



July 2004

A MONTHLY COMMUNICATION FOR THE MEMBERS OF PDA—
AN INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL AND
BIOPHARMACEUTICAL SCIENCE AND TECHNOLOGY

PDA Interview with Roger Williams concludes, page 18

Technical Resources Augment PDA Career-Long Learning

New Books Available; Technical Reports Pending

The PDA library of career-long learning resources is expanding in 2004 with the addition of new technical books, technical reports, training videos and interactive computer-based programs, and conference proceedings.

These technical resources augment the valuable career-long learning opportunities PDA offers to our members and the pharmaceutical and biopharmaceutical communities as a whole.

The textbooks PDA publishes in cooperation with Davis Healthcare International Publishing address a wide variety of technical topics, helping experts both in industry and in the regulatory bodies perform at a higher level professionally and contribute to their

career advancement. Like PDA meetings, courses and audio conferences, PDA relies on the expertise, hard work and commitment of our members to provide these valuable resources.

In July, PDA and Davis Healthcare International Publishing present a comprehensive examination of perspectives on pharmaceutical quality from industry and government, from large companies and small companies, and from countries around the globe, in the new book, *Pharmaceutical Quality*. By defining quality from these various points-of-view, the book provides a blueprint for the production and delivery of consistently high-quality products.

continues on page 34

2004 PDA/FDA Joint Regulatory Conference: *The New Guidances*

A Message From Program Committee Chair, Allen L. Burgenson (Cambrex)

As a career-long learning resource for more than 57 years, PDA strives to keep a finger on the pulse of the ever-evolving needs of pharmaceutical and biopharmaceutical professionals around the world. Over the last 15 years, the PDA/FDA Joint Regulatory Conference has been an important resource for leading-edge information and training on FDA regulatory and science issues affecting our industry.

In 2002, FDA announced its "21st Century Initiative" to complete the first major overhaul of its current Good Manufacturing Practices (cGMP) for pharmaceutical products in 27 years. Significant changes have transformed our environment, including: resource constraints; advances in pharmaceutical sciences and manufacturing

technologies; the application of biotechnology in drug discovery; advances in the science and management of quality; and globalization of industry. These changes have resulted in FDA's effort during the past two years toward designing effective, risk-based, innovation-friendly cGMPs, design controls and quality systems for our industry.

The 2004 PDA/FDA Joint Regulatory Conference, themed *The New Guidances*, will provide a unique opportunity to meet with FDA, industry and academic experts and our peers to discuss the impact and implications of the new guidances for today, and learn, as we move forward with FDA down the Critical Path, what long-term measures are necessary for our future success.

Turn to page 30 to learn more about this exciting PDA event. Go to www.pda.org/pdafda2004 to view the conference brochure and to register online.

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1
Filtration Handbook: Integrity Testing
By Maik W. Jornitz and Theodore H. Meltzer (Item #17197, US\$185/member, US\$229/nonmember)

2
PDA Technical Report No. 13 (Revised) – Fundamentals of an Environmental Monitoring Program
Prepared by the PDA Environmental Monitoring Task Force (Item #01013, US\$75/member, US\$550/nonmember)

3
Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations – PDA Technical Report No. 3
(Item #01032, #01132, US\$100/member, US\$575/nonmember)

4
Laboratory Validation: A Practitioner's Guide
By Jeanne Moldenhauer (Item #17201, US\$250/member, US\$309/nonmember)

5
Excellence Through Validation: A Practitioner's Guide
By U.G Barad (Item #17205, US\$160/member, US\$199/nonmember)

6
Microbiology in Pharmaceutical Manufacturing
By Richard Prince (Item #17185, US\$240/member, US\$299/nonmember)

7
Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2002, Sixth Edition (The Orange Guide)
(Item #12001, US\$45/member, US\$60/nonmember)

8
GMP in Practice: Regulatory Expectations for the Pharmaceutical Industry, Third Edition
By James Vesper (Item # 17199, US\$105/member, US\$129/nonmember)

9
Steam Sterilization: A Practitioner's Guide
By Jeanne Moldenhauer (Item #17183, US\$215/member, US\$269/nonmember)

10
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The PDA Archive gives you easy access to more than 50 years of research papers written by highly qualified research scientists in the pharmaceutical/biopharmaceutical industry. (Item # 01101 / #01002, US\$395/member, US\$1200/nonmember)



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Important Dates...

- **August 31**—EMEA API Master File guideline becomes effective
- **September 7-8**—PDA/BFS Inter'l. Operators Association Joint Workshop on Blow/Fill/Seal Processing Holopack Verpackungstechnik GmbH, Germany
- **September 20-24**—2004 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits: The New Guidances Omni Shoreham Hotel, Washington, D.C.

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Neal G. Koller
PDA President

President's Message

PDA Thanks Its Technical Contributors

On the cover of this month's issue, PDA highlights the technical resources that the Association makes available to our members and the pharmaceutical and biopharmaceutical communities as a whole. These textbooks, technical reports, training videos and conference proceedings are valuable resources that truly augment the career-long learning that PDA provides as part of our mission.

This month, I would like to use this column to express PDA's appreciation for those members who contribute to these important resources.

Writing is a time-consuming and isolating exercise. Finding the requisite time, peace and quiet to write is often more challenging than the subject matter covered in the various textbooks and technical reports we offer. Those members who actually make that commitment to write a textbook, chapter or technical report on top of their "day jobs" and personal commitments truly deserve to be recognized.

By making this commitment, PDA's authors share their knowledge, experience and expertise with all the membership and the pharmaceutical/biopharmaceutical communities as a whole. Sharing knowledge is one of the fundamental goals of science, and PDA's authors represent some of the finest scientists in the communities.

While it is not possible in this column to name all PDA's authors and task force members who have contributed to the PDA library of technical resources over the years, I would like to recognize our most recent contributors. The following authors have written or edited technical books on topics ranging from quality control and validation to rapid microbiology and cleanroom clothing:

- U.G. Barad, PhD, Tabuk Pharmaceutical;
- Maik Jornitz, Sartorius Corp.;
- Bengt Ljungqvist, PhD, Swedish Royal Institute of Technology;
- Theodore Meltzer, PhD, Capitola Consulting Co.;
- Jeanne Moldenhauer, PhD, Vectech Pharmaceutical Co.;
- David Nettleton, industry consultant;
- Richard Prince, PhD (editor), industry consultant;

· Berit Reinmuller, PhD, Swedish Royal Institute of Technology;

This list does not include the non-PDA members who authored books, nor the large number of authors who contributed essays to Dr. Prince's recent textbook, *Pharmaceutical Quality*. To all of you, please accept PDA's gratitude as well.

On behalf of PDA, I want to specially thank Amy Davis, CEO of Davis Healthcare International Publishing, the publishing house that PDA partners with to bring to the membership the valuable technical books referenced above. A longtime PDA member, Amy works hard finding topics that are important to the daily work of our members, and then she finds the experts to author the books.

I wish I had the space to list all those involved with creating PDA technical reports. These valuable industry guidelines are put together by a large number of PDA experts, from the task force participants who draft the documents to those who volunteer as technical reviewers, and all those who vet the documents for relevance and applicability, including experts on the PDA Science Advisory Board and the PDA Regulatory Affairs and Quality Committee and the PDA Board of Directors. In the coming months, PDA anticipates publishing several new technical reports. When these are released, please take a moment to review the list of task force members who worked on the projects. Their valuable work is well-appreciated.

Lastly, I want to remind you that the PDA E-store is the best place to learn about all of the technical resources in PDA's library. There you can learn about all the textbooks, technical reports, technical bulletins and training media produced by your colleagues. A 2004-2005 PDA publications catalogue will be sent to every member later this year, so please take the time to review that as well.

I encourage all our authors to continue with their efforts. By sharing your expertise and knowledge in these books and technical reports, you strengthen the ability of manufacturers in the communities to produce high quality medicinal products. You also make outstanding contributions to the career-long learning opportunities provided by PDA.

On behalf of all of us at PDA, I thank you!

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August 30-31:

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George A. Robertson
VP, Science & Technology

Vice President's Message

Rapid Micro Method Approved

I would like to share with you the following monumental news from a Pall Corporation press release (use of this information does not imply a PDA endorsement of Pall products):

GlaxoSmithKline Process Using Pall Rapid Microbiological Test Is First Approved By FDA

East Hills, NY (May 27, 2004) - - Pall Corporation announced today that the U.S. Food and Drug Administration granted GlaxoSmithKline approval to use the Pallcbek(TM) Luminometer as part of the quality control process for its prescription nasal spray product in its Parma, Italy facility....GSK is the first pharmaceutical company to obtain approval to release a prescription product to market using a rapid detection technology under the FDA Process Analytical Technologies (PAT) program.

This is the first of what promises to be a scientific revolution in the pharmaceutical industry: Process Analytical Technology (PAT).

The purpose of my article this month is to describe the scientific underpinnings of the test cited in the press release. The analytical test method detects *bioburden*. Products or components used in the pharmaceutical or medical field require control of microbial levels during processing and handling. Bioburden or microbial limit testing on these products proves that the requirements are met.

Microbial limit testing of raw material as well as finished pharmaceutical products can help to determine whether the product complies with the compendial requirements of the major pharmacopeias in the United States (USP), United Kingdom, Europe and Japan. Bioburden testing of components can show the use of adequate control measures during preparation and handling.

The current U.S. method, USP <61> *Microbial Limit Tests*, uses the Total Aerobic Microbial Count method (plate counting) or the Most Probable Number method in tubes. I won't go into details, but both methods require 48-72 hours of incubation time to see visible evidence of growth.

The rapid method, alluded to in the press release, does not require the long incubation

period to see evidence or growth; it directly measures evidence of cellular respiration, the chemical ATP (adenosine tri-phosphate)

Bacterial metabolism requires ATP and this can be used as a measure of viable bacteria in biological samples. Standard microbiological techniques for culturing bacteria from samples take a minimum of five days to complete. The ATP bioluminescence assay reduces this testing time to 24 hours.

ATP bioluminescence is a sensitive technique, which detects bacteria by measuring light emitted when their ATP reacts with firefly luciferase and luciferin. The light measurement is based on the reaction described in *Illustration 1*, below.

The typical components of the testing method using the *Pallcbek* system include:

- Filtration of product through membrane
- Wash membrane to remove product
- Membrane incubated in growth medium (Tryptic Soy Broth) for 18-24 hours
- Extract the cellular ATP with a disrupting reagent
- Add the luciferase/luciferin reaction solution
- Measure emitted light

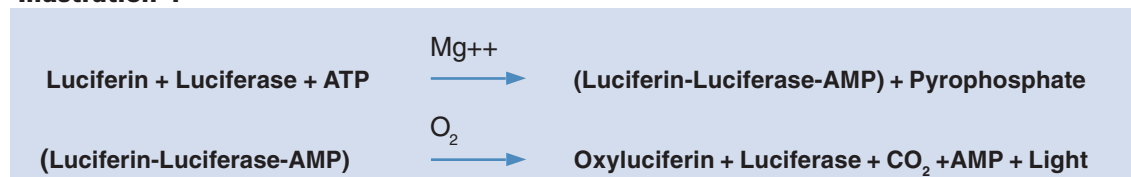
The advantage obtained is time. The manufacturer claims a turn around time of 24 hours for their system, and this would compare very favorable with the 5-14 days compared to conventional growth-dependent methods. An economic question for the manufacturer would be whether the increased costs of ATP bioluminescence testing would be outweighed by the savings associated with quicker testing/release cycles.

In my column this month, I have presented an example of how a new approach to an established assay method can and will increase its utility to the industry. Rather than relying on a technology that has been around for centuries, it makes use of our modern understanding of molecular/cellular biology to make test methods more relevant and applicable to the automated manufacturing methods of today.

In October, the PDA Training and Research Institute is holding a course on rapid microbiological methods. Also, the written transcript and audio CD for a PDA audio conference on the topic is available.

In 2003, PDA published a new book entitled, "Rapid Analytical Microbiology", by Wayne Olsen. Also, PDA Technical Report #33 addresses rapid micro methods. Both can be bought at the PDA E-store, www.pda.org/estore.

Illustration 1



Recent Sci-Tech Discussions

The following, unedited remarks are taken from the Pharmaceutical Sci-Tech Discussion Group, a PDA-sponsored Online Forum at www.pda.org. PDA Online Forums are free of charge and open to the public. They serve as a platform for exchanging practical and sometimes theoretical, ideas within the context of some of the most challenging issues confronting the pharmaceutical industry. If you are not currently a member of a discussion group, we encourage you to visit our Web site and join. Visit www.pda.org to sign up via the Web or send an e-mail to requests@www2.pharmweb.net.

Question 1: "Validation and Post-Approval Changes"

It would be nice to hear your opinions on following issue: How many process validation batches are needed if two tablet presses from different SUPAC-subclasses (one from power assisted and one from centrifugal subclass) are to be used? Is the needed amount of batches three, six or something between them?

Response 1

I think you are approaching this issue backwards. The key issue is as follows: What kind of information and data will allow to believe that your process is working and under control? The answer to this question should also be the answer to your validation questions. The key is that you do not want to face recalls because of incomplete studies of process changes.

Validation means three batches. If you are investigating two options, I suggest do three for each option. Otherwise you cannot be sure of what you have.

Response 2

I would do three batches of granules and run half on each press.

Response 3

Validation does *not* mean three batches. Validation means as many batches as are necessary to establish sufficient evidence that you understand the process; that you are in control of the process; and that the process produces a consistent reproducible output.

Response 4

You hit the nail on the head when you said, "Validation does *not* mean three batches...."

However, *because* validation is a journey and not a destination, I would recommend a slight change to your cogent comments and recommend changing the last phrase from, "and that the process produces a consistent reproducible output" to "and that the process IS PRODUCING a consistent reproducible output that meets the *uniformity minimums set forth by cGMP.*"

Response 5

I agree with the forum responses. In my perspective, seems the issue is not how many

batches you should perform for your process validation, but what critical parameters you should establish before you perform it.

I believe you will have no significant problem to establish the parameters for "powder-assisted" / regular tableting machine. However, you should pay more attention to some parameters for your "centrifugal" tableting machine, especially for tableting speed (since it will be tightly related to tablet weight and granules distribution), initial time and tableting speed before you can collect the tablet at startup, also granules flowing and particles distribution properties. Since "centrifugal" tableting machine is usually applied for relatively "closed system" tableting (e.g. for hormones, carcinogenic materials, etc), you may also perform "leakage" powder level around the machine to ensure the environment does not contain the materials powder above the PEL number.

Response 6

OK. Stand corrected. At least three batches. But if you need more than three batches, there is need to review leading up to the validation exercise.

The rule of validation is always the same. A validation exercise must not fail. If it does, this indicates validation was done before you're ready.

Question 2: "Stability Studies"

What are the requirements for the length of time after product manufacture that the stability study has to be initiated?

Response 1

There is no official period of time from manufacture to date of study initiation, but a common interval is 30 days from TOM. However, if the time interval stipulated in the appropriate stability SOP is exceeded, you will probably need to repeat the stability analytical monograph for this batch and use it as your Time-zero point. Some companies use the time from Quality Testing and release as time-zero if and only if study initiation does not exceed 30 days from Assay, Impurities and other critical testing.

Response 2

Your query is perplexing because, in general, primary stability studies are *required* BEFORE the general manufacture of a drug product is initiated—these are required to establish and support the expiration dating applied to the product. (SEE 21 CFR 211.137, that states: Sec. 211.137 Expiration dating.

(a) To assure that a drug product meets applicable standards of identity, strength, quality, and purity at the time of use, it shall bear an expiration date determined by appropriate stability testing described in Sec. 211.166.

(b) Expiration dates shall be related to any storage conditions stated on the labeling, as determined by stability studies described in Sec. 211.166.

(c) If the drug product is to be reconstituted at the time of dispensing, its labeling shall bear expiration information for both the reconstituted and unreconstituted drug products.

(d) Expiration dates shall appear on labeling in accordance with the requirements of Sec. 201.17 of this chapter.

(e) Homeopathic drug products shall be exempt from the requirements of this section.

(f) Allergenic extracts that are labeled “No U.S. Standard of Potency” are exempt from the requirements of this section.

(g) New drug products for investigational use are exempt from the requirements of this section, provided that they meet appropriate standards or specifications as demonstrated by stability studies during their use in clinical investigations. Where new drug products for investigational use are to be reconstituted at the time of dispensing, their labeling shall bear expiration information for the reconstituted drug product.

(h) Pending consideration of a proposed exemption, published in the Federal Register of September 29, 1978, the requirements in this section shall not be enforced for human OTC drug products if their labeling does not bear dosage limitations and they are stable for at least 3 years as supported by appropriate stability data.

In addition, 21 CFR 211.166 states: Sec. 211.166 Stability testing.

(a) There shall be a written testing program designed to assess the stability characteristics of drug products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates. The written program shall be followed and shall include:

(1) Sample size and test intervals based on statistical criteria for each attribute examined to assure valid estimates of stability;

(2) Storage conditions for samples retained for testing;

(3) Reliable, meaningful, and specific test methods;

(4) Testing of the drug product in the same container-closure system as that in which the drug product is marketed;

(5) Testing of drug products for reconstitution at the time of dispensing (as directed in the labeling) as well as after they are reconstituted.

(b) An adequate number of batches of each drug product shall be tested to determine an appropriate expiration date and a record of such data shall be maintained. Accelerated studies, combined with basic stability information on the components, drug products, and container-closure system, may be used to support tentative expiration dates provided full shelf life studies are not available and are being conducted. Where data from accelerated studies are used to project a tentative expiration date that is beyond a date supported by actual shelf life studies, there must be stability studies conducted, including drug product testing at appropriate intervals, until the tentative expiration date is verified or the appropriate expiration date determined.

(c) For homeopathic drug products, the requirements of this section are as follows:

(1) There shall be a written assessment of stability based at least on testing or examination of the drug product for compatibility of the ingredients, and based on marketing experience with the drug product to indicate that there is no degradation of the product for the normal or expected period of use.

(2) Evaluation of stability shall be based on the same container-closure system in which the drug product is being marketed.

(d) Allergenic extracts that are labeled “No U.S. Standard of Potency” are exempt from the requirements of this section.

Hopefully, a careful study of the preceding cGMP requirement MINIMUMS should provide you the answers you, or, failing that, help you shape your questions more precisely.

Response 3

I do not recall anything in the regs for this requirement. We are using a 3 month time frame from the date of manufacture. Also we have a 30 day requirement from release to the stability initiation or the project teams need to perform T0 testing or justify why they can still use the initial release for T0.

Call for Papers

2005 PDA Annual Meeting

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Scientific abstracts of papers not previously published or presented at scientific meetings are being sought for presentation at **2005 PDA Annual Meeting, which will be held April 4–8, 2005 in Chicago, Illinois.**

This conference offers many opportunities for academicians, practitioners, consultants, and other subject-matter experts to present in a variety of forums—breakfast, luncheon and presentation sessions, keynote addresses, and panels.

ABSTRACTS MUST BE RECEIVED BY AUGUST 30, 2004 FOR CONSIDERATION.

PDA is seeking presentations 30-35 minutes in length, that present major challenges and practical approaches to resolution in the following areas:

- Aseptic processing of medicinal products
- International regulatory and harmonization initiatives
- Industry manufacturing/product trends
- New technology
- Combination products
- Risk management and risk-based GMP
- Process analytical technologies (PAT)
- Quality management systems for pharmaceuticals
- Industry case studies—compliance and quality issues
- Microbiology initiatives and trends

COMMERCIAL ABSTRACTS PROMOTING OF PRODUCTS AND/OR SERVICES WILL NOT BE CONSIDERED.

Send via e-mail an electronic copy of the abstract and the presenter's biography (approximately 100 words in length) by August 30, 2004 to: Deborah Stokes at Stokes@pda.org.

Please include the following information. Submissions received without full information will not be considered:

Title ♦ Presenter's biography ♦ Additional authors ♦ Full mailing address ♦ Phone number ♦ Fax number ♦ E-mail address of the presenter ♦ 2-3 paragraph abstract, summarizing your topic ♦ The type of forum you can present your topic in (traditional, case study, discussion/debate, panel) ♦ Target audience (by job title or function) ♦ Explanation of specific take home benefits to target audience for attending this presentation ♦ Key objectives of your topic and the benefits of someone hearing what you have to say.

Upon review by the program committee, submitters will be advised in writing of the status of their abstract after August 30, 2004. PDA will provide one complimentary meeting registration per presentation. Additional presenters will be required to pay appropriate conference registration fees. With the exception of health authority speakers, all presenters are responsible for their own travel and lodgings.

PDA Interest Groups & Leaders

The following is a list of PDA Interest Groups (IGs). Starting in 2004, PDA began establishing "Branches" of each IG in the various regions of the world that we serve. The list below includes the names of the Leaders for each Branch of the IG, the Leader's affiliation and their e-mail address. More detailed information on PDA's Interest Groups and contact information is available on the PDA Web site at: www.pda.org/science/IGs.html.

Biotechnology

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Drug-Device

Delivery Systems

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Isolation Technology

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Vice President's Message

PDA's Evolving Regulatory Strategy

Today's market dynamic requires that we continually evaluate our role and strategy in the marketplace and to remain abreast of constantly changing regulations, procedures and trends on a global basis. PDA has a strong track record and a 57-year history of providing its members with the strategy and expertise required to leverage emerging scientific and technology opportunities within today's complex regulatory framework.

PDA's efforts in this regard are encapsulated in the PDA Strategic Plan strategy number 2, "*Build a stronger liaison with regulatory bodies.*" Since I

joined PDA in February, the PDA Quality and Regulatory Affairs Department has worked closely with the member volunteers on the PDA Regulatory Affairs and Quality Committee (RAQC) to develop a "PDA regulatory strategy" to better fulfill strategy number 2.

Thus far, a two-pronged approach is being utilized with execution support from RAQC, PDA worldwide Chapters and global staff activities. It is also supported by all PDA functional activities, e.g., training, education, meetings and publications. The two-pronged approach we are developing is as follows:



Victoria Ann Dedrick
VP, Quality and
Regulatory Affairs

1. Raise awareness of PDA to health authorities worldwide by:

Interacting with health authorities and organizations worldwide to develop working relationships via visits, attending public meetings and provision of PDA technical resources and publications.

Providing scientific expertise to national and international health authority and organization committees, task forces, working groups, forums and round-tables to ensure promulgation of regulation that is science-based, and ensure that decision-making is not burdensome to industry.

Proactively working to ensure the needs of members are met by conducting a review and appraisal of the worldwide regulatory environment, the relevant guidelines, existing precedents and ongoing regulatory initiatives which may affect members and industry.

Submitting relevant science-based comments and/or recommendations regarding new guidelines/policies to the issuing authorities.

Providing training, educational and networking opportunities to share views and build consensus.

Acting as a neutral (3rd party) forum/facilitator between the health authorities and the private sector portion of the pharmaceutical and biopharmaceutical communities (see my discussion of the PDA/FDA drug shortage initiative below).

Maintaining and continuing to build scientifically strong ties with regulatory bodies worldwide.

Becoming the "Go To" partner on projects and activities.

2. Assist PDA Chapters worldwide interact with health authorities by:

Accompanying PDA Chapter members to meetings with health authorities and organizations to provide support, expertise and aid in the development of working science-based working relationships.

Providing education, training and programming to support Chapter needs in working with health authorities and other organizations.

Developing and maintaining relationships with sister and allied associations that will be beneficial to all parties involved.

Promoting the harmonization of regulation, policy and guidance development worldwide.

continues on page 14

Strategy Implementation

During the last few months a number of activities have been carried out to begin implementing this regulatory strategy. Following are some examples:

RAQC submitted written comments on new guidelines and policies to multiple authorities, including the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and World Health Organization (WHO).

PDA met five times with FDA on topics including aseptic processing, drug shortages, and conference support.

PDA participated in two direct meetings with EMA and one phone conference to discuss several issues including Annex 1, development of stronger working relationship and closer ties, improved transparency, drug shortages and training opportunities.

PDA initiated relationships with the European Commission Directorate Generale Enterprise, the Minister of Health in Jordan and the health authorities in Canada, China, Taiwan and Singapore.

PDA met twice with the European Directorate for Quality Medicines (EDQM) to continue relationship development, discuss potential joint conferences and begin contributions to the *PDA Letter*.

PDA continues building its relationship with the U.S. Pharmacopeia (USP), meeting several times recently to explore joint educational opportunities, explore ways for PDA to support the work of USP's Expert Committees and develop of Memorandum of Understanding (MOU) between the pharmacopeia and PDA.

PDA has met with the Risk Management Center for Applied Sciences in Health Products and Processes at Virginia Tech (VPISU) to develop a relationship and potential opportunities to benefit members.

I sincerely hope that this beginning flurry of regulatory activities at PDA has your interest and will be of support to you in your career. PDA is always looking for volunteers to help us out. If you are interested in providing regulatory updates on a region, providing analysis of new proposed regulations and/or case studies of how your company has handled regulatory issues, please contact us and get involved. PDA and you colleagues around the world need your support.

Drug Shortage Initiative

I want to conclude this column with some words on the drug shortage initiative:

PDA has embarked on an initiative to assist the U.S. FDA in responding to the serious problems caused by drug shortage situations. In doing so, both parties are striving to develop processes to ensure that products are available for needy patients, all stakeholders are educated and clear communication pathways are established. This information will be shared with manufacturers and health authorities worldwide to assist patients everywhere in need of treatment.

The goals of the initiative are to:

- establish a system to help FDA facilitate the identification of pharmaceutical manufacturers worldwide who have the willingness, dosage form availability, and capacity (or desire to develop capacity) to supply medically necessary products

that are experiencing emergency, short-term or long-term drug shortages;

- identify manufacturers willing to take up production of medically necessary discontinued products through either the transfer or purchase of an existing NDA/ANDA or through pursuing a new NDA/ANDA. This can lead to the development of new niche markets;
- improve voluntary/mandatory notification procedures for drug shortages; and
- look at the economic and other incentives, and the opportunities available to manufacturers who participate in drug shortages supply programs.

The first step in this process is to collect information from worldwide manufacturers on the willingness to participate in resolving drug shortages. We invite you to complete the Drug Shortages Survey and to attend a free audio conference to be held with FDA in late July to discuss the drug shortages problem, the reasons why you should participate, incentives, opportunities and have the opportunity to ask questions about the process.

For more information and to answer the survey, please visit the PDA Web site, www.pda.org.

Thank you.

Aseptic Processing Harmonization Moving Forward

Manufacturers Submit Case Studies to EMEA to Help Process

22 April 2004

Emer Cooke
 Inspections, Head of Section
 EMEA
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 United Kingdom



Dear Mrs. Cooke,

On behalf of EFPIA and PDA, I would like to present EMEA with the following case study comments collected and compiled from manufacturers regarding inspectional concerns and issues arising from the differences between EU GMP Annex 1 and the draft FDA Guidance on aseptic processing. I would also like to take this opportunity to thank you and your staff again for joining us by conference call in Basel, CH on 18 February to participate and contribute to our session on Harmonisation of the EU Annex 1 "Manufacture of Sterile Medicinal Products" and the FDA "Sterile Products Produced by Aseptic Processing Draft" and presenting us with the opportunity to submit these observations for consideration.

EFPIA and PDA desire to work closely with EMEA on scientific, technical and regulatory issues and we applaud your efforts to increase the transparency of processes. You discussed the future development of a Q&A document to address inspectional issues and questions regarding interpretation of Annex 1. Both EFPIA and PDA would like to actively participate and contribute to that development process. We hope that the provided examples of inspectional issues and differences compiled from member experiences assist you in identification of issues that require elaboration.

PDA will also be following up with the FDA on harmonisation and inspectional issues identified during the Basel meeting and by sharing these findings jointly developed with EFPIA. We would be happy to share the content of those discussions with you.

Again, thank you on behalf of EFPIA and PDA for the opportunity to provide these comments to you.

Sincere regards,
 Victoria Ann Dedrick
 Vice President, Quality and Regulatory Affairs

The compilation of case studies submitted to the EMEA in April appears on pages 16 and 17.

Aseptic Processing Case Studies

The lack of apparent harmonization between EU GMP Annex 1 for manufacture of sterile medicinal products and the FDA draft guidance on Aseptic Processing is creating some difficulties and additional financial burden for manufacturers. In order to be in compliance with both sets of requirements from an inspectional basis, manufacturers are taking steps to implement procedures and processes that comply with both EU and FDA perceived regulations. In some cases, these may conflict with current regulatory practice being applied and/or are additive to the process without affording any additional safety that is scientifically justifiable.

Where there are requirements by one regulator that are not clearly required by the other, or where there are specific differences in requirement(s), manufacturers should be afforded the opportunity to justify their positions and practices to an inspector on a scientific, technical and logical basis taking into account the assessment of risk to the patient. These justified positions should be acceptable to both regulatory parties.

The following points taken from case situations presented by manufacturers serve to highlight those areas where clarification regarding inspectional consistency may be required.

Case	Difference in requirement	Comment
EU inspection requirement in the EU to include all personnel in media fills twice per year rather than once.	FDA draft guidance requires 'at least once per year' which contradicts this interpretation.	Our understanding of industry practice is the inclusion of all personnel once per year.
Different EU regulators are interpreting the requirement for continuous monitoring in different ways.	The formal EMEA perspective regarding continuous monitoring is that discrete samples (perhaps using manifold systems) totalling >1 cubic metre over a working period is acceptable, whereas some national authorities require true uninterrupted continuous monitoring, where manifolds are not acceptable.	Since companies with facilities in different member states are being held to different standards on the same point, it is requested that a common position be published on this issue by the regulatory authorities.
EU inspector in the US indicated that Annex 1 would be changed to require a passing criterion of zero positives at media fill.	Potential differences in media fill philosophy and actual requirements as stated in the FDA draft guidance.	Confirmation of scientific rationale for acceptance criteria in media fills.
FDA regards videotapes of media fills as raw data, and reviews them as such.	EU tend to regard this type of record as more of a help with deviations, rather than as a fundamental part of the validation system.	It is recommended that videotapes of media fills may be viewed and utilized as raw data, under defined circumstances.
EU inspections carried out in the EU emphasise the requirement to monitor 5 micron particles at specified levels, and to take 1 cubic metre air samples.	FDA draft guidance does not require monitoring at 5 microns and states only that an appropriate sample volume should be taken.	Re-evaluation of the scientific, technical and rational requirement of the 5 micron requirement alongside the ISO 14644-1 requirement.
EU inspections in the US require the monitoring of 5 micron particles.	Company did not routinely do this (facility not designed to achieve this) as it is not required by FDA	Re-evaluation of the scientific, technical and rational requirement of the 5 micron requirement.
Total sample air volume of 1 cubic metre for EU requires the use of many sampling machines and significant time.	FDA requires only appropriate volume based on risk. Different interpretations result in different requirements during inspection.	Companies should define a justified scientific and rational basis for the selection of an appropriate air volume.
EU inspectors in the US have cited firms for failure to use settle plates in Grade A/B areas.	US sites have traditionally used active air samples and contact plates. This is accepted by FDA. Some companies justify based on interpretation of Annex 1 to mean that different methods are alternatives rather than additional requirements to each other.	Companies should provide a rationale and justification for the usefulness of the monitoring methods employed, and/or demonstrate equivalence.
EU inspections in US require physical measurements for primary steam sterilisation validation, rather than the use of biological indicators.	EU philosophy on steam sterilisation is different to that applied in the US. EU requires steam pressure, as well as temperature, be used with steam sterilisation. Additional non-regulatory standards are enforced (HTM 2010). FDA guidance and recommendations have not required this.	It is recommended that a harmonised consensus position be found.

Case	Difference in requirement	Comment
EU inspections require facility qualification studies under static conditions.	FDA requirements are for dynamic conditions only.	Provide rationale for the use of static conditions in facility qualification.
US firm cited by EU inspector for failing to classify the final stage of change to be the same as the room into which it lead.	Not required by FDA.	Companies should document and justify the conditions under which their personnel change.
US firm cited by EU inspector for failing to have changing rooms between Grade C and Grade B areas, even though the clothing regime was Grade B for all.	Changing access requirements to Grade B/Class 10,000 are not defined in the FDA document.	It is recommended that a harmonised consensus position be found that is scientifically and technically justifiable.
US firm cited by EU inspector for failing to have changing facilities into a Grade C area, and for inappropriate Grade C gowning.	Changing conditions and gowning for Grade C/Class 100,000 dynamic, is not specified in the FDA draft guidance.	Companies should document and justify the conditions under which their personnel change.
EU requires sealing of aseptically filled, stoppered vials in Grade A.	Vial stoppering background has not been defined in the US.	Companies should scientifically justify and document the conditions under which vials are stoppered.
EU requirement at inspection for demonstration of validation of laminarity in Grade A.	FDA requirement is for unidirectional, which is more reasonable. Some EU inspectors have asked for a similar position 'low turbulence unidirectional'.	Companies should justify their positions and practices.
EU inspection in the US required leaks in Grade A HEPA filters not be patched, but that filter(s) be replaced.	Acceptable industry practice, supported by FDA viewpoint, has been to patch to a limited degree, as this is less risky than filter replacement.	Companies should justify their practices based on appropriate risk assessment.

The following points are not specific inspectional issues, but represent areas of concern with regard to interpretation and clarification.

Case	Difference in requirement	Comment
Recommended limits for microbial contamination	Annex 1 – 'average' value: FDA – 'individual' value.	Different companies have different interpretations of 'average'.
Redundant filtration	Annex 1 and FDA guides recommend this. Interpretation of what this means is variable.	Because of confusion over interpretation, some companies have gone from 1 sterilising filter to 3, with bio burden sample taken after the first in order to comply with the spirit.
Cubic metre sampling	It is unclear how cubic metre samples are to be taken, regarding the current state of technology. Can the sample be comprised of numerous cubic foot samples?	Clarification of the intent of monitoring a cubic metre.
Grade A air velocity	Multiple EU inspectors from different authorities have expressed that they believe that the Grade A air velocity figures in Annex 1 are excessive.	Reword to include design philosophy within Grade A zones to minimise potential for contamination.
This document was compiled and prepared with the assistance of Martyn Becker, Merck and Co., Inc. PDA and EFPIA would like to extend their thanks to Mr. Becker and all of the many companies and individuals that contributed to this document for their contribution and assistance.		

Stakeholders Drive USP's Success

Part 3 of PDA's Interview with Roger Williams

This is the final installment of PDA's interview with USP CEO and Executive Vice President Roger Williams. The interview was conducted by PDA Senior Editor Walter Morris at USP's headquarters in January and February.

In this installment, Dr. Williams discusses a number of issues regarding the type of standards found in the pharmacopeia and how USP chapters become official in the eyes of the U.S. FDA.

Throughout the discussion, Dr. Williams alludes to the important role USP's stakeholders play in the success of the pharmacopeia. Finally, the interview concludes with

Dr. Williams' reflecting on his career as the head of the Office of Pharmaceutical Science in FDA's Center for Drugs Evaluation and Research.

PDA: The U.S. Pharmacopeia includes information that can be found elsewhere. One example is Chapter <1208>, *Sterility Testing – Validation of Isolator*

Systems. There are two issues here, first this information exists in PDA Technical Report #34, *Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products*. Second, the USP chapter references Federal Standard 209e, which is no longer an active standard having been replaced by an International Organization for Standardization (ISO) standard long ago. What is the purpose of including this information and how does USP monitor this external information for current applicability?

Dr. Williams: First of all, USP wants to work with other parties very closely. There are things that USP can do and then there are things that other groups can do. Sometimes there is overlap and USP's goal is to minimize any conflict about overlap. It may occasionally arise with the technical reports by PDA, but I would draw a strong distinction between the standards that appear in USP-NF and the technical reports that come from PDA. Both are extremely valuable to the industry, but I would say in terms of a standards-setting body, USP's documents serve a different purpose.

Regarding standards, anybody can create documents that provide information and describe ways of doing things. Standards generally apply to products, processes and people. That is an ISO concept, which also talks about a standard just being a document. So the question also then becomes: What do people do with the standards that USP creates and what makes them official? The term 'official' is an interesting concept that

represents, in part, a decision by other bodies. For example, USP standards were adopted in the Food, Drug and Cosmetic Act under various provisions of the law. By adopting USP standards in the legislation, the U.S. government made most of the contents of the USP-NF official from its perspective. Official, from my perspective, can mean providing safe harbors to pharmaceutical manufacturers and compounding professionals. So the standards that appear in USP-NF are extremely valuable to makers of therapeutic products and compounding professionals because they create an appropriate approach that is acceptable to FDA and other health authorities.

How does all this relate to the technical reports of PDA? The technical reports of PDA can be extremely valuable for providing further information, more detailed information, and an amplification of a general approach. This can happen in other contexts as well.

THE TECHNICAL REPORTS OF PDA CAN BE EXTREMELY VALUABLE FOR PROVIDING FURTHER INFORMATION, MORE DETAILED INFORMATION, AND AN AMPLIFICATION OF A GENERAL APPROACH. THIS CAN HAPPEN IN OTHER CONTEXTS AS WELL.

For example, with USP's sterile compounding guidelines [USP General Chapter <797>] obviously has some impact on community pharmacists who compound sterile preparations. But the USP standard can be supplemented by additional technical guides and standard operating procedures from an organization like the American Society of Hospital Pharmacists (ASHP). USP might create the general approach with the detailed approach being handled by the organization that speaks to a specific cadre of interested parties. In this context, I like to think that what USP does can synergize very well with PDA's work, ASHP's work and the work of many other talented individuals and groups. The challenge is to make sure that everybody agrees up front and to make sure that there is a lot of input from involved parties. With this in mind, I believe that USP can do better job communicating with the involved parties to make sure all voices are heard.

PDA: There is some concern that USP sometimes overlaps with the guidances of the U.S. FDA?

Dr. Williams: For the most part, USP does not want to compete with FDA's guidances. However, there is a big difference between guidance from FDA, which frequently is a recommendation on information needed to support an application, and a product standard that can be used to assess conformity. As you know, I spent a lot of time on guidances over at FDA and I hope they continue to get the attention they deserve. USP's general chapters greater than 1000 at times are more along the lines of FDA's guidances in that they

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Regulatory Briefs

Important Dates

- Aug. 23** Deadline for public comment on **U.S. HHS** program to expedited approval of new drug and biologic products
- Aug. 31** **EMEA** API Master File guideline becomes effective

U.S. Department of Health and Human Services

HHS Wants Public Comment on Critical Path

Coming in the wake of the publication of a U.S. FDA report on the problems and potential solutions to the “drug pipeline problem” (see the PDA Letter, *June 2004*, “Regulatory Briefs, p. 22), FDA’s parent agency, the U.S. Department of Health and Human Service, is getting into the act. In June, HHS established a public docket for input into how the department can expedite the development and approval of new drugs and biologics. HHS is seeking comments on the following topics:

Strategies HHS could implement to accelerate the development and application of new technologies;

Ways HHS can help its operating agencies work together more effectively to eliminate obstacles to the development of novel technologies;

How HHS scientific and regulatory agencies can cooperate more effectively with CMS to eliminate obstacles to development; forums HHS should use—such as public meetings, contract research organizations and focus groups, etc.—to survey constituents about obstacles to innovation;

Optimizing the portability of information between HHS agencies;

Policies and programs that spur innovation, as well as those that pose obstacles to innovation; and

The role of nongovernmental partners in assisting the federal government in the process.

Interested parties may submit written comments to the Division of Dockets Management, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Electronic submissions can be made at www.fda.gov/dockets/ecomments. Comments will be accepted through Aug. 23.

U.S. FDA

FDA Rescheduled GMP Meeting

The U.S. Food and Drug Administration (FDA) announced that a public meeting on its current good manufacturing practice (cGMP) regulations has been rescheduled for July 19. FDA previously announced three public meetings intended to obtain comments about the cGMPs, the first to be held on June 11. However, the meeting was postponed due to the closure of all federal agencies in observance of the death of former U.S. President Ronald Reagan.

The rescheduled meeting will be held in College Park, MD, on Monday, July 19, 2004, from 9 a.m. to 12 p.m.

FDA also announced the cancellation of the public meeting originally scheduled for July 2, 2004, in Monterey, Calif. A new date will be announced. The public meeting scheduled for July 21, 2004, in Chicago, Ill., will occur as originally planned.

FDA is soliciting the comments as it works on revisions to the regulations. FDA believes that public comments may be useful in determining appropriate revisions to the cGMP regulations.

FDA Makes ICH “Q1E” Official

In June, FDA published the International Conference on Harmonisation guidance, entitled, “Q1E Evaluation of Stability Data.” The document provides recommendations on how to use stability data generated in accordance with the principles detailed in the “parent” ICH guidance, “Q1A(R2) Stability Testing of New Drug Substances and Products,” to propose a retest period or shelf life in a registration application. This guidance describes when and how extrapolation can be considered when proposing a retest period for a drug substance or a shelf life for a drug product that extends beyond the period covered by available data from the stability study under the long-term storage condition (long-term data).

The guidance covers:

The evaluation of stability data that should be submitted in registration applications for new molecular entities and associated drug products.

Recommendations on the establishment of retest periods and shelf lives for drug substances and drug products intended for storage at or below *room temperature*. Stability studies using single- or multifactor designs and full or reduced designs.

It is recommended in the document that ICH Q6A and Q6B, product specifications, be consulted for recommendations on the setting and justification of acceptance criteria, and ICH Q1D, bracketing and matrixing, be referenced for recommendations on the use of full- versus

reduced-design studies. A link to Q1E is available at the in the regulatory news archive at www.pda.org/regulatory/RegNewsArchive.html.

FDA Postpones SPL Formatting Deadline

FDA has pushed back the timeline for implementing its structured product labeling (SPL) file format requirement, effectively extending the deadline for companies to begin using the new standard when submitting drug-labeling data.

The change from portable document format (PDF), the current labeling specification, to SPL will require a longer transition period stretching from June 8 to roughly about the middle of next year, said Randy Levin, director for health and regulatory data standards and associate director for medical information at the FDA's Center for Drug Evaluation and Research. As a result, the year-end deadline originally envisioned by the FDA will be extended by at least six months.

The actual date for the shift to SPL is being pegged to the launch of the electronic labeling information system, which reviews the content of label changes to prescription drugs. That system is expected to be up and running by mid- to late June 2005, said James Rinaldi, the FDA's chief information officer. The transition date to SPL for the labeling data of all drugs is planned for 2006, when the electronic listing system, which will include product codes, is fully functional, said Levin.

FDA Cancels Part 11 Meeting

The June 11 FDA meeting on 21 CFR Part 11 was called off in observance of the national day of mourning for former U.S. President Ronald Reagan. The meeting was not rescheduled. The public docket for comments on the rule, remained open, however, but closed in early July.

FDA Publishes Med. Imaging Guides

In June, the FDA Center for Biologics Evaluation and Research (CBER) and Center for Drugs Evaluation and Research (CDER) published a three-part guidance on medical imaging drug and biologic development. Part 1 covers safety assessments, part 2 covers clinical indications, and part 3 addresses clinical studies. Links to the documents are available in the regulatory news archive at www.pda.org/regulatory/RegNewsArchive.html.

FDA Guidance Clarifies Botanical Drug Regs

In July, CDER published a final guidance covering botanical drug products. The document explains when a botanical drug may be marketed under an over-the-counter (OTC) drug monograph and when FDA regulations require approval for marketing of a new drug application (NDA). The guidance also provides sponsors with guidance on submitting investigational new drug applications (INDs) for botanical drug products, including those botanical products (or *botanicals*) currently lawfully marketed as foods (including

conventional foods and dietary supplements) in the United States. CDER also made available a new Manual of Policies and Procedures (MAPP) concerning the review of new botanical INDs and NDAs. The MAPP is intended to ensure quality and consistency in the review of botanical products. Links to the documents are available in the regulatory news archive at www.pda.org/regulatory/RegNewsArchive.html.

EMEA

EMEA Supports Orphan Transparency

In June, the European Medicines Agency (EMA) Management Board approved a proposal to publish the name of the active substance, the orphan condition and the name of the sponsor for all designated orphan drugs submitted for marketing authorization.

The Board met to consider the "EMA Road Map to 2010," a document outlining the Agency's strategy to further develop as one of the leading regulatory authorities that is public health oriented, science driven and transparent in the way it operates (*see the PDA Letter, June 2004, "Regulatory Briefs, p. 25*). Focusing on how to improve transparency, communication and information to patients in its discussion the Board welcomed the Agency's initiative for a European communications strategy that focuses on the information needs of patients, healthcare professionals and the public in general. The Agency put forward 23 recommendations in October 2003 to promote transparency and communication, including the provision of information on applications for new medicines for the treatment of rare diseases ('orphan drugs').

As part of its corporate governance role, the Management Board adopted a new financial regulation and implementing rules for the EMA. These bring the EMA rules in line with those of other EU bodies. One important change in the rules will help the long-term financial stability of the EMA, which will now for the first time be entitled to establish a financial reserve in years when there is a surplus of fee revenue.

The Board also revised the fee implementing rules. The new rules, which come into force on 11 June 2004, now include fees for certification of plasma master files and also changes that reduce the fee burden for companies involved in parallel distribution of centrally authorized medicines.

The next meeting of the Management Board is on 30 September 2004.

Williams, from page 18

provide an authoritative view, but are not 'standards' applicable to an article unless they are specifically referenced in a monograph for that article.

There are a lot of synergies between the guidances and the standards of USP. If you go back again to what a product standard is, there is some general information that appears in a monograph, but then the bulk of a monograph and the related general chapters are the specifications for the article—the specification being the test, procedures and acceptance criteria. USP has a general goal, to the extent possible, that the private specification becomes the public specification.

One of the ways to achieve this is to get away from is the 'one size fits all monograph' because when that is the goal, it becomes difficult for five different private specifications to become a single public standard. That relates to some of the information I provided earlier [*Editor's Note: see the first installment of this interview in the May PDA Letter, cover*]. Many times, general

chapters provide techniques that can become procedures in a particular test provided in a monograph. For example: Dissolution. If you look at <711>, dissolution has a lot of apparatus and media that form the technique of dissolution. <711> also provides a 'study design and analysis' approach with acceptance criteria. The end result is a general procedure. But a specific manufacturer must adapt the general technique and procedure to their specific dosage form so that it satisfies the Performance test of the monograph. For dissolution—and particularly for modified release dosage forms, USP has generally recognized that the dissolution procedures in a single monograph may need to differ. This may become increasingly true for other monographs as ingredients and dosage forms become more complex.

So how is that useful to a manufacturer working with a regulatory agency? Procedures or techniques in the *USP-NF* can be used as much in development as in post-marketing control. When you are building a dosage form, USP dissolution approaches can be used to study the dosage form. This information then becomes part of characterization studies that can be incorporated in an application to support a private specification. In this regard, USP has created maps of the general chapters in USP27-NF22 that are designed to help all manufacturers understand the value of general chapters both in development and control. The texts thus provide 'off-the-shelf' approaches beyond dissolution that must surely be of assistance of all manufacturers. The end result is some kind of continuous cycle between public general approaches that support private specifications that in turn support public ones. When it works, it can work very well.

For example, if you look at the [U.S. FDA draft guidance on chemistry, manufacturing and control submissions for drug products] that just came out from the agency last year, there is a lot of allusion in there to USP. Now, if USP has a monograph for an excipient, the application requirement may generally be satisfied. There may need to be some additional information, but the monograph should provide a validated set of tests, procedures and acceptance criteria for the excipient. In this setting, the USP document can assist both manufacturers and reviewers in advancing the availability of safe, effective, good quality dosage forms.

PDA: USP General Information Chapter <1208> addresses isolator technology, as does PDA Technical Report #34. What makes USP preferable if the USP is more general and the technical report is more specific?

Dr. Williams: There is another aspect to it. Let's say there is a monograph that alludes to an isolator system referenced in a General Chapter. In this instance, the monograph makes the general chapter official for that particular article. We talk

continues on page 24

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Williams, from page 22

about general chapters above 1000 as being interpretative, informative, authoritative, but as independently derived publications of unbiased experts, they can also be made mandatory by third parties. But in direct answer to your question—I see only synergy between the USP and PDA approaches, just as there should be synergy between a TR and an FDA guidance. Probably the larger question is one of detail—the TR could provide more detail. I suppose TRs could also become a requirement if a regulatory body adopted them by reference or if a manufacturer cited them in one of their SOPs. But at heart, PDA may not want to aspire to be a standards-setting body, just as USP shouldn't try to duplicate the kind of excellent service that PDA provides to its members.

PDA: Do you think that is where the confusion comes in industry where they say FDA comes in and enforces general chapters?

Dr. Williams: There is confusion, but the General Notices section of the USP-NF clarifies this for the most part: General chapters above 1000 are not mandatory so far as it relates to FDA. However, they can become mandatory, in my mind, in at least three ways:

One: It is referenced in a monograph.

Two: FDA or another regulatory body refers to it in regulation or law as a standard, or

Three: A company puts it in their own SOPs to conform to cGMPs. In the latter case, they also could use a PDA technical report.

PDA: Could a company reference a PDA technical report in a monograph?

Dr. Williams: A manufacturer could amplify a monograph by referencing a PDA technical report in their private specification and approach. In so doing, it becomes mandatory and subject to inspection.

PDA: PDA has been working on cold chain management for the shipment of temperature sensitive biologics and other drug products. The effort has been led by Eli Lilly's Rafik Bishara. USP has been working on similar issues for over a decade. How do you see PDA's effort fitting in or complementing USP's efforts? Would USP be receptive to having PDA technical reports and guides incorporated into the Compendia?

Dr. Williams: My view is whatever synergies that can be promoted should be. Now basically USP drew upon a broad range of talented experts like [Dr. Bishara] to serve on our Project Team on Packaging, Storage and Distribution. They did an excellent job, and their work can help guide USP in coming years. They published their deliberations as a stimuli article in the

Pharmacopeia Forum [May-June 2003]. It is an excellent article, which I read it with great pleasure. The team executed a HACCP [hazard analysis and critical control point] analysis of how a drug in its packaging moves from the point of manufacturing to the point of use by the patient. Now, a HACCP analysis looks at severity of risk and frequency of risk. Essentially a lot of the risk in HACCP analysis is associated with repackers. And of course a pharmacy in some ways repacks when they dispense it in the little yellow vial. That committee worked very well.

USP is creating General Chapters in this entire area. Some of these general chapters have been contentious. Probably the most contentious one is on labile preparations. It is under continuing discussion. How this all flows out into a coherent way in this cycle and the next cycle remains to be determined. I hope PDA stays involved in this

undertaking, given the considerable expertise of your organization.

PDA: Now, a little history: Many changes occurred at CDER while you were there. You've been credited for establishing the Office of Pharmaceutical Science, spearheading the SUPAC [scale-up and post-approval changes] initiative and bringing to industry a vision of a "product quality research

initiative", which of course has become the Product Quality Research Institute. Which of your many accomplishments with FDA do you look back upon and feel has made the greatest difference in the industry and for the U.S. public at large?

Dr. Williams: I had some wonderful years at the agency at a time of great ferment. I suppose the main thrust that I championed related to the use of applied regulatory research to support and undergird regulatory policy. That is exactly what PQRI [Product Quality Research Institute] is suppose to be doing—It is suppose to be doing applied regulatory research to support the agency's guidances. And every time we put out a guidance, there was a lot of underlying science discussion that informed the guidance. One problem is that research takes a long time. But I always felt that you couldn't delay a guidance while you did research for five years because industry needs to know now what to do and guidances can be refreshed and updated later based on new information.

An interesting example was the problem of gelatin capsules forming pellicles in dissolution media. Understanding the problem took a lot of research, and it was a very interesting resolution. That entire matter could have been much more problematic to industry, but FDA used applied regulatory research, working closely with industry,

GENERAL CHAPTERS ABOVE 1000 ARE NOT MANDATORY SO FAR AS IT RELATES TO FDA. HOWEVER, THEY CAN BECOME MANDATORY, IN MY MIND, IN AT LEAST THREE WAYS:

and actually solved the problem in a good way for both the agency and the industry.

PDA: PQRI has been in operation for four years, how do you feel with your “child” out there? Are you proud of it?

Dr. Williams: I went to a recent steering committee and I told them I was very impressed with the way they set it up to function and to create a forum for dialogue. Some of the technical committees and working groups are doing very well and will continue to do so. If I had any particular concern, it is that PQRI has always struggled to get the resources it needs. Now, in its forming years, the idea was that industry itself would support it, and maybe that was a view that needs to be supplemented or expanded now. I see no reason why the federal government shouldn't provide some funding, or maybe there are other sources of funding. But it has actually done very well on constrained resources and a lot of ‘sweat equity’—you know people volunteering a lot of their time. These are extremely busy people and I always admire the people who have day jobs and then they come down and do all this other stuff.

PDA: What is your opinion on the FDA aseptic concept paper, which went to a PQRI working group, whose recommendations, in turn, were used by FDA to create a draft guidance?

Dr. Williams: That is an interesting use of PQRI where the group was used as a sounding board. There are substantial challenges in building consensus, because the Steering Committee is based on trade association representation. Getting consensus within a trade association might be as difficult as getting consensus at PQRI. I hope PDA's members see a correspondence between the Stakeholder Forums and Project Teams, which can function in similar ways vis-à-vis the Council of Experts. I'm also pleased that PQRI can provide information to support the work of the Council of Experts. USP has staff and Council experts on some of the working groups. That is an approach that I would like to see expanded.

PDA: Finally, what would you say to PDA members who aren't sure of USP's role or relevance to their professions? What advice would you give those who want to become involved?

Dr. Williams: If I can become very philosophical at this point, I would like to talk about social contracts. For citizens of the United States, our social contract began in 1776 [The Declaration of Independence]. That social contract has endured to the present and has had success that the founding fathers could hardly have imagined.

USP has a different, yet quite complementary social contract. It is based on getting practitioners together to create standards that they agree to abide by. Now, that social contract began in 1820

for USP and continues on to this day. As long as people in industry accept this social contract, it becomes a very powerful way for them, if you will, to take control of their own destiny. It is not something that is imposed on them from the federal government. It is something that they themselves create. And I would hope that PDA members continue to support USP. Most importantly now, PDA members should sign on to become members of the Council of Experts [www.usp.org/volunteer/nominate].

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Standards help ensure
products are made
correctly batch after
batch after batch by
all manufacturers**

USP is an independent body that allows the standards-setting process to occur at the grassroots level. Now some people would say, why do you need public standards? I would argue that public standards are extremely valuable for many reasons, not the least of which is that practitioners and patients should see the standards for

the articles they use in daily practice—the medicines that are prescribed, dispensed and administered. Without USP, it all would be opaque and behind closed doors. Good public standards, on the other hand, demonstrate to the public at large [that medicines are manufactured] to very rigorous standards. USP standards, in a sense, support commercial transactions—and in this case I'm speaking about the practitioner writing a prescription for a patient and the patient going to the pharmacy to get the medicine and then taking it. [For most commercial products,] we don't see the standards, but given the [nature] of healthcare and medicine, isn't important for people to see those standards?

PDA: When you say practitioners, you are no longer referring just to doctors and pharmacists?

Dr. Williams: No, if you go back to the early pharmacopeia, it contained recipes for therapeutic products that were compounded by professional practitioners of the day. Now those people have been supplanted, for the most part, by people like your membership, manufacturers who make excellent and increasingly sophisticated therapeutic products.

PDA: What advice do you give to PDA members who want to be involved with USP?

Dr. Williams: Volunteer for our committees, that is one. Watch for stakeholder forum opportunities. Pay attention to PF and of course to USP-NF. I am delighted to not that George Robertson [PDA VP, Science and Technology] will be PDA's formal representative to the Prescription/Non-Prescription Stakeholder Forum.

PDA: Dr. Williams, PDA and all its members thank you for taking time to answer these questions. We look forward to continuing working with you and USP in the future.

PDA Chapter Focus: Canada Chapter

“Bingo!” cried a woman in a black business suit as she made her way to the side of the exhibit hall amidst sighs from the men and women still holding tickets in their hands. After placing her hands on the M3P Player, she gave a quick smile to the presenter and shuffled triumphantly back to her spot near the door.

Her excitement echoed that of others attending the prize drawing following the Canada Chapter’s “2004 Conference on Current Regulations and Compliance” held on April 26, 2004 at the Holiday Inn in Montreal, Quebec, Canada. More than fifty people attended the event. But the excitement wasn’t bred by prize drawings alone.

The conference featured several speakers covering a variety of topics about current regulation and compliance issues. Speakers included: France Dansereau, Manager of Drug GMP Inspection Unit, Compliance and Enforcement Coordination Division, Health Products and Food Branch Inspectorate, Health Canada; Stephen Desroirs, Projects Director, Sabex, Inc.; Harvey Greenawalt, President, Audit Repository Center, LLC.; Jeff Priem, Principal Consultant, Barnett International; and Peter Woodhouse, Professional Engineer, SNC Lavalin Pharma, presenting on behalf of Warren Campbell, independent industry consultant.

“The Chapter wanted to provide a valuable meeting for the PDA members in this region,” said Chapter President Hein Wick (HWMR Ltd.).

Attendees circulated through vendor exhibits during breaks in the sessions and took part in a cocktail hour following the conference. Nothing, however, trumped the overall quality of the presentations for the attendees.

“I feel that professionals can regard the PDA Chapter meeting as an essential annual update on pertinent issues as well as an opportunity to reestablish contacts and share ideas with the local community,” stated Jeffrey Brooks, President, Kinsale Consulting, Inc., in a letter dated May 26.

“I FEEL THAT PROFESSIONALS CAN REGARD THE PDA CHAPTER MEETING AS AN ESSENTIAL ANNUAL UPDATE ON PERTINENT ISSUES AS WELL AS AN OPPORTUNITY TO REESTABLISH CONTACTS AND SHARE IDEAS WITH THE LOCAL COMMUNITY,”

The conference had a special meaning for Chapter officers because many of them were meeting each other face-to-face for the first time. Planning for the conference followed the Chapter’s elections and a few of the newly elected officers had only officially met via conference calls. (The Chapter holds meetings in Montreal and Toronto on an annual basis, often alternating between the two cities. Vancouver, British Columbia, is also under consideration for the annual meeting for 2006.)

“It was fantastic placing faces with names after all the time we spent planning and coordinating with each other,” said a newly-elected Vagiha Hussain (Chapter Treasurer) QA Validation

Manager, Serologicals Biomufacturing Corp.

Chapter officers discussed their new plans to promote free seminars to take place several times a year (starting this year) as a way to acquaint more people with PDA and the PDA Chapter events in Canada.

Holding these seminars goes hand-in-hand with the *PDA Points Program*,

achieving a goal the Chapter set for the upcoming year.

Past-Chapter President Grace Chin (SNC Lavalin Pharma) helped PDA with the PDA Chapter Points Program “from the beginning so I think the Canada Chapter will definitely be more involved with the *Program* in upcoming months,” Wick said.

The other Canada Chapter officers are: Chapter VP Patrick Bronsard (SNC Lavalin Pharma), Chapter Secretary Ronald Marchesani (Shire Biologics), Chapter Program Chair Jacques Pilon (Validapro Inc.), and Chapter Program Chair Arun Malaviya (Bimeda MTC Animal Health, Inc.).

For more information about the PDA Canada Chapter, please contact KiKi Coffman, Chapter Coordinator, at coffman@pda.org. Soon you will be able to visit the Chapter’s Web site at: www.pdacanada.org, which is currently under development.

By KiKi Coffman, Chapter Coordinator

2004 CHAPTER EVENTS CALENDAR

Please visit www.pda.org/courses/index.html for lodging, registration, and event description information.

August

- 5-6 **Japan**
Topics & Current Tendency of QA/QC & Reg.
—Engineering Course for GMP
Tokyo, Japan
- 9 **India**
PDA Course on Pharmaceutical &
Biopharmaceutical Inspections
Mumbai, India
- 19 **Midwest**
Modern Consideration for Test Method
Validation
Northbrook, Illinois

September

- 2-3 **Japan**
Education & Training courses: "API GMP &
Qualification/Validation," "How to prepare &
receive FDA Inspection"
Tokyo, Japan
- 9 **Southern California**
Compliance with FDA Change Control
Regulations & Validation Management
Irvine, CA
- 22 **Delaware Valley**
Aseptic Processing
Malvern, PA

October

- 1 **New England**
Workshop on Combination Product
Development
Cambridge, MA
- 6-7 **Central Europe**
Visual Inspection Course
Berlin, Germany
- 18-19 **Italy**
Biosafety Forum
ISPE/AFI/PDA Meeting
Rome, Italy
- 18-19 **Central Europe**
The Universe of Pre-filled Syringes
Hannover, Germany

October (cont.)

- 19 **Israel**
Seminar: Process Validation
Tel Aviv, Israel
- 20 **Southeast**
Annual Fall Meeting
Research Triangle Park, NC
- 25 **Spain**
Science-, Risk-Based Approach to
Validation
Barcelona, Spain
- 27 **UK & Ireland**
Biotechnology Conference
OSI Pharmaceuticals
Oxford, England

November

- 9-10 **Japan**
Japan Chapter Annual Meeting
Tokyo, Japan
- 17-19 **Central Europe**
Aseptic Processing Course
Basel, Switzerland
- 17 **Delaware Valley**
Environmental Monitoring
Malvern, PA
- 19 **Metro**
Current Compliance Trends
Clark, NJ
- 19 **Midwest**
Rapid Methods
Northbrook, IL

December

- 6-7 **France**
New Success Factors for Bio/
Pharmaceutical Manufacturing in Europe
Paris, France
- 27 **Israel**
Annual Meeting
Tel Aviv, Israel
- TBD **New England**
Dinner Seminar on PAT
Cambridge, MA

New member contact information is forwarded to Chapters on an ongoing basis. For immediate notification of Chapter events, please contact your local representative and ask to be placed on the Chapter mailing list.

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LTR 07/04

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Manufacturing: Last Barrier on “Critical Path”

PDA/FDA Joint Conference to Address Important Component of the Critical Path Program

The 2004 PDA/FDA Joint Regulatory Conference will feature more than 25 FDA officials who will discuss the evolution of the “21st Century” risk-based cGMP initiative and the steps FDA will take to implement new policies and guidances. Ample time will be provided during the conference for questions and answers. Among the senior FDA officials involved with the 21st Century initiative appearing at the meeting are:

- David Horowitz, Director, Office of Compliance, CDER
- James Cohen, Associate Director, Office of Compliance and Biologics Quality, CBER, and
- Joseph Famulare, Director, Division of Manufacturing and Product Quality, OC, CDER.

September marks the two-year anniversary of the 21st Century quality initiative and the close of the policy development phase. As such, the conference will cover various elements of the initiative, including FDA’s risk-based quality system approaches to regulation, regulatory relief for new technologies, new expert pharmaceutical inspection teams, new communication and dispute resolution systems, and the international cGMP harmonization.

Manufacturing on the Critical Path

The importance of the 21st Century initiative was elevated recently when an FDA committee identified the switch from laboratory production to full-scale industrial manufacturing as a large barrier on the “Critical Path” from drug discovery to marketing authorization.

FDA announced that “Critical Path” initiatives will be developed to “fix” the pharmaceutical, biopharmaceutical and medical device “pipeline problem”—the declining number of new medical therapies. The “pipeline problem” is particularly acute for pharmaceutical and biopharmaceutical

therapies with a sharp decline in the number of submissions for new chemical entities and biologics products over the last ten years in spite of a sharp rise in private and public research and development budgets.

A report titled “Challenge and Opportunity on the Critical Path to New Medical Products,” published by FDA’s Office of the Commissioner in March, targets for reform the safety, efficacy and manufacturing components of the submission process in order to correct the “pipeline problem.” The report notes that the transition from laboratory prototype to industrial product one area of the drug development process where “many product failures” occur. As such, FDA writes, the 21st Century quality initiative is identified as a key initiative in FDA’s effort to facilitate more new product submissions.

The 21st Century Initiative

FDA launched the 21st Century quality initiative in September 2002 to overhaul its cGMP and Chemistry, Manufacturing and Control (CMC) regulations. The emphasis of the initiative has been to establish a risk-based quality systems approach to the regulations and inspection practices in order to facilitate the adoption of modern manufacturing and control technologies by the pharmaceutical and biopharmaceutical industries, i.e., PAT.

Several draft cGMP and CMC guidances related to the initiative were released at the initiative’s one-year anniversary in September 2003. FDA anticipates those drafts will be final for implementation at the two-year anniversary this September. FDA also will have an expert group of pharmaceutical inspectors—known as the pharmaceutical inspectorate—in place, as well as new warning letter and other communications procedures.

PDA/FDA Joint Regulatory Conference Exhibitors

ACCUGENIX	Genesis Machinery	Phoenix Imaging	Virtis an SP Industry
American Stelmi	Products	PML Microbiologicals	Company
Applied Biosystems	ITW Texwipe	Prudential Cleanroom Svcs.	VTS Consultants, Inc.
BD Diagnostics	Lloyd’s Register	PSI	
BioScience International	Serentec	Quality is Learned, Inc.	
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Charles River Laboratories	NovaTek	Sparta Systems, Inc.	
Clarkston Consulting	Noverant	Vectech Pharmaceutical	
Drumbeat Dimensions, Inc.	Pall Life Sciences	Consultants, Inc.	
General Physics	PharmaSys, Inc	Veltek Associates, Inc.	

PROGRAMS AND MEETINGS CALENDAR

Please visit www.pda.org/courses/index.html for lodging, registration, and event description information.

2004	2005
<p>July</p> <p>22 Audio Conference: Implementing a Global Risk Standard to Assess Risk and Improve Quality Processes</p> <p>28 Audio Conference: Justify ROI and Obtain Management Buy-In for Rapid Microbial Methods</p> <p>September</p> <p>7-8 PDA/BFS Inter'l. Operators Association Joint Workshop on Blow/Fill/Seal Processing Holopack Verpackungstechnik GmbH, Germany</p> <p>9 PDA Audio Conference: "GERM 3: Models Document"</p> <p>20-24 2004 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits: The New Guidances Omni Shoreham Hotel, Washington, D.C.</p> <p>November</p> <p>TBD PDA Regulatory Summit Brussels, Belgium</p>	<p>February/March</p> <p>28-2 PDA International Congress, Courses & Exhibitions Rome, Italy</p> <p>April</p> <p>4-8 PDA Annual Meeting, Courses and Exhibitions TBD</p> <p>May</p> <p>16-18 PDA Viral Safety Conference TBD</p> <p>September</p> <p>12-16 2005 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits Washington, D.C.</p> <p>October</p> <p>TBD Taormina Conference Taormina, Italy</p>

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2004 TRAINING AND RESEARCH INSTITUTE CALENDAR

Please visit www.pda.org/courses/index.html for lodging, registration, and course description information.

Laboratory Courses

August

9-11 Developing a Moist Heat Sterilization Prgm Within FDA Requirements

16-20 Aseptic Processing Training Prgm: Week 1

September

1-3 Adv. Environmental Mycology Workshop

13-17 Aseptic Processing Training Prgm: Week 2

October

4-8 Aseptic Processing Training Prgm: Week 1

14-15 Fundamentals of D, F, and z Value Analysis

18-22 Rapid Microbiological Methods

25-27 Designing, Operating, and Controlling High Purity Water Sys for Regulatory Compliance

November

1-5 Aseptic Processing Training Prgm: Week 2

11-12 Developing and Validating Cleaning & Disinfection Prgms for Controlled Env'n.

15-17 Cleaning Validation

18-19 Remediation of Existing Computer Sys

December

2-3 Environmental Mycology Identification Workshop

6-7 What You Need to Know to Select Adequate Thermal Validation Equipment

Lecture Courses

August

23-27 CGMP Trainer's Qualification Prgm
PDA-TRI, Baltimore, MD

September

6-8 Pan European
Fundamentals of Aseptic Processing
UBS Ausbildungs-und Konferenzzentrum
Basel, Switzerland

7-8 PDA-BFS Joint Workshop on Blow/Fill/Seal
Processing
Schwabish Hall
Sulzback-Laufen, Germany

October

4-5 Visual Inspection
Location TBA
Berlin, Germany

December

6-7 Computer Products Supplier Auditing Process
Model: Auditor Training

Course Series

August-September

30-1 Chicago, Illinois

A Comprehensive Guide to OOS Guidance & Regulations
A Practical Approach to Aseptic Processing
& Contamination Control

Assessing Packaging & Processing Extractables/Leachables
Pharmaceutical Water Sys: A Practical Approach
Preparing for an FDA Pre-Approval Inspection
CGMP & Compliance

Application of Clean-In Place to the Pharmaceutical Industry
Environmental Monitoring in Pharmaceutical Manufacturing
Risk Management

Z1.4 Attribute Inspection Sampling in a GMP Environment

September

20-24 2004 PDA/FDA Joint Reg. Conference,
Courses and Tabletop Exhibits
Washington, DC

Change Control & Documentation

Auditing Pharmaceutical Microbiology Laboratories

Basic Concepts in Cleaning & Cleaning Validation

Compliance Auditing of Cleanrooms and Controlled
Environments

Qualification and Validation of API Manufacturing Ops.

Auditing Techniques for CGMP Compliance

October

18-20 Boston, Massachusetts

Analytical Problem Solving for CAPA Sys.

Design and Validation of a Cleaning & Disinfection Prgm

Intro. to Writing and Auditing CGMP Doc.

CGMPs for Bioprocesses

Pharmaceutical Water Sys. Design & Validation

Maximizing SOPs - An Untapped Resource of Trng. Solutions

Everything You Wanted to Know About Environmental
Monitoring but Were Afraid to Ask

Qualification and Validation of API Manufacturing Ops.

Achieving CGMP Compliance During Development of a
Biotechnology Product

Annual Product Reviews: How to Comply with
FDA & ICH Req.



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New Technical Resources, from cover

Considering the qualifications and expertise of the authors, this book should prove to become an invaluable resource for all those in the communities concerned with quality assurance/quality control, regulatory affairs, production and training. Essays were provided by health authority experts, senior industry officials, consultants and academics. **[Editor's Note: See page 35 for a complete list of authors.]**

Pharmaceutical Quality was skillfully edited by PDA member Richard Prince, PhD, who brought a wealth of pharmaceutical and biopharmaceutical quality control experience to the project. Dr. Prince currently consults for the biopharmaceutical industry.

In 2001, he was the editor of the PDA/DHI, *Microbiology in Pharmaceutical Manufacturing*, which to this day remains PDA's best selling book.

Pharmaceutical Quality is divided into three sections. The first includes ten chapters that provide an in-depth review of the quality control expectations in Australia, Britain, Canada, Germany, Israel, Japan, Singapore and the United States. The second section of the book, encompassing six chapters, focuses on industrial "quality systematics," a term describing the interplay of quality systems in commercial pharmaceutical manufacturing. The third section of the book contains four chapters on the perspectives of quality from top industry thought leaders.

PDA members can purchase *Pharmaceutical Quality* at the PDA E-store (www.pda.org/estore) for US\$240. Nonmembers can buy the book for US\$299. Government employees receive a substantial discount and can purchase the book for US\$160.

A recent addition to the PDA/DHI library is *Cleanroom Clothing Systems*, by longtime PDA contributors and cleanroom experts Bengt Ljungqvist, PhD, Professor, Swedish Royal Institute of Technology, and Berit Reinmuller, PhD, Senior Researcher, Swedish Royal Institute of Technology. Over the years, the two experts have teamed up to help the pharmaceutical and biopharmaceutical communities understand how to control cleanroom environments.

In *Cleanroom Clothing Systems*, the two scientists provide a comprehensive scientific analysis of this critical aspect of environmental control. This book provides detailed specifications on various "clean" garment systems. Increasing cleanliness demands in a variety of industries require an in depth knowledge of the performance of modern cleanroom clothing systems. This superb set of

observations from case studies performed in a dispersal chamber, or "body box," will help manufacturers determine the effectiveness of the clothing systems used at their facilities.

Cleanroom Clothing Systems covers testing methods, test series, source strength, test results, presentation of the Results, and guidelines for pharmaceutical production from the European Union, United States and the International

Organization for Standardization. This book promises to be an indispensable resource for the aseptic processing operator and manager, as well as all the production, QA/QC and validation professionals involved with the processing of

sterile medicines in a cleanroom environment. (Editor's Note: This book was originally published in May, but is being re-released due to a publishing error.)

PDA members can purchase *Cleanroom Clothing Systems* at the PDA E-store (www.pda.org/estore) for US\$135. The nonmember rate is US\$169 and the government rate is US\$75.

PDA members are encouraged to visit the PDA E-store to learn about all the PDA/DHI books available, including the following titles that were added to the PDA/DHI library in 2003:

- *The Essence of GMPS: A Concise Practitioner's Guide*, U.G. Barad;
- *Excellence Through Validation: A Practitioner's Guide*, U.G. Barad;
- *Filtration Handbook: Integrity Testing*, Maik Jornitz and Theodore Meltzer;
- *Quality and Safety of Gene Medicines: A Practical Guide*, Anthony Meager;
- *Laboratory Validation: A Practitioner's Guide*, Jeanne Moldenhauer;
- *Commercial Off-The-Shelf Software Validation for 21 CFR Part 11*, David Nettleton and Janet Gough;
- *Rapid Analytical Microbiology: The Chemistry and Physics of Microbial Identification*, Wayne Olson; and
- *Supply of Chemicals in the Pharmaceutical Industry: Regulatory Guidelines and Rulings*, Mark Selby.

One of the most substantial contributions PDA members have made to the communities over the years has been the publication of the PDA technical reports. In total, PDA has published 36 technical reports on a wide variety of subjects relating to pharmaceutical production, validation and quality assurance.

CONSIDERING THE QUALIFICATIONS AND EXPERTISE OF THE AUTHORS, THIS BOOK SHOULD PROVE TO BECOME AN INVALUABLE RESOURCE FOR ALL THOSE IN THE COMMUNITIES

These reports are put together by PDA task forces, which are assembled by the PDA Science Advisory Board or the PDA Regulatory Affairs and Quality Committee. Task forces are composed of PDA members with expertise in the area under consideration and representing a wide-swath of the PDA membership, i.e., industry, government, academia, large and small companies, and multiple countries. In order to be published, a technical report must be approved by the appropriate committees and the PDA Board of Directors.

In the coming months, two new technical reports and two newly revised reports will be available. In what represents a major elevation of the service PDA provides to its non-U.S. members, PDA has just published four technical reports in Chinese. These valuable PDA resources are even more valuable when available in our member's native tongues. From now on, PDA members in Asia who speak Chinese can benefit from having the following documents translated into their language:

- PDA Technical Report #26: *Sterilizing Filtration of Liquids*;
- PDA Technical Report #29: *Points to Consider for Cleaning Validation*;
- PDA Technical Report #33: *Evaluation, Validation and Implementation of New Microbiology Testing Methods*; and
- PDA Technical Report #35: *A Proposed Training Model for the Microbiological Function in the Pharmaceutical Industry*.

The Chinese versions of these documents are available to PDA members for only US\$75 and to government officials for US\$30. The nonmember rate is US\$550.

PDA is adding to its conference proceeding offerings in 2004. To date, proceedings from the following conferences have been published:

- 2004 PDA International Congress, Basel, Switzerland;
- 2004 PDA SciTech Summit and Annual Meeting, Orlando, Florida;
- 2004 PDA Singapore Conference; and
- PDA/IABs 2001 Proceeding – Process Validation for Manufacturing of Biologics and Biotechnology Products, Berlin Germany.

All these can be purchased at the PDA E-store (www.pda.org/estore).

Missed a PDA audio conference? You can purchase transcripts and audio compact disks at www.pda.org/audio/past.html. Topics covered so far this year include barcodes, risk-based validation, and product recalls.

Video and interactive computer-based training is another career-long learning opportunity available to PDA members. Through a special arrangement, two professional training companies—Micron Training and Shepherd

Training—offer their videos and interactive compact disk (CD) products to PDA members at a significant discount.

So far in 2004, Micron Video has added twenty titles of interest to PDA members, in both the Video and interactive CD format, including: *Introduction to Lab Skills, GMP, Engineering & Maintenance*, and *Introduction to Microbiology & GMP*. Shepherd Training's 2004 new narrated systems audit CDs address technology transfer, QC laboratory operations, out-of-specification results investigations, and drug product component control.

PDA has made similar arrangements with CRC Press and Marcel Dekker with regard to their textbook offerings. Whenever a PDA member purchases a textbook from one of these companies through PDA, they receive a significant discount.

To learn more about PDA's technical resources and the discounts available to members, please visit the PDA E-store at www.pda.org/estore. Also, look for the 2004-2005 PDA Publications Catalogue which will be sent to all PDA members in the fall.

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John L. Turner, regulatory consultant

James L. Vesper, President, LearningPlus, Inc.

E. Günter Winkmann, PhD, German Institute for Medical Documentation and Information, ret.

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Pharmaceutical Quality

EDITED BY **Richard Prince**

How do you define quality?

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Is this publication for me?

If you need a comprehensive understanding of pharmaceutical quality from a variety of perspectives, **Pharmaceutical Quality** is a must-have reference guide. This book will benefit pharmaceutical and biopharmaceutical professionals, including:

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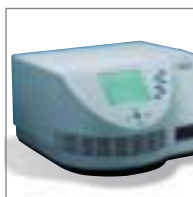
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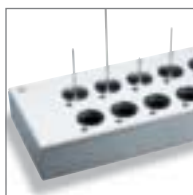
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