relation to types of contamination in an aseptic production area by **Peter Koger**, Technical Sales Manager, Veltek. It was followed by lectures on environmental monitoring for viable particulates by Veltek's Trombetta, and environmental monitoring for non-viables by **Joerg Dressler**, Director, PMT Partikel Messtechnik. The latter two presentations initiated a discussion on the latest changes to the EU GMP Guide through recently revised Annex I. Of most interest were arguments and implications in the Annex on sampling time, sampling speed, and sampling point location. In addition there were issues of setting alert and action levels, and best practices for executing investigations on alert/action level violations and their respective batch disposition decisions.

It was interesting to follow the discussion about disinfectant rotation, the rationale behind it, and the frequency suggested by the experts present. In brief, rotation is not to prevent developing resistance to the disinfectant. Rather, the suggestion was to avoid the constant use of very aggressive disinfectants that eventually will corrode equipment very fast by rotating less aggressive disinfectants with more aggressive but less frequently applied disinfectants—thus eliminating possible contaminants like spores that can survive other cycles.

Veltek's Koger introduced a hot topic in his presentation entitled, "People in an Aseptic Production Area (APA)." The impact of people and their behavior was further addressed by two lectures given by **John Lindsay**, President, Aseptic Solutions, called "Aseptic Manufacturing, the Strands of the Rope" and "Smoke Studies, Air Made Visible." His lecture contained examples of the visualization of correct behavior to avoid or reduce contamination risks and to safeguard the integrity of the product.

In the end, the workshop was very interesting and valuable as supported by the attendee evaluations. It is the intent of PDA to continue this series with another event within a year's time.

70 Regulators Attend 2nd PDA/EMEA Conference

Walter Morris, PDA

In February, PDA and EMEA teamed up for a second time to hold a Joint Conference on European regulatory initiatives. The week-long event in Budapest, Hungary included PDA Training and Research seminars, two preconference workshops, and two days of enlightening conference sessions. By all measures, the second Joint Conference surpassed the inaugural October *2007 PDA/EMEA Joint Conference* in London, which in itself was a spectacular event.

Opening the conference, PDA Chair **John Shabushnig,** PhD, Pfizer, drew parallels between the Joint Conference with EMEA and the model PDA adopted in 2006 of *Connecting, People, Science and Regulation*™. "I would like to think that, especially the people comment, that we are really connecting scientists and regulators, and I cannot think of a better meeting than this one…that really exemplifies that goal, that objective," stated Shabushnig.

"It is really quite exciting to see this meeting grow from the first meeting in London in 2006," he said. "We see now more people, more countries, more regulatory authorities here today, and so I can only hope that this meeting continues and continues to grow in this manner. This is really an exciting opportunity and I am really happy to be here today."

Shabushnig acknowledged the EMEA officials who helped plan the meeting alongside PDA volunteers and staff.

"I want to take this opportunity to thank **Emer Cooke** and **David Cockburn** of EMEA. I can say this with all sincerity, this meeting would not be possible without their cooperation, without their support. So my thanks go out to them. I would also like to thank **Scott Lambert,** from the World Health Organization and the many EU nation participants who are here today. Again, your participation will make this a more interesting and more valuable meeting.

"I also want to extend my thanks to **Lothar Hartmann,** PhD, F. Hoffmann-La Roche, and the program committee who put together the wonderful program that we have in the next two days. I think the topics are very timely and will stimulate some very good discussion. And lastly, I would like to thank the PDA staff. They make this kind of meeting look easy, but I know how hard they work to put this together in order to make things work smoothly and well for all of us while we are here."

Finally, Shabushnig encouraged conference participants to make the most of the opportunity presented by the conference: "So please, take the opportunity to listen, to question what you hear, to discuss what is being spoken about, and finally to learn from each other. This is truly your meeting. And so we can make the most of the time that we have together in the next few days."

EMEA's Cooke, before introducing the first conference speaker, took a moment to thank the program committee chairs. "I would like to take this opportunity before I start the first plenary session to thank PDA for putting this together, and particularly the program chairs Lothar, David Cockburn and **Steve Bellis**."

She also highlighted how unique the event truly was: "It is fantastic that we have 400 people here. We have, I understand, in the region of 70 regulators and representatives from over 40 countries."

Opportunities to Connect

The ensuing two days of plenary and breakout sessions provided attendees ample opportunities to hear first-hand the thoughts of European regulators on a wide variety of topics. Most sessions ended with Q&A, allowing attendees a chance to get to the heart of issues impacting them.

In between sessions, well-presented breaks and luncheons further facilitated networking. Attendees also had the opportunity to learn about new products and services from over 14 vendors participating in the exhibits area.

Following the first day of sessions, PDA's Regulatory Affairs and Quality

Budapest painted the perfect backdrop for nighttime networking

8 hours of regulatory talk drove some attendees to dance Hungarian style at the gala dinner

Committee had a reception and was joined by a number of the regulators at the conference. Later that evening, most attendees participated in the bus tour of Budapest and gala dinner at Ladik Csarda.

The bus tour provided the perfect transition from the busy first day sessions to the festive gala dinner. The bus stopped at a city overlook that provided the perfect place to take a picture. At Ladik Csarda on the island Obuda, participants were treated to traditional Hungarian food, drink and dance. The rustic restaurant with its large eating hall reminded this author of the beer hall in the recent Hollywood adaptation of *Beowulf*—good thing Grendel didn't make an appearance! Some participants were even invited on stage for a dance.

Prior to the meeting, PDA's Training and Research Institute hosted six different lecture courses. Meeting organizers also agreed to two focused workshops to precede the meeting—one on cleaning and disinfection (see article, p. 18) and the other on revised EMEA GMP Annex 2 (see cover story).

Three Times a Charm?

In closing the four-day event, it seemed there was momentum for PDA and EMEA to host a third Joint Conference sometime in 2009.

PDA VP for Europe, **Georg Roessling,** PhD, tagged communication as the key driver for the Joint Conference. "The last two days I heard a lot from the inspectors and the industry how important communication is. I think this conference can help really to improve the communication. I am looking forward to having it next year again."

EMEA's Cooke followed Roessling to help close the meeting, and focused on the quality of the information presented. "I have to say for me, it has been a great learning experience. It has been a great opportunity to meet with a large number of industry representatives, but also a large number of regulatory representatives, some of those we don't see at the meetings in the EMEA. So really what I would like to do in these closing remarks is just to thank everybody for their participation."

Cooke offered special thanks to her regulatory colleagues for preparing excellent talks. "I particularly would like to thank the regulatory speakers for all of the work that they put into their presentations, because…think of the demands on regulators." In order to appear at a meeting like PDA/ EMEA, she said, they are "probably" working "on their own time with very little feedback."

Lastly, Cooke thanked the audience "very active participation in all the sessions" and PDA "for proposing" a second PDA/EMEA conference. "I think that we are very pleased that we've had the opportunity to participate."

Finally, PDA President **Bob Myers** closed the meeting with praise for the EMEA and other regulatory representatives, the planning committee, the quality of the program and the host city:

"What I want to do is to thank our co-sponsors, the EMEA. They have done a tremendous job over the last year putting this together. They spent a lot of time on the podium answering questions. The attendance here—400 people—speaks to the importance to our membership to have that many people here in Budapest. I want to thank the inspectorates. It has been very interesting and informative, those on the podium, especially those from the Eastern European countries who are speaking for the first time publicly. I thought that was a great addition to the program, and I think that is the result of the volunteers who put together the program as well as our staff getting them here and providing the content from all of the people that did present.

"I want to make one comment on the venue: I did not know Budapest before I came here. For those of you who didn't get a chance to take a scenic tour, it is a great city. On a tour that I was on, the guide described the city as an Eastern city in the west at times or a Western city in the east, so you get a complete blend of cultures here. It is a great spectacular city.

"Finally, I do want to comment on the dialogue. It is very important to PDA to provide this kind of forum.

"It is essential to a lot of what we do and stand for to have regulators and industry speaking to each other to try and understand what is expected. That is what I have enjoyed over the years as part of PDA—that is the dialogue between people with a joint mission—PDA, the regulators and the industry. And that mission is to keep safe and effective drugs on the market and present them to the global public and to ensure the highest quality.

Thank you all for your attendance and I look forward to seeing you all again in the near future."

Inspector Highlights Quality Management Deficiencies

Emily Hough, PDA

At the *2008 PDA/EMEA Joint Conference,* **Tor Gråberg,** Chief Pharmaceutical Inspector of the Swedish Medical Products Agency, gave a presentation entitled "Inspections Update: Major Observations."

Gråberg presented data from inspections done by his Agency from 2003 to 2006. During that time frame, the Agency's performed 136 inspections and recorded 2,809 distinct deviation observations.

Breaking down the numbers, Gråberg listed the top ten deficiency categories. Consistent with data presented by the U.S. FDA and other regulatory authorities over the years, documentation led all categories.

While it wasn't the most cited deficiency, quality management was the most serious, according to Gråberg. "If you have a lack of quality systems, the most important thing is, what signal does it send out to the company? Normally, quality systems are the responsibility of the QA department, and if there is a lack in the QA department, it sends out the message throughout the company that quality is not that important, instead of sending out the opposite message. That is why these deficiencies are so valuable to look for. It is our belief that if you consider quality risk management, Q9, the new Annex 20—the Annex 20 itself is not mandatory, but quality risk management is—so in the future you will see the deficiencies cited to Chapter 1 when it comes to lack of quality risk management. That's why it is important to have a thorough knowledge of Chapter 1 of the GMP."

The Swiss inspector was not surprised that about the number of times quality management was cited because it is a relatively new concept. He likened the current experience with quality management to that of validation when it was a new concept. For a few years following the official expectation for process validation, it became a top category in the inspection data, but began to drop as "internal knowledge" about validation grew. Gråberg said he imagined that the quality management deficiencies will follow the same path.

"I expect what we will see is more deficiencies with quality management, and you can compare that to the development of validation." In the beginning many firms were written up for not conducting process validation at all. Once process validation became ubiquitous, inspectors honed in on the content, leading to additional violations. "So you always start on the helicopter pad and go further down, depending on how well the company has understood the task—you will see the pattern. Although you have increased your workload for validation at the same time the outcome appears normally, you have increased the number of deficiencies as well. And then [the number of deficiencies] turns around again and decreases as a result of internal knowledge."

Gråberg listed a variety of specific deficiencies that fell into the broader quality management category, starting with the quality system. "So that includes dealing with deviations, change controls and rejected materials." Inspectors also cited firms for problems with "technical agreements" between contractors and customers. "In this case, the technical agreement between contract giver and contract taker did not explicitly point out who was responsible—responsibility for quality control, approval and release of starting material to production. Once again if you fail this very simple issue, it could be a disaster further down chain."

Problems defining the quality person's responsibilities also was cited. "This type of deficiency makes me wonder what is actually happening at that company because responsibly of the QP should not be something new for the industry. It should be in the back door; it should be very easy to understand and to implement the responsibility for the QP throughout the whole organization. So if you fail on this small patch, it sends us the signal that something else might also be lacking."

Training was another "quality management" issue. "The training of personnel was inadequate. No program for introduction was in place. Same for repetition of GMP had not been performed. No system was in place to incorporate personnel who were absent during the training when training took place as well as external personnel. So even if you have a good system you need to follow-up; what about those who were sick that day, how can they take part of the training that was given?"

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.

Europe

Draft Annex 13 to be Revised

Revisions to draft Annex 13, Manufacture of Investigational Medicinal Products, have been proposed. The European Commission has deemed it necessary to clarify certain points related to reference and retention samples, the two-step release procedure for investigational medicinal products and to the principle of independence between production and quality control functions.

The following changes would be made to Section 3, in order to reinforce the principal of independence between production and quality control functions in cases where the number of personnel involved is small; Sections 36 and 37, in order to supplement, for investigational medicinal products, the guidance for reference and retention samples given in Annex 19; and Section 44, which has been reworded to enhance the understanding of the two-step release procedure that applies to investigational medicinal products.

Comments should be sent to entr-gmp@ec.europa.eu and GMP@emea.europa.eu by October 31, 2008.

International Harmonization

GHTF Releases Regulatory Auditing Guideline

The Global Harmonization Task Force (GHTF) Study Group 4: Regulatory Auditing has released a final report entitled, Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufac-turer–Part 3: Regulatory Audit Reports.

The guideline provides a structure that is expected to assist auditors in preparing reports in multiple jurisdictions and promotes consistency and uniformity. The intent of this and related documents is to facilitate review and exchange of audit reports and the acceptance of audit reports by multiple regulators. This document is anticipated to ultimately reduce the number of audits for medical device manufacturers.

North America

U.S. FDA to Establish Offices in China

The U.S. FDA has received approval from the U.S. State Department to establish eight full time permanent FDA positions at U.S. diplomatic posts in the People's Republic of China—pending authorization from the Chinese government.

According to the FDA, the permanent overseas offices in China would allow greater access for inspections and greater interactions with manufacturers to help assure that products that are shipped to the United Sates meet U.S. standards for safety and manufacturing quality.

U.S. FDA to Extend Presence Beyond the U.S.

FDA Commissioner Andrew Von Eschenbach, MD, announced on March 26 at the Food and Drug Law Institute's Annual Conference FDA's plans to set-up offices with FDA personnel in India, the Middle East, Central and Latin America.

Earlier in the month, FDA announced plans to open offices in China, upon authorization of the Chinese government.

Eschenbach said that because many products are imported, FDA is striving to expand its "gatekeeper" position and is trying to "extend [its] presence…." That effort is a mission we call "Beyond Our Borders."

The "Beyond Our Borders" initiative facilitates the building of stronger cooperative relationships with FDA's counterpart agencies around the world and enhanced technical cooperation with foreign regulators.

U.S. FDA Requests Comments on Measures to Safeguard Prescription Drugs

FDA is requesting comments and information on technologies used for the identification, validation, tracking and tracing, and authentication of prescription drugs, as well as on issues related to standards for identification, validation, tracking and tracing, and authentication for prescription drugs. The requests are linked to FDA's efforts to secure the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded or expired drugs.

FDA has posed a number of specific questions that they are seeking input from on both documents.

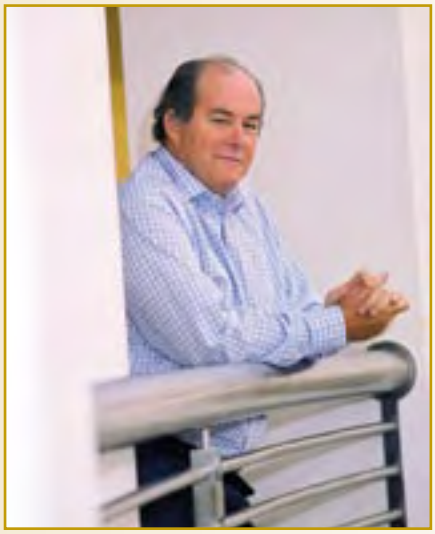
Comments and information are requested by May 19, 2008.

U.S. FDA Withdraws Direct Final Rule

FDA is withdrawing the direct final rule which would have amended certain regulations as the first phase of an incremental approach to modernize or clarify some of the cGMP regulations for finished pharmaceuticals, as well as to harmonize some of the cGMP requirements with those of other foreign regulators and other FDA regulations.

The Agency is withdrawing the direct final rule because they received significant adverse comments. FDA will consider the comments received under a companion proposal as part of their normal comments and rule-making procedures.

Volunteer Spotlight



…[In] the PDA Ireland Chapter…we have a variety of very busy people who consistently put in a great effort to get an exciting chapter off the ground…

Frank Hallinan, PhD

Company: Wyeth Biotech

Title: Senior Director, Quality

Education:
PhD, Molecular Biology, University of Southampton

Diploma in Pharmaceutical Manufacturing, Trinity College Dublin

PDA Join Date: 1990

Areas of PDA Volunteerism:
President of PDA Ireland Chapter

Interesting Fact about Yourself
I am a big Munster Rugby and Cork hurling fan.

Why did you join PDA and start to volunteer?
I really liked the way in which PDA brought together interesting speakers from industry and regulatory authorities to discuss topics of common interest. I felt there was a need to promote this in Ireland.

Of your PDA volunteer experiences, which stand out the most?
There are two; one is being President of the PDA Ireland Chapter, where we have a variety of very busy people who consistently put in a great effort to get an exciting chapter off the ground and the other, is a small PDA meeting held a few years ago in Taormina, Sicily where the location, people and wine added up to an intoxicating experience in every sense!

How has volunteering through PDA benefited you professionally?
Through learning new things at meetings.

Which member benefit do you most look forward to?
The meetings.

Which PDA event/training course is your favorite?
The PDA/FDA and now PDA/EMEA meetings.

What would you say to somebody considering PDA membership?
Go right ahead…you won't regret it.

Volunteer Spotlight

Glenn E. Wright

Company: Eli Lilly and Company

Title: Director, Quality

Education:
Masters Microbiology, Southern Illinois University

PDA Join Date: 1989

Areas of PDA Volunteerism:
Multiple Technical Committees

President of PDA Southern California Chapter

Science Advisory Board

PDA Board of Directors

Professional Awards Won:
At this point I really have no idea. But the one that means the most to me professionally is the PDA's Frederick J. Carleton Award for lifetime contributions. It really came as a complete surprise and I was very honored to receive the award.

Why did you join PDA and start to volunteer?
I have always felt strongly about PDA's mission and importance in the industry. Its all about the science and how it can be applied to everyday activities we perform. I still remember when I heard the phrase "PDA, providing scientific based answers to regulators' concerns." That one statement summed up for me PDA's importance and its value. The one thing that really drew me into PDA was its openness to new members and its willingness to give new members the chance to get involved and contribute right from the start. Over my many years of being involved in PDA, I have never seen this philosophy change.

I have always felt strongly about PDA's mission and importance in the industry. Its all about the science and how it can be applied to everyday activities we perform.

Of your PDA volunteer experiences, which stand out the most?
That's a hard question. I have really been fortunate to work with PDA in so many areas. The work to bring the PDA's Southern California Chapter into existence (with the help of many others) certainly is one that stands out from an organizational standpoint. I think we (PDA) had a significant impact in that region as a result and were able to help meet the needs of the industry professionals by providing local PDA events. From a technical standpoint, contributing on the PDA Science Advisor board, the work on the "PDA Points to Consider for Aseptic Processing" document and later the work through PDA on the Product Quality Research Institute Aseptic Processing Task Force have been some of the most memorable from a scientific contribution standpoint.

But probably the one that would stand out the most was the chance to meet and talk with new PDA members at the PDA new member breakfast sessions. It was always great to help them understand the PDA mission, see there excitement, and hear there ideas.

How has volunteering through PDA benefited you professionally?
My involvement with PDA has provided me a great deal both professionally and personally. Over the years I have had the opportunity to develop many strong professional friendships through PDA as we have worked through significant challenges facing the industry. If we truly are a sum of our experiences then PDA, and the experiences it has provided, has certainly been a significant factor for me. Personally it has given me the opportunity to make a contribution—to be involved in improving an industry that is dedicated to improving life and has the demonstrated ability to make products that are truly life changing for the patents that receive them.

Which member benefit do you most look forward to?
I always like receiving the *PDA Letter.* It is a great read.

What would you say to somebody considering PDA membership?
Get involved, PDA is a great organization with opportunities for volunteers in almost every area. It's a great way to contribute both personally and professionally to an organization that has been helping our industry develop for over 50 years.

2008 North America Event Calendar

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

Conferences

May 13–16, 2008
PDA Risk Management and Aseptic Processing Conference and Training Course
(Conference and Course)
Bethesda, Maryland

May 19–23, 2008
2008 PDA Biennial Training Conference
(Conference, Courses and Exhibition)
New Orleans, Louisiana

June 12, 2008
2008 PDA Technical Reports: A Fresh Look
San Francisco, California

June 26–27, 2008
Seminar on PDA Technical Report No. 1, Revised 2007, Validation of Moist Heat Sterilization Processes: Cycle Design, Development, Qualification and Ongoing Control
Montreal, Canada

September 8–12, 2008
2008 PDA/FDA Joint Regulatory Conference
(Conference, Courses and Exhibition)
Washington, D.C.

October 6–7, 2008
The Universe of Pre-filled Syringes & Injection Devices
(Conference and Exhibition)
San Diego, California

October 20–23, 2008
PDA's 3rd Annual Global Conference on Pharmaceutical Microbiology
(Conference, Courses and Exhibition)
Chicago, Illinois

November 10–11, 3008
Clinical Trials
Boston, Massachusetts

Training

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

Lab Courses

May 19–21, 2008
Cleaning Validation

June 4–6, 2008
Developing a Moist Heat Sterilization Program within FDA Requirements

June 9–13, 2008
Pharmaceutical and Biopharmaceutical Microbiology 101

August 4–8, 2008
Rapid Microbiological Methods

September 24–26, 2008
Advanced Mycology Identification Workshop

October 2–3, 2008
Developing and Validating a Cleaning and Disinfection Program for Controlled Environments

Lecture Courses

May 13–14, 2008
Elements of Risk Management

June 11–13, 2008
Environmental Monitoring Database and Trending Technologies

August 14–15, 2008
Computer Product Supplier Auditing Process Model: Auditor Training

September 24–26, 2008
Environmental Monitoring Database and Trending Technologies

Course Series

June 2–4, 2008
Raleigh Training Course Series
Raleigh, North Carolina

October 21–23, 2008
New Brunswick Training Course Series
New Brunswick, New Jersey

Web Seminars

June 5, 2008
Steam Sterilization Validation to Meet European Requirements

May 22, 2008
Responding to FDA-483's

Chapters

May 14, 2008
Metro Chapter
Role of Internal Auditing in GMP Management

May 16, 2008
New England Chapter
TR13 Fundaments of Environmental Monitoring/Facility Tour

May 22, 2008
Puerto Rico Chapter
Particles in Solution: A Visual Inspection Challenge

June 11, 2008
New England Chapter
Business and Organizing Committee Meeting

June 12, 2008
West Coast Chapter
Dinner Meeting

June 13, 2008
Southeast Chapter
Eighth Annual PDA Southeast Chapter Golf Social

June 22, 2008
West Coast Chapter
2008 PDA Technical Reports: A Fresh Look

June 26, 2008
Canada Chapter
Technical Report No. 1, 2007 Revision

June 13, 2008
Southeast Chapter
Eighth Annual PDA Southeast Chapter Golf Social

August 13, 2008
New England
Business and Organizing Committee Meeting

September 17, 2008
New England
Facility tour and Glass Defects Meeting

October 8, 2008
New England
Business and Organizing Committee Meeting

November 12, 2008
New England
Facility tour and Cleaning Validation

December 10, 2008
New England
Business and Organizing Committee Meeting

Europe/Asia-Pacific Event Calendar

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

Europe

May 14, 2008
Israel Chapter
Pharmaceutical Water Systems

June 3–5, 2008
2008 PDA Virus and TSE Safety Forum
In cooperation with FDA, European Health Authorities and Paul-Ehrlich-Institut
(Conference and Exhibition)
Berlin, Germany

June 12, 2008
United Kingdom Chapter
Board Meeting

June 24–25, 2008
2008 PDA/EBE Biopharmaceutical Development and Manufacturing Meeting Global Challenges in Europe
Dublin, Ireland
(Conference, Exhibition, Workshop and Courses)
Training Courses: June 26–27, 2008

September 23–24, 2008
2008 Pharmaceutical Freeze Drying Technology
(Conference and Exhibition)
Brussels/Wavre, Belgium
Training Course: September 25, 2008

October 7–8, 2008
2008 PDA Conference on Quality by Design: Practical Applications in Development and Manufacturing of Pharmaceuticals
(Conference and Exhibition)
Frankfurt, Germany
Training Course: October 9–10, 2008

October 14–15, 2008
2008 PDA Visual Inspection Forum
(Conference and Exhibition)
Berlin, Germany
Training Courses: October 16–17, 2008

November 4–5, 2008
Pharmaceutical Cold Chain Management
(Conference and Exhibition)
Berlin, Germany
Training Courses: November 6–7, 2008

November 13, 2008
PDA/ISPE Workshop with PIC/S
Geneva, Switzerland

November 19, 2008
Sterilization Technologies in Development and Manufacturing of Parenterals
Milan, Italy

December 8–12, 2008
Practical Aspects of Aseptic Processing
Basel, Switzerland

Asia-Pacific

November 11–12, 2008
Japan Chapter
PDA Japan Annual Meeting

Chapters

November 11–12, 2008
Japan Chapter
PDA Japan Chapter Annual Meeting

Please Welcome the Following Industry

Suzanne Adamczak, Genzyme

Kristian Agnew, Amgen

Sarah Aherne, Saic-Frederick

Mihaela Akl, Bayer Healthcare

Fred Albertini, GlaxoSmithKline

Idiculla Alexander, Middlesex Community College

John Alfano, Astellas Pharma Mfg.

Hassan Almoazen, University of Tennesse

Amy Anderson, King Pharmaceuticals

Melissa Baca, Amgen

Julie Baker, Genmab

Victor Balala, Middlesex Community College

Deborah Baly, Genentech

Ernie Bancroft, Korber Medipak

Vincenzo Bassi, Bristol-Myers Squibb

Tracie Beaver, Emergent BioSolutions

Ashley Bell, Middlesex Community College

Michele Bellay, Morphotek

Paul Belliveau, Middlesex Community College

Soline Berend, LFB

Paal Berg, Alpharma AS

Trupti Bhagat, Middlesex Community College

Palak Bhatt, Middlesex Community College

Alexander Bijman, Nobilon

Lorenzo Bindi, Novartis Vaccines and Diagnostics Srl

Mariluci Bladon, Middlesex Community College

Katie Bloom, Immunogen

Ross Blum, Sensitech

Ildiko Bodor, AstraZeneca

Jesus Bolivar, Eli Lilly

Ryan Bourque, Middlesex Community College

Michael Boychyn, Amgen

Ruth Brady

Joan Brandt, Joan Brandt Enterprises

Monica Briggs, Bausch & Lomb

Celeste Brooks, GE Healthcare

Ulrica Brunsberg, Medical Products Agency

Jennifer Bukowinski, Bayer

Tyson Burrows, Glaxosmithkline Biologicals

Ann Carraher, ECC

Chris Castro, Amgen

Zahira Cepero, Nephron Pharmaceuticals

Jimmy Chanthamasinh, Middlesex Community College

Emmanuelle Charton, EDQM

Samphas Chuun, Middlesex Community College

Liliana Clemente, Global Biologics Supply Chain

Eric Clifford, Hollister-Stier Labortories

Catherine Collins, Alexion Pharmacuetical

Rebecca Connors, Baxter Pharmaceutical Solutions

Michael Cooper, Boehringer-Ingelheim Vetmedica

Deborah Corcoran, Middlesex Community College

Robert Cormier, Middlesex Community College

Yvonne Cotti, Wyeth

Leslie Cox, Bausch & Lomb

Thelma Crommnell-Moss, Middlesex Community College

Gretchen Crossen, Amgen

Julie Czanstkowski, PDL BioPharma

Edward Daniel, Validation Technologies

Chalnicia Darby-Snyder, Wellstat Biologics Corporation

Carrie Dasconio, Lyophilization Technology

Pankaj Dave, Navinta

Alan Davis, Global Transportation

Christian De Muynck, Nycomed

Abhaya Deb, Middlesex Community College

Benito Delgado, SAFC Biosciences

Christopher Derby, Gilead Sciences

Manisha Deshmukh, BioMarin Pharmaceutical

John Duguid, Genzyme

Amy Durocher Matthews, Eli Lilly

David Eakins, CSL Bioplasma

Michelle Eldridge, Genzyme

Miriam Estrano, Tigenix

Mauro Faccio, EZEM Canada

Brenda Fairweather, Genzyme

Brooks Fardy, BE&K

Milan Fillmore, Korber Medipak

William Fisher, GlaxoSmithKline

Gary Floyd, YM BioSciences

Terrish Floyd, Bayer Healthcare

Emily Ford, HHS/ASPR

Amy Ford Davison, GlobeImmune

Bruce Forman, Advanced Electron Beams

Heidi Fronheiser, Sanofi Pasteur

Steven Galavotti, Talecris Biotherapeutics

Stephen Gantt, AAIPharma

Pamela Garcia, Cell Genesys

Sandip Garg, Glenmark Pharmaceuticals

Joel Gates, Talecris

Lisa Gebbia, Wyeth

Diana Gee, Bayer

Denisa Gilaj, Genzyme

Miguel Gonzalez, Baxter Bioscience

Robert Graves Graves, Carbon

Eric Gruff, E4 Pharmaceutical Consulting

Raphael Guidos, Genentech

Dipti Gulati, Biomerieux

Joseph Guthrie, Middlesex Community College

Amanda Hallowell, Middlesex Community College

Leaders to the PDA Community

Jessica Hays, Bayer Healthcare

Christian Helbig, Schott

Shelia Hinnant, Microbac Laboratories

James Hogan, Gen-Probe

Stephen Holcroft, Johnson & Johnson

Keith Holland, Schering-Plough

Michelle Hora-Welch, Middlesex Community College

Elmer Huey-Nazareno, Amgen

Shane Humphreys, Bayer Healthcare

Yoshiaki Igarashi, Yakult Honsha

Emily Illo, Bayer Healthcare

Monina Inumerable, Baxter Bioscience

Priya Jagasia, Nuvelo

Deborah Jamieson, AstraZeneca

Sohail Jarrahian, CMC Icos Biologics

Jason Ji, Astrazeneca

Zhi Qiang (John) Jiang, APP Pharmaceuticals

Ashish Jobanputra, Alembic

Brian Johnson, Bristol-Myers Squibb

Sylvie Jorajuria, Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSA)

Rishi Kapur, Archimedes Pharma

Anupama Karwa, Nellix

Iftah Katz, Protalix Biotherapeutics

Beth Keij, Cell Genesys

Tom Keohane, The Tech Group

Mher Ketchedjian, Middlesex Community College

Samira Khalifa, Middlesex Community College

Ash Khorzad, Baxter Healthcare

Catherine Killion, TissueReg Services

Chung Ryeol Kim, LG Life Science

Yong Bin Kim, Boryung Pharm

James Kirnon, Middlesex Community College

Jessie Klein, Middlesex Community College

Kazuhiko Konno, Towa Pharmaceutical

Emily Krawczyk, JHP Pharmaceutic

Lynne Krummen, Genentech

Ellen Lacebal, Bayer Healthcare

Timothy Largen, Molecular Insight Pharmaceuticals

Stacy Lewis, Glaxosmithkline Biologicals

Marva Loblack, DJA Global Pharma

Nathanael Lowe, Genentech

Edgar Luciano, Amgen

Susan Lukie, Schering-Plough

Jon Lundquist, The Tech Group

David Maes, Vical

Sai Mann, Sanofi Aventis

Hadar Marcus, Israel Institute for Biological Research

Jill Mariano, Bionique Testing Laboratories

Marla Tammy McGonigle, Alcon Labs

Steven McLaaughlin, Middlesex Community College

Edgar Mejia, Middlesex Community College

Lawrence Mignot, Merial

Michelle Miller, Baxter Healthcare

Christopher Miller, Bayer

Patrick Milliken, Auxilium Pharmaceuticals

Kurosaki Misawo, Teika Pharmaceutical

Hoang Mitchell, Baxter Healthcare

Leandra Mollanazar, Catalent Pharma Solutions

Arlene Monnar, Agensys

Malcolm Montgomery, Microbac Laboratories

Allyimn Mood, Middlesex Community College

Kevin Moore, United States Pharmacopoeia

John Morelli, Shire

Dianne Moustafa, Middlesex Community College

Amol Mungikar, Bristol-Myers Squibb

Justin Nadeau, Cell Genesys

Vijay Naringrekar, Bristol-Myers Squibb

Berry Narron, Talecris Biotherapy Critics

Masao Nasu, Osaka University

Janet Neeley, Allos Therapeutics

Oanh Nguyen, Middlesex Community College

Patel Nisha, Middlesex Community College

Kevin Norgeot, Sanford Rose Associates

Ulrich Nuetz, IDT Biologika

Nnamdi Nwachuku, Middlesex Community College

Paul O' Sullivan, Shire

Jose Ochoa Faure, The ZDM Group

Robin Ochs, Sandoz

Junichi Okada, Daiichi Sankyo Pharma Development

Deji Oloruntoba, AERAS Global TB Vaccine Foundation

James Oterreau, Bayer Healthcare

Annie Ouellet, EZEM Canada

Micheal Paden, Xoma

Lackhena Pak, Middlesex Community College

Christine Palus, Althea Technologies

Prerna Patel, Middlesex Community College

Komal Patel, Middlesex Community College

Nash Patel, Gilead Sciences

Dipti Patel, Middlesex Community College

Paul Patev, Middlesex Community College

Kevin Pelin, Indevus Pharmaceuticals

Juan Perez, Middlesex Community College

Bonnie Petersen, Middlesex Community College

We welcome more of this month's new PDA members on the next page ➤

Please Welcome the Following Industry Leaders to the PDA Community

continued from previous page

Ralt Pfirmann, IDT Biologika

Bo Pham, Shire

Keady Phelan, Genentech

Matthew Piasecki, Middlesex Community College

William Pietz, Bnbkennel

Isabelle Pilon, Bioniche

Wyatt Ping, PDLBioPharma

Irene Quenville, Bausch & Lomb

Kristen Quevedo, Global Quality Alliance

Stacy Rager, Aderans Research Institute

Jorge Rayo, Middlesex Community College

Abbas Raza, Astellas Pharme

Jillian Regier, GBSC

Isabel Rivero, Alcon

Becky Rivoire, Colorado State University

Loretta Roach, Millenium Pharmaceutical

Robin Rondeau, Middlesex Community College

Thomas Rosahac, Sanofi Pasteur

Alix Rucinski, Baxter Healthcare

Cammie Sagerdahl, Biomarin

Yoshikazu Sakagami, Kinki University

Richard Sanchez, GCA Services

Mary Sanders, Colorado State University

Richard Sands, RTS Training Services

Rebecca Santorios, CEL-SCI Corporation

Nathan Schaus, GOJO Industries

Eli Schmell, Bio-Technology General

Sandra Schroeder, F. Hoffmann-La Roche

Laura Segalen, Merial

Robert Shaw, Ark Therapeutics Oy

Ayaz Sheikh, Middlesex Community College

Greg Shoffner, Amgen

Roman Shumylo, LifeCell

Michael Shutty, Lonza Walkersville

Kristine Siemer, Bioserv Corporation

Danielle Simard, Wyeth

Shirley Simmons, WuXi AppTec

Christina Siniscalchi, Covidien

Beth Slater, Salix Pharmaceuticals

Kimberly Smith, Middlesex Community College

Bill Smutny, SeraCare Llfe Sciences

Ursula Snow, GE Healthcare

Dustin Sorel, Shire

Ulrike Sorger-Herrmann, Bayer Healthcare

Patrick Spain, Genzyme

Daniel Spangler, Microbial Contamination Solutions

Frances Stack, Amgen

Denise Stevens, LifeCell

David Stinehelfer, PDL BioPharma

Jorge Sugranes, Alcon Manufacturing

Christopher Sullivan, Sartorius Stedim Biotech

David Surace Kapitula, Cell Genesys

Ganesh Swaminath, HCL Technologies

Jeff Swehla, Emergent Bio Solutions

Kenichi Takashima, ParticleMeasuringSystems

Shannon Thomas, Genentech

Abhinaya Thummala, Amgen

Robert Tomaselli, Johnson & Johnson

Vikki Tomasko, Schering-Plough

Minh-Luan Tran, Draxis Pharma

Dang Troung, Middlesex Community College

Blair Tyson, Eisai

Julie Upole, GOJO Industries

Sabien Van der Schoot, Solvay Pharmaceuticals

Alan Varlack, Pall Life Sciences

Romain Veillon, GlaxoSmithKline

Tata Venkata, Hospira

Ramarao Vepachedu, National Jewish Medical and Research Center

Mark Walker, GeneEd

James Waterbury, Genentech

Roger Webb, Wyeth

Beth Wescott, Wyeth

Cheryl White, Baxter International

Mark Whithaus, University of Missouri Research Reactor Center

Byron Wingerd, Bioport Corporation

Robert Wittorf, Eli Lilly

Franklin Wood, Talecris

Joseph Wrafter, Pfizer Ireland Pharmaceuticals

Mukesh Yadav, MassBiologics

Ava Yap, Allergan

Michael Young, Cubist Pharmaceuticals

Sau-Gee Yung, Stryker Biotech

Dimitri Zacharenko, UPS

P. Zamora, BioMarin Pharmaceutical

Nick Zecherle, BioMarin Pharmaceutical

Adam Zerda, BD

Yi Zhang, Farmaprojects

Xianzhi Zhou, Pfizer

Ronald Ziance, University of Southern Nevada

Ilana Zigelman, Zigelman Consulting

Catherine Zune, GlaxoSmithKline

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

Chapter Contacts

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

Asia-Pacific

Australia
Contact: Robert Caunce
Email: robert.caunce@hospira.com
www.pdachapters.org/australia

India
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Email: dmakhey@hotmail.com

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Korea
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Southeast Asia
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Taiwan
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Capital Area
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Delaware Valley
Areas Served: DE, NJ, PA
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Email: artjr@sterile.com
www.pdadv.org

Metro
Areas Served: NJ, NY
Contact: Nate Manco
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www.pdachapters.org/metro

Midwest
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Contact: Peter Noverini
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www.pdachapters.org/midwest

Mountain States
Areas Served: CO, WY, UT, ID, NE, KS, OK, MT
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New England
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www.pdachapters.org/newengland

Puerto Rico
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Email: manuelm@amgen.com
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Southeast
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Email: patrick.sabourin@novartis.com
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Southern California
Areas Served: Southern California
Contact: Saeed Tafreshi
Email:
saeedtafreshi@inteliteccorporation.com
www.pdachapters.org/southerncalifornia

West Coast
Areas Served: Northern California
Contact: John Ferreira
Email: jferreira@banzigersystems.com
www.pdachapters.org/westcoast

2008 PDA/EMEA Joint Conference: New Member Breakfast

Astrid Guenther, PDA

For the first time, PDA hosted a New Member Breakfast in Europe to support new PDA members in their orientation with the Association. The event was held at the PDA/EMEA Joint Conference and was a great success.

Thanks to the enthusiasm of the PDA Board Members and staff who were involved, the breakfast was a hit. PDA Chair **John Shabushnig,** PhD; PDA Europe VP **Georg Roessling**, PhD; and long time PDA volunteer **Susan Schniepp** gave insightful presentations on their membership experiences and informed members how to utilize PDA's *career-long learning*™ opportunities.

Because of the positive feedback and support received from the attending new members, PDA will continue to host the New Member Breakfast at future PDA/EMEA Joint Regulatory Conferences.

If you are a new PDA member and were unable to attend the breakfast, you can view the PDA membership orientation presentation online at www.pda.org/membership. The next PDA New Member Breakfast will be hosted at the *2008 PDA/ FDA Joint Regulatory Conference* in September. If you would like more information please visit www.pda.org/ annual2008 or contact the Member-ship Department at info@pda.org.

We would like to thank all the new PDA members who attended the breakfast; the experience was successful and memorable to all. We look forward to making the next New Member Breakfast just as spectacular!

Three EMEA Speakers Confirmed: QBD for Tangible Benefits Conference

Frankfurt, Germany • October 7–8

Mohammed Barkat, Draxis and Volker Eck, PhD, PDA

Quality by Design (QbD) is becoming a very often used, but not so well understood term. Therefore, after its very successful Workshop in 2007, PDA is organizing a conference on this topic to be held in Frankfurt, Germany, October 7–8. The conference will strive to demonstrate the tangible benefits of QbD, if applied correctly, with presentations illustrating practical examples of such applications. The committee has titled the conference *Quality by Design for Tangible Benefits: Charting the Path from Pharmaceutical Development to Regulatory Flexibility.*

The programming committee is extremely pleased to announce the confirmation of three speakers representing the EMEA, who will provide updates on the uptake of QbD in Europe. They are:

- **Mats L. Welin,** Senior Expert, Quality Assessment, MPA, Sweden
- **Jacques Morenas,** Assistant Director (Inspectorate and Companies Department), AFSSAPS, France; Chair of PIC/S
- **Kowid Ho,** Pharmaceutical Assessor, Evaluation of Biological Products Department, AFSSAPS, France

If looked at more closely, QbD can be defined as a project to establish a solid knowledge of the product and the process leading to it. Therefore, the conference will highlight the critical steps that lead to this knowledge and define desired quality. Inherent in QbD are:

- Risk assessment and risk evaluation
- Determination of critical parameters
- Statistical analysis
- Definition of design space
- Control strategy

Identification of the "design space" should be the goal of the QbD project. The design space can be understood as a multidimensional space encompassing combinations of product design and processing variables that provide assurance of suitable product performance. It is necessarily coupled to a control strategy to ensure the process will render the desired quality. The conference will demonstrate that this concept is not only applicable to the many well-publicized oral solid cases, but also to parenterals and other dosage forms.

We hope you will join us in Frankfurt!

[Editor's Note: In the next issue of the *PDA Letter,* the committee will discuss the positive impact of QbD on a freeze-drying processe.**]**

Achieving a Future Vision with the *2008 PDA/FDA Joint Regulatory Conference*

Washington, D.C. • September 8–12 • www.pda.org/pdafda2008

Susan Schniepp, Schniepp and Associates

By announcing the GMP's for the 21st Century initiative in 2002, the U.S. FDA gave the bio/pharmaceutical industry its first glimpse of the future of regulatory oversight for pharmaceutical production. The intent of the original initiative was to offer the industry the necessary tools to provide more post-approval flexibility, making continual improvement less of a regulatory burden, and to promote better self-regulation to improve their regulatory compliance status.

In the five years that have passed since the announcement, regulatory health authorities and industry have partnered by harmonizing requirements and implementing new systems for assuring and maintaining pharmaceutical quality. The *2008 PDA/FDA Joint Regulatory Conference* will provide examples of how these new approaches have been successfully implemented. In addition, the conference will examine what is working well and where the industry and regulatory health authorities still need to work to achieve modernized quality systems.

In order for today's pharmaceutical companies to operate in a global environment, they must understand the various regulations and standards that are utilized throughout the world.

Harmonization of these regulations and standards would reduce the regulatory burden and allow for consistency in company filings and applications.

The conference will devote a significant portion of the program to the issue of global harmonization for standards, regulations and supply chain qualification. The opening plenary session will kick off the conference by featuring speakers who will discuss harmonization from the pharmacopoeia, importation and product safety perspectives.

Concurrent sessions will offer more in-depth insight into harmonization by discussing consensus standards, International Conference on Harimonisation quality system implementation, and harmonization of GMP inspections, including the PIC/S initiative.

Day two of the conference will start off with a discussion of how to transition from a standard operating procedure driven approach to a comprehensive quality system using the principles defined by the ICH Q8, Q9 and Q10 documents. This concept will also be discussed in concurrent break out sessions with respect to product development and legacy products.

In addition to harmonization and quality systems, this year's conference will also focus on the product life cycle (i.e., supply chain, product development) as well as global emerging issues such as importation safety.

Mark your calendar to attend the *2008 PDA/FDA Joint Regulatory Conference* held September 8–12 in Washington, D.C.

Pre-filled Syringes and Injection Devices Conference Celebrates Five Years of Success

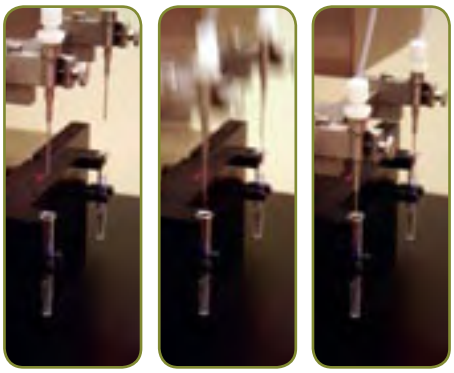
San Diego, Calif. • October 6–7 • www.pda.org/prefilled2008

Committee Co-Chairs Shawn Kinney, PhD, Hyaluron Contract Manufacturing and Thomas Schoenknecht, PhD, Amgen

The PDA *Universe of Pre-filled Syringes and Injection Devices* conference is coming back to the United States and will celebrate its fifth year anniversary with a two-day conference and exhibition in San Diego, Calif. This conference is the largest international technical forum focusing on pre-filled syringes and injection devices.

A growing interest in pre-filled syringes is evidenced by the attendance at this conference series, which has grown from 70 participants in Hannover, Germany in 2004, to more than 450 participants in Bethesda in 2006, and followed by an increase again at last year's conference in Berlin, Germany—which was for the first time combined with special syringe related workshops after the conference.

A larger attendance is expected this year with representatives from user organizations, suppliers of equipment and syringes and regulatory authorities in attendance. *The Universe of Pre-filled Syringes and Injection Devices* forum has established itself as the premier industry conference covering the needs of pharmaceutical industry working with pre-filled syringes and injection devices.



To answer the growing interest in the use of pre-filled syringes, aid in understanding regulatory requirements and to highlight new developments and directions in this exciting area, a dual track program will be offered allowing the attendees the opportunity to attend a broader variety of actual presentations. We are excited to have a focus on new developments and actual case studies from companies involved in new approvals and late phase clinical studies with pre-filled syringes and injection devices.

This event presents an outstanding opportunity to meet colleagues and network with professionals involved in all aspects of pre-filled syringes and injection devices. The conference promises to assemble the largest group of experts and users of pre-filled syringes and injection devices.

On behalf of the program planning committee and PDA, we invite you to join us to be part of this unique event, October 6–7 at the Manchester Grand Hyatt San Diego Hotel.

We look forward to seeing you there.

Current Best Practices Provided at Upcoming Meeting: *2008 PDA Technical Reports – A Fresh Look*

San Francisco, Calif. • June 12 • www.pda.org/techreports

Program Chair Jean Bender, Genentech

PDA is embarking on many new programs to bring you the latest information on key issues and topics relevant to the pharmaceutical and biotechnology industries. Not only has PDA expanded training facilities and programs at the Bethesda headquarters, but it is working with local PDA chapters to bring new conferences and programs to your neighborhood!

We are pleased to announce an exciting new conference, *2008 PDA Technical Reports – A Fresh Look*, to be held June 12 in the San Francisco Bay Area. PDA global headquarters and the West Coast Chapter invite you to learn more about the progress made in revising multiple technical reports which have served as invaluable industry guides for many years.

Presentations will be made by members of task forces working on the following PDA technical reports:

- TR- 45, *Filtration of Liquids Using Cellulose-Based Depth Filters*
- TR-26, *Sterilizing Filtration of Liquids* (revision)
- TR-14, *Industry Perspective on the Validation of Column-Based Separation Processes for the Purification of Proteins* (revision)
- TR-15, *Industrial Perspective on Validation of Tangential Flow Filtration Systems in Biopharmaceutical Applications* (revision)
- TR-41, *Virus Filtration* (revision)

Presenters will provide an overview of each technical report and, in the case of revisions, discuss current best practices, technological advances and changes in regulatory and validations strategies necessitating the updates.

Attendees also will hear from one of a group of PDA members who met with an EMEA Expert Working Group in September 2007 to explain PDA's responses to the EMEA *Draft Guideline on Virus Safety Evaluation of Biotechnological Investigational Medicinal Products*. In addition, a member of the PDA Mycoplasma Contamination and Control Task Force will discuss issues facing the industry related to current and alternative detection methods, media contamination, filtrative removal and other emerging issues. And last but not least, attendees will be able to participate in an interactive discussion on bioburden monitoring in APIs.

The Technical Report update event will take place in conjunction with the PDA West Coast Chapter dinner meeting on June 12. **Hal Baseman,** ValSource, will discuss Technical Report No. 44 at the dinner meeting.

On behalf of the Program Planning Committee, I invite you to join your colleagues and chapter members at the *2008 PDA Technical Report – A Fresh Look* meeting in San Francisco, Calif. in June.

PDA technical reports deliver our membership the definitive consensus report on best practices in the industry.

The latest release, TR-44, *Quality Risk Management for Aseptic Processes,* is only the first of the year—several more are scheduled for 2008.

2008 PDA Technical Reports – A Fresh Look is a great opportunity for discussion of today's key issues featured in PDA Technical Reports.

Make a Safe Bet in Vegas: Attend the 2009 Annual Meeting!

Las Vegas, Nev. • April 20–24, 2009 • www.pda.org/annual2009

Program Chair Ian Elvins, Lonza Biologics

The *PDA 2009 Annual Meeting* will focus on a subject that none of us can ignore—the role that computers and automation play in the modern pharmaceutical industry. Few can disagree that the microchip has placed enormous power at our disposal. A power that has been (and will continue to be) a tremendous force for good within our industry. The microchip has arguably been one of the greatest factors of modern times in moving our industry towards the goal of ever safer, more reliable and more effective products.

Even a few moments reflection reveal the countless ways in which the industry has been transformed by "the chip." Analytical technology has achieved levels of speed, precision and sophistication undreamed of just two decades ago, and entire production plants can be run automatically by complex computer control systems. But it is not just the development of advanced technology that has achieved such progress. Individuals and small groups working within the industry itself have devised countless new ways to monitor, control, problem-solve, analyze, and generally do things quicker, smarter and better.

By popular demand we are returning to the Red Rock Resort and Casino—site of the successful 2007 meeting

The *PDA 2009 Annual Meeting* will provide a unique opportunity to learn, not only about the capability of the latest technology. The meeting will present attendees with an opportunity to share ideas about the myriad of ways in which computers and automated systems can be used to resolve problems and improve reliability in the many tasks that make up all stages of the modern drug process.

It is ironic that in a world increasingly dominated by electronic communication and data management, there is not a better arena for stimulating new ideas than the face-to-face discussion with peers and like-minded professionals that results at conferences like the PDA Annual Meeting.

Above all the 2009 event will be about the future of our industry, and in particular how we can devise and use even more powerful tools in ever more imaginative ways to better serve the needs of the patient. So on behalf of the Program Planning Committee, I cordially invite you to join us at the *PDA 2009 Annual Meeting*.

Faces and Places: PDA/EMEA Conference Sessions

Both plenary and breakout sessions covered a variety of topics, attracting large numbers of attendees

Tim Marten and Jacque Morenas, program committee members

(l-r back row) Bob Myers, PDA; John Shabushnig, Pfizer; Lothar Hartmann, F. Hoffmann-La Roche; Georg Roessling, PDA
(l-r front row) Emer Cooke, EMEA; Sabine Atzor, European Commission; Michael Doherty, F.Hoffmann-La Roche; Katrin Nodop, EMEA; Eija Pelkonen, National Agency for Medicines

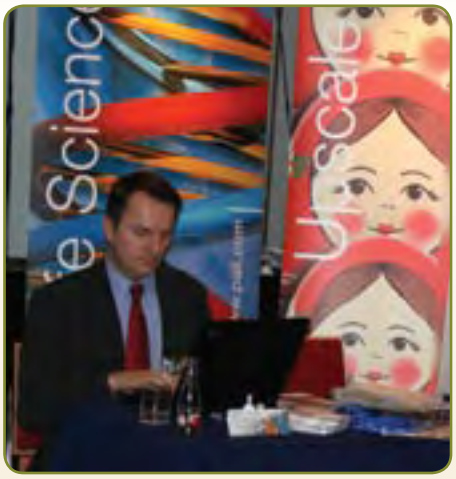
The registration desk kept attendees happily moving along

The Closers (l-r): Tim Marten, Emer Cooke, Paul Hargreaves, Tor Gråberg, Jacques Morenas, Christian Siebert, David Cockburn, Chris Oldenhof

Faces and Places: PDA/EMEA Conference Exhibits

Sarah Graham, Allergan, won a digital camera in the PDA raffle and stands with Astrid Guenther, PDA.

Faces and Places: PDA/EMEA Conference Exhibits



Faces and Places: PDA/EMEA Conference Dining and Social

Faces and Places: PDA/EMEA Conference Dining and Social

Faces and Places: Cold Chain Conference

(l-r) Kevin Linde, cGMP Consulting; Diane McLean, Pfizer; David Ulrich, Abbott

David Ulrich, Abbott, drove home a solid presentation on quality systems for the pharmaceutical supply chain

(l-r) Debbie Smith, Eli Lilly; Ed Smith, Packaging Science Resources; Gary Hutchinson, Amgen

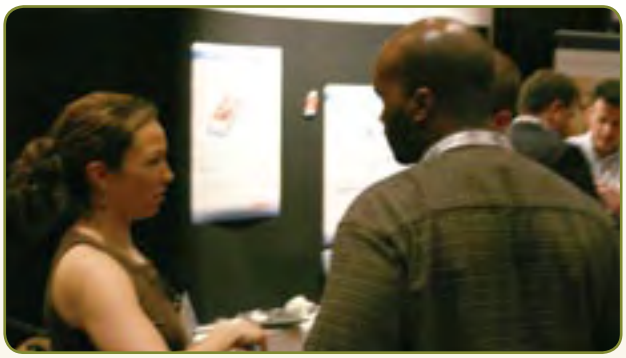
Committee members and attendees engaged in hot cold chain topics

Bob Dana, PDA; Rafik Bishara, PDA

(l-r) Jeff Seeley, Merck; Ben Romero, Bristol-Myers Squibb; Jeff Wells, Franwell

Cindy Tabb, PDA and Tony Choudhury, Bax Global, tested a new method of cold chain transportation—ultimately concluding it is not up to current standards.

Jeff Simpson, Cold Chain Technologies;
William Pelletier, University of Florida



TRI Treks Globe to Teach Industry

In the first four months of the year, TRI has offered courses in a number of spots convenient to the PDA membership.

It all started in February when TRI and its faculty traveled to the PDA/EMEA conference in Budapest to offer six courses to our members attending that event. In the spirit of the regulatory conference, these courses addressed various topics of interest to regulatory affairs personnel. The topics covered were: drug product registration in Europe, ICH Q10, GMP inspections, quality systems for investigational drugs, risk management, and product registration meetings with EMEA.

In March, TRI sponsored six courses in San Francisco with a mix of topics addressing regulatory concerns and scientific topics, all relevant to biotech manufacture. The various courses included "What Every Biotech Start-Up Needs to Know about CMC Compliance," "Process Validation for Biopharmaceuticals," and "CGMP Manufacturing of Human Cell Based Therapeutic Products."

With little rest, TRI next traveled to Colorado Springs in April to offer eleven courses which followed the conclusion of the *2008 PDA Annual Meeting*. Topics addressed a variety of regulatory issues relevant to various PDA core competencies like aseptic processing, microbiology, parenteral delivery systems, filtration and biotechnology.

PDA would like to thank all of the faculty who traveled to these locations to lead these courses and also local PDA Chapters for helping in some cases.

Coming up, TRI plans to visit the following locations New Orleans (in conjunction with the 2008 Biennial Training Conference); Raleigh, N.C.; Frankfurt, Germany; and then Berlin. Of course, the Institute always offers lectures and lab courses at its facility in Bethesda, Md.

We hope to see you at one.

On the Horizon: Investigational Medicinal Products in Europe

Bronwyn Phillips, MHRA

At PDA's January *Investigational Medicinal Products–Negotiating the GMP/GLP/GCP Interface* conference in Paris, **Hans Smallenbroek,** IZG, The Netherlands, provided a preview of the latest developments in the regulatory scheme for IMP production and use in Europe. He covered 11 specific areas:

1. **Qualified Person Responsibilities: Annex 13, Paragraph 42**
   The text of a series of Q&A's has been agreed. These will be added to the EMEA website when its update has been completed.

2. **Local Packaging Sites**
   A modification has been made to the clinical trial application form to clarify that all packaging at authorized manufacturing sites should be included but not sites where local packaging under exemption from a manufacturing authorization takes place. Reference should however be made if this activity is to occur.

3. **Definition of "Certification by a QP"**
   There are some inconsistencies in the GMP guide regarding the words used to describe certification by a Qualified Person (QP). The new definition proposed by the group will ultimately appear in Annex 16 when that is opened for revision (not scheduled at present). The definition will remove the term "QP release" and clarify that it is the QP's duty to certify the batch, while it is the sponsor who is responsible for the actual act of release to the clinical trial site.

4. **Content of the Batch Release Certificate**
   In the same vein as topic 3 above, the certificate will be referred to as a batch certificate, eliminating the word "release."

   The wording will be changed to be specific for IMPs rather than the same as for marketed products. It was agreed, following feedback from the consultation, that it was not appropriate to use a single document for the purposes of both MRA batch certificate and the certificate referred to in Art. 13.3 of Directive 2001/20/EC.

   The author explained that the purpose of the certificate is to facilitate the transfer of IMPs from one member state to another and is not intended for importation. The final document will be considerably simpler than that put out for consultation

   The ICH GCP Guidance refers to a need for a Certificate of Analysis for IMPs. A footnote has been added to the recommendations for the content of the trial master file and archiving published in Volume 10 of Eudralex to indicate that the QP Batch Certificate will meet this requirement.

   [Editor's Note: PDA submitted comments on this proposed statement of content in 2007. To view the PDA comments go to www.pda.org/regulatorycomments.**]**

5. **Two Tier Release Procedure: Annex 13, Paragraph 13.44**
   The wording has been revised to more clearly separate the role of the sponsor and that of the Qualified person (refer to no. 3). The change will only be made when Annex 13 is opened for revision.

6. **QP Responsibilities for Intermediate Manufacture Prior to Clinical Trial Application (CTA) Submission/Approval**
   This topic will appear as Q&A's on the EMEA website following acceptance by the GMP and GCP Inspectors working groups. A technical agreement should be in place between QPs and between QPs and Sponsors, where a batch is manufactured prior to approval of the CTA. The agreement will need to assign responsibilities for compliance and for notification of changes made during the approval process.

7. **Guidance on Transport and Storage Conditions at the Investigator's Sites and related documentation**
   This is a GCP led topic that was helped by input from GMP inspectors regarding current industry practice at pharma manufacturers. The text of the Q&A's was agreed by the subgroup and will now go to the Inspectors' Working Groups for GMP and GCP for their approval. The final approved text will eventually appear on the EMEA website.

8. **Reference and Retained Samples for IMPs**
   The group is close to agreeing on wording to modify Annex 13 regarding reference/retained samples for IMPs, but again this will depend on a timeline for opening Annex 13 to revision.

9. **Independence of Quality Assurance and Production**
   This aspect of GMP has proven challenging for small operations. "Softer" wording has been agreed to the strict requirement presently in place for total separation of these functions. However, again this has to wait for Annex 13 revision.

10. **Harmonized definition of Reconstitution**
    The act of reconstitution of an IMP is exempt from the requirements of a manufacturing authorization.

    However there is no agreed definition of the word and examples have been seen in CTA's of manufacturing activities being classified as "reconstitution" to avoid the need for an authorized facility. The UK has a definition in place for medicinal products and this has been used as the basis for a proposal under development.

11. **FDA Draft Guidance on GMPs for Phase I**
    This guidance was on the subgroup's workplan. However, since the FDA has withdrawn the guidance and it was therefore removed from the agenda, since it was no longer appropriate to comment.

Italian Inspectorates Receive Training on Moist Heat Sterilization

Giuseppe Fedegari, Fedegari Autoclavi SpA and Volker Eck, PhD, PDA

The Italian health authority, Agenzia Italiana del Farmaco (AIFA) and the Italian national health service, Istituto Superiore di Sanità (ISS) organized a meeting on moist heat sterilization in Rome on Jan. 21, 2008. The objective of the meeting was to illustrate to the Agencies' inspectors current best practices, the minimum technological requirements for moist heat sterilization processes, as well as underlying scientific and technological principles. AIFA and ISS, respectively, conduct GMP inspections of small molecule/chemical and the biologics/biotechnology sectors of the industry.

The meeting was attended by approximately 40 members of the inspectorates and led by **Giuseppe Pimpinella,** PhD, and **Carlo Pini,** PhD. The discussions included a presentation by **Vittorio Mascherpa** on general principles of moist heat sterilization. This was followed by a series of Fedegari experts including **Mario Barbini,** PhD, on technological features of autoclaves; **Massimo Guelfi** and **Daniela Martigani** on the development and validation of automated process control features integrated into sterilizers, which have resulted in a robust and reliable process control.

These topics were put into an application perspective by **Luca Del Freo,**PhD and **Daniele Soliani,** PhD, who delineated the steps to validate a saturated steam sterilization process. **Vittorio Cerasaro,** PhD, addressed the validation of a steam-air mixture sterilizer.

The discussions showed that the concepts laid out in TR-1 were generally accepted and referenced by both the inspectors and the industry representatives.

Volker Eck, PhD, contributed an overview on the essential suggestions in PDA Technical Report No.1, Revised 2007, Validation of Moist Heat Sterilization Processes Cycle Design, Development, Qualification and Ongoing Control. It was clear from the talks given, that TR-1 is the reference document that suppliers, like Fedegari, and users, like GSK and BMS, would use to define necessary steps in validation and qualification of processes and equipment.

During the discussion with inspectors, the biological and physical qualification strategies of moist heat sterilization and the use of integrators and indicators in qualification and validation raised many questions. The minimum checks for ongoing process control necessary to establish sterilizer system suitability was also an area of concern. Another topic that garnered discussion centered on the bracketing and standard load definitions in qualification and validation activities and related strategies in the requalification programs.

The discussions showed that the concepts laid out in TR-1 were generally accepted and referenced by both the inspectors and the industry representatives. It seems that following the recommendations in TR-1 will aid in meeting the inspectors' expectations.

PDA's Who's Who?

Giuseppe Pimpinella, PhD, Director Inspections, Istituto Superiore di Sanità

Carlo Pini, PhD, Director Research, Istituto Superiore di Sanità

Vittorio Mascherpa, Ing, Senior Consultant, R&D, Fedegari Autoclavi SpA

Mario Barbini, PhD, Technical Operations Manager, Fedegari Autoclavi SpA

Massimo Guelfi, Ing, Supervisor, Electronic Systems, Fedegari Autoclavi SpA

Daniela Martigani, Ing,Process Engineer, R&D, Fedegari Autoclavi SpA

Luca Del Freo, PhD, Responsible Manager, Validation, Calibration and Compliance, GlaxoSmithKline SpA

Daniele Soliani, PhD, Responsible Manager, Environment, Health and Safety and the Sterile Manufacturing Plant, GlaxoSmithKline SpA

Vittorio Cerasaro, PhD, Manager, Aseptic Technique and Equipment Qualification, Bristol-Myers Squibb SpA

Volker Eck, PhD, Sr. Director, Science and Technology, PDA

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Joint Industry/Inspector Training Session Raises Many Questions

Peter Reichert, Novo Nordisk; Pete Gough, David Begg Associates; Luisa Paulo, Hovione; Stephan Rönninger, F. Hoffmann-La Roche; and Jim Lyda, PDA

On Dec. 17, 2007, the EMEA hosted a joint industry/inspector training session for inspectors from EU member states and PIC/S members. The London event was in support of the PIC/S Expert Circle on Quality Risk Management (QRM). This was a first step in defining the future role of inspectors when auditing QRM activities during inspections of medicinal product manufacturers.

Chairing the meeting was **Emer Cooke,** Head of the EMEA Inspections Sector. Assisting were **Paul Hargreaves**, Senior Inspector, MHRA, UK; **Tor Gråberg**, Chief Inspector, MPA, Sweden; and **David Cockburn**, EMEA Inspections Sector. Both Hargreaves and Gråberg are members of the PIC/S Executive Bureau.

The day started with a series of industry presentations (PDA, EFPIA, ISPE, EGA, and APIC) and open discussions. The afternoon was a closed inspectors' session for discussion of the industry presentations and identification of training needs for inspectors. The outcomes of the day will be shared with the PIC/S Expert Circle on QRM.

Prior to the meeting, the EMEA asked for three questions to be answered by each attending association:

1. How Industry uses or hopes to use ICH Q9?
2. How Industry thinks inspectors should inspect the use of Quality Risk Management during site inspection?
3. Industry's views on how GMP inspectorates should be using ICH Q9 within inspectorates?

EMEA and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) recently agreed to strengthen their cooperation in the field of GMP. The agreement covers the training of GMP inspectors, the exchange of information on guidance documents and audits of GMP inspectorates. It is in accord with the PIC/S Blueprint for the future and recognizes the developing role of PIC/S in the training of European inspectorates (as well as inspectors from non-EU countries).

The Discussion

The following are notes on the key discussion points during the session. *Caution: These notes reflect the tone and nature of the open discussion as recorded by the authors. Comments are sometimes attributed to inspectortes or industry but are not actual quotations. Readers should be cautious making regulatory or compliance interpretations based on these notes. They should not be interpreted as policy statements or requirements.*

QRM Output vs. Outcome*:* The inspectorates commented that industry QRM activities often result in information outputs rather than decision *outcomes.* Industry needs to start thinking in terms of *outcomes*, e.g., the patient receives the right drug, the right quality, with the correct expiry date, etc. Risk analysis only adds value when we act upon the information generated. There was a comment that risk outputs are well documented by industry, however, risk rationales are not equally well documented.

Retrospective Risk Analysis: The inspectorates suggest that today they see more examples of retrospective risk analysis (when there is a problem) than prospective activities. This is part of the challenge in shifting to the more proactive, preventive-action mindset. In the end, such a mindset offers better quality, safety and saving of resources.

Human Error: Human error represents a very large risk and is a common cause of failures in pharmaceutical manufacturing. The impression is that human error is often overlooked in QRM root cause analysis. Industry would benefit by ensuring that the recognition of human error is appropriately reflected in the QRM program.

Shared Examples: There was agreement that open sharing by regulators of QRM problems found during inspections would be useful for the industry and all interested parties. The identity of the company involved must be kept anonymous. Sharing inspection findings promotes openness and transparency that will lead to better understanding and effective use of QRM. The Inspectors would be the best presenters of such case studies, as they are familiar with the context.

Can QRM (or ICH Q9) be implemented as stand alone?: There was consensus that a useful QRM program could be implemented alone. GMP regulations have always required companies to perform QRM to some extent and ICH Q9 offers a more structured way to do it. This structured approach can add value in many circumstances. A valuable benefit of QRM is that the level of effort, formality and documentation of the QRM process will be commensurate with the level of risk. The full benefit of the new approaches to pharmaceutical quality will be obtained best by implementing

the concepts in ICH Q8, Q9 and Q10 together.

What is the cost of implementing QRM (or ICH Q9)?: There is not believed to be a large upfront expenditure to implement a QRM system. There was a general feeling that implementing better QRM will enable cost savings by prioritization of quality efforts by a focus on value-added activities.

How will "QRM proficiency" be recognized by the inspectorates?: Can there be a *company rating* and if so, how will this be done? The inspectorates have suggested in the past that there will be no *certification* process. Nevertheless, there may be some objective criteria both for companies deemed *QRM proficient* as well as for those deemed *high risk.* If they are *high risk,* this should be conveyed to the company. Assessment of QRM activities should be part of the internal independent audit system of the company. **[Author's Note:** MHRA has proposed a Risk Based Inspection system that is described as transparent and objective. A MHRA Chief Inspector referenced the following document, UK MLX345, closed consultation January 15, 2008.**]**

Regarding FMEA (Inspectorates point of view): A process map is critical for Failure Mode and Effects Analysis (FMEA). FMEA originally was applied to engineering disciplines and associated with quantifiable data. How well can it be adapted to pharma process risks where inputs are not always quantifiable? It is important when using FMEA to have a good rationale for the choice of the risk threshold. A risk threshold should not be considered a specification.

FMEA (Industry's point of view): Inspectors should focus on the severity (i.e., consequence) rating given by the FMEA. When ranking risks a clear demarcation of high, medium and low risks, it is frequently evident. The presentation of the output from a structured approach to QRM, such as FMEA, is the key to gaining acceptance by regulators. We must avoid with QRM what we did with validation—creating an industry over-reaction. QRM is a simple, structured and logical approach and we should not complicate it.

Differences Between Compliance and QRM: Compliance is sometimes viewed as something done to comply with the regulations and satisfy the regulators. QRM coupled with six sigma tools, for example, may result in better processes and a higher level of quality that satisfies the manufacturer's business needs. Many unregulated companies implement QRM quite well with a reduction in the costs of quality. They use QRM to run the company better, not to satisfy regulators.

The Future: Going forward we have many more questions than answers at this time. We need to plan more frequent opportunities for these discussions. PDA will report on these activities as they develop.

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