Volume XXXIX, No. 2

PDA Letter

February 2003

A Monthly Communication for the Members of PDA—
An International Association for Pharmaceutical Science and Technology

Kathryn Zoon, Ph.D., Moves to NIH, page 10

# PDA Presents "Dispute Resolution" Comments to FDA

PDA presented comments to the FDA at the December FDA OPS (Office of Pharmaceutical Science) Trade Association Meeting. The FDA had asked the Trade Associations to comment on FDA's dispute resolution process, part of GMP for the 21st Century, A Risk Based Approach. The working group co-chairs are David Horowitz, Director, Office of Compliance, and Helen Winkle, Acting Director Office of Pharmaceutical Science.

PDA thoughts on "Dispute Resolution" were presented by Russell Madsen, PDA Acting President. Highlights of the presentation begin on page 5.

*continues on page 5*

# PDA's Spring Conference Focuses on Biotechnology Issues

Time is fast approaching for the first-ever PDA Spring Conference that will focus on biotechnology issues for pharmaceutical manufacturers. The conference promises to provide you with updated information on regulatory requirements; the skills to identify and meet new compliance expectations; opportunities to interact with FDA representatives and the ability to benchmark with your peers from other companies.

## Changing Members

The PDA 2002 Strategic Plan Update indicates a rapid rise of biotechnology, and with it, biopharmaceutical manufacturing has drawn more and more interest from PDA members. The rapid growth of this sector supports the need for more biopharmaceutical issues in PDA conference offerings. In addition, PDA has a unique opportunity to attract from the San Diego region's numerous private and public biotech companies.

## Speakers

Thought leaders from industry and agencies have been invited to address the impact of today's regulatory environment on biopharmaceutical product development and approval. The impressive list of presenters includes:

**E.J. Brandreth** is the Senior Director of Quality Assurance at BioMarin Pharmaceuticals. In his 20 years of cell culture experience he has validated nine biotech facilities, worked on BLAs, MAAs, INDs, and both bacterial and mammalian biotech products.

**Jeffrey C. Baker, Ph.D.** Senior Research Scientist (Validation), Eli Lilly and Company, is a frequent speaker on the strategy and tactics of bioprocess development, and has been a guest lecturer in graduate programs in biotechnology in the United States and the United Kingdom.

**Patrick Shannon**, Ph.D. is Senior Director of Pharmaceutical Development at ILEX Oncology, Inc., a pharmaceutical company specializing in oncology drug development.

**Lisa Sperry** is the Director of Regulatory for Lonza Biologics, Inc. and is responsible for all Regulatory functions in a global environment.

**Anders Vinther, Ph.D.** is co-founder and Chief Quality Officer, CMC Biopharmaceuticals A/S, a contract process development and manufactur-

*continues on page 33*

**2003 PDA Spring Conference, Courses and Tabletop Exhibits**

March 17–21

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*Manager, Publications & Production*


## Important Dates...

- **March 1—deadline for Call for Papers, PDA Annual Meeting, page 33**
- **March 2—Comments on ICH Draft Guidance on M4 Common Technical Document, Quality, page 7**
- **March 17–21—PDA Spring Conference, cover**

## IN THIS ISSUE...

*Russell E. Madsen, Acting President PDA*

# PDA to Provide Regulatory Compliance Courses for the Italian Inspectorate

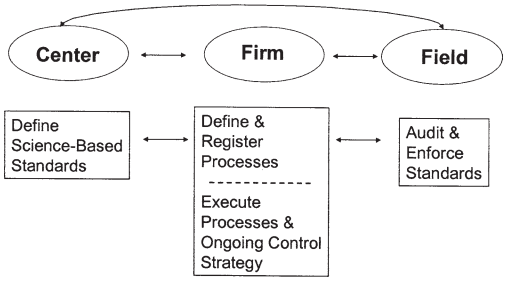
PDA has been selected to design and direct a course for members of the Italian Inspectorate. The course, entitled *Regulatory Compliance for the Italian Inspectorate*, will be delivered in Rome, Italy in 2003. The course is intended to enhance the experience of senior Italian inspectors. Through a series of courses the participants will review global GMPs, and their applications, with emphasis on European regulations. Participants will also receive training in all the major aspects of drug production, and will learn additional ways to prepare for inspections, to communicate, and to appropriately interpret regulations and assess the importance of inspectional findings. The program will bring into the Italian arena the leading PDA faculty, mostly European, with expertise in each of the topic areas. Case Study discussions will provide an opportunity to examine "real life" experiences and solutions.

The PDA effort is lead by the US PDA Headquarters, with support of the PDA Europe Office and the PDA Italy Chapter. Carmen M. Wagner, Ph.D., president of Strategic Compliance International, Inc., is the Course Director and is working closely with Dr. Carlo Pini, the Italian Government Representative for this project. Dr. Wagner and Dr. Pini are supported by an expert cadre of instructors, primarily based in Europe, and by Gautam Maitra, Director, PDA Europe and Robert J. Mello, Ph.D., VP Education from the PDA Training and Research Institute. The PDA Chapter in Italy, represented by Antonino Giannetto and Vincenzo Baselli, has also been instrumental in helping coordinate this effort. The first course section scheduled in early February, 2003, will be taught by James C. Lyda, KMI-Parexel Europe, and Joerg Neuhaus, from the German Inspectorate. ■

Overall Comments on Dispute Resolution

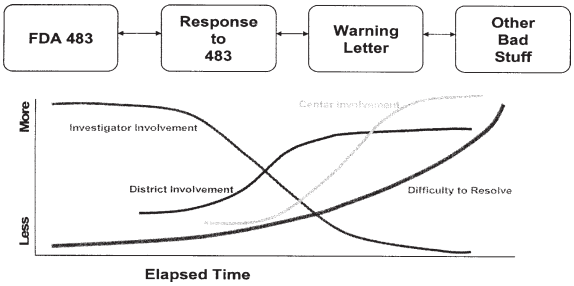
- Disputes should be resolved at the earliest time point and at the lowest possible level
- The Dispute Resolution Process should be clearly defined and easy to follow
- The ideal situation would include:
  - Clear standards
  - Consistent interpretation
  - Clear roles and responsibilities
  - Clearly identified technical decision makers

## Clearly Defined Processes, Roles/Responsibilities, and Excellent Communication are Necessary



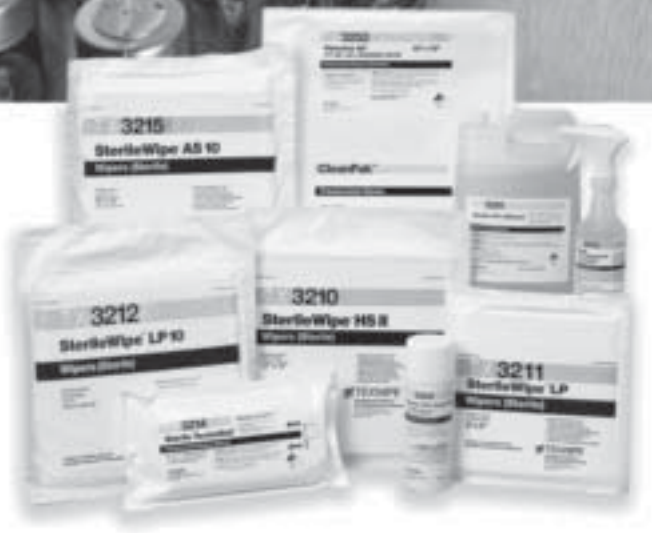

- Experience with existing dispute resolution processes
  - PDA members have examples where existing informal processes have worked well, and many examples where they have worked very poorly
  - Formal dispute resolution currently not practical or effective
  - Success largely dependent on people involved
  - Need to make the process stronger, clearer, and less people-dependent
  - Today, companies agree to approaches that lack scientific basis or do not make sense
    - Fear of retaliation/damaging relationships
    - NDAs held hostage
    - Unfortunately, this then sets precedent for other companies
- What types of issues should trigger a dispute resolution?
  - Differences in interpretation
  - Compendial issues (USP)
  - Regulations
  - Guidance
- Differences in opinion/jurisdiction between Field Operations, Office of Compliance, and Review Divisions (OPS)
  - Who is the decision maker?
  - Industry is put in a difficult position in this case
  - Need coordination and synergy between review, compliance and inspection programs
- Should there be different types or levels of disputes?
  - Yes, different levels of disputes will occur and are appropriate
  - Pre-483/Post-483/Post-Warning Letter/ Pre-OBS (Other Bad Stuff)
- Need to ensure that communication is strong at all levels
  - Ensure resolving the dispute, not resolving communication issues
  - Beneficial for the firm to have the EIR as soon as possible
  - Include key people in all conversations

## Dispute Resolution Continuum




- Who from industry should initiate the dispute resolution process?
- Category dependent
  - Pre-observation: person(s) coordinating the inspection
  - Post-observation: local or divisional QA/RA representative
  - Post-Warning Letter: divisional/corporate management
- How can we create a dispute resolution process that minimizes disruption to the inspection process?
- Process
  - Clear, easy to follow
  - Consistent and transparent
- Timelines defined
- Decision makers identified
  - Roles and responsibilities of review, compliance and field organization clearly defined
- Should dispute resolution outcomes be publicly available?
  - Yes—through Freedom of Information
- What can FDA/industry do to help prevent/ reduce disputes?
  - Disputes should be resolved at earliest time point, and lowest possible level
  - When necessary to use dispute resolution process, process must be easy to follow with defined decision makers
    - Quick resolution necessary (applications on hold)
    - No fear of retaliation when process is used
  - Improve overall process
    - Clear standards defined
    - Consistent interpretation of the standards
    - Clear technical decision makers (roles and responsibilities defined)
  - Industry has role and responsibility as well
    - Current on requirements
    - Scientifically strong
    - Use discretion when raising disputes ■

***—Russell E. Madsen and William Stoedter***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# U.S. Regulatory Briefs

***Federal Register* Notice, Published December 30, 2002: Docket No. 02N-0509, CDER 2002152. International Conference on Harmonization (ICH); Draft Guidance on the M4 Common Technical Document, Quality: Questions and Answers, and Location Issues. Comments due March 2, 2003.** This draft guidance provided further clarification for preparing the quality components of an application file in the Common Technical Document (CTD) format. This document should be read in conjunction with CTD-Q Modules 2 and 3. Content of an application is not addressed in this document, the applicants should refer to regional guidances. The draft guidance addresses:

1. The relationship between linked sections for certain parameters (such as polymorphism and particle size); and
2. Location issues, by indicating the section in which to place requested information.

Submit written comments on the draft guidance to the Dockets Management Branch (HFA-305), FDA, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments.

For further information, contact Charles P. Hoiberg, CDER, (HFD-800) FDA, 5600 Fishers Lane, Rockville, MD 20857, (301) 827-5918; or Christopher C. Joneckis, CBER, (HFM-20) FDA, 1401 Rockville Pike, Rockville, MD 20852, (301) 827-0833.

For questions regarding the ICH, contact Janet J. Showalter, Office of International Programs (HFG-1) FDA, 5600 Fishers Lane, Rockville, MD 20857, (301) 827-0864.

***Federal Register* Notice, Bioavailability and Bioequivalence Requirements; Abbreviated Applications; Final Rule 21 CFR Parts 314 and 320. Docket No. 98N-0778. Effective February 19, 2003.** The FDA is amending its regulations on Bioavailability and Bioequivalence and on the content and format of an abbreviated application to reflect current FDA policy and to correct certain typographical and inadvertent errors. This action is intended to improve the accuracy and clarity of the regulations.

The final rule changes the term "enteric coated" to "delayed release" and the term "controlled release" to "extended release." To conform to the new terminology, the final rule also amends Title 21 CFR Part 320.25 (f) by changing "noncontrolled release" to "nonextended release."

In the proposed rule it was stated that blood or urine samples should be taken on three or more consecutive days to establish that steady-state conditions have been achieved. Some comments stated that obtaining samples on consecutive days may be impractical and, for drugs with long half-lives, may be less sensitive to the establishment of steady-state than data obtained over a longer period of time. The final rule requires that "appropriate dosage administration and sampling should be carried out to document steady-state." Specific advice about dosage administration and sampling may be obtained from the appropriate review division for the drug product.

For further information, contact Christine F. Rogers, CDER (HFD-7), FDA, 5600 Fishers Lane, Rockville, MD 20857, (301) 594-2041.

**International Conference on Harmonization; Draft Consensus Guideline, Addendum to ICH E2C, Clinical Safety Data Management, Periodic Safety Update Reports for Marketed Drugs.** The FDA has posted the International Conference on Harmonization (ICH) addendum to ICH E2C for consultation at step 2 of the ICH process. At step 2 of the ICH process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Steering Committee to the regulatory authorities of the three ICH regions (the European Union, Japan, and the USA) for internal and external consultation, according to national or regional procedures.

The original guideline has been interpreted in different ways by both Marketing Authorization Holders (MAHs) and Regulatory Authorities. The objective of this addendum is to provide clear guidance for the preparation of the Periodic Safety Update Report (PSUR) as recommended in the ICH Guideline E2C entitled Clinical Safety Data Management.

The PSUR should represent a practical and achievable mechanism to summarize interval safety data, especially covering short periods (e.g. six months or one year) in order to conduct an overall safety evaluation. It is meant to serve as a stimulus for MAHs to conduct systematic analyses of safety data on a regular basis.

The guideline strongly recommends one report for one active substance. This single report would include information on all indications, dosage forms and dosing regimens. Whenever possible, PSURs should be based on the International Birth Date (IBD) of the product (approval date).

The addendum can be found at http://www.fda.gov/cber/guidelines.htm#ichsafety.

**Drug Center Ombudsman Retires.** Jim Morrison, a 38-year FDA veteran, retired as the Drug Center's ombudsman on January 3. Morrison joined the Agency in 1965 and became the Drug Center's first ombudsman in 1995, investigating citizen complaints against the FDA.

**FDA Searchable Data Base of Inactive Ingredients.** FDA has released a searchable database for information on inactive ingredients present in FDA-approved drug products. This information can be used by industry as an aid in

*continues on page 8*

*Regulatory Briefs from page 7*

developing drug products. The database can be found on the CDER Web site at www.fda.gov/cder.

**FDA Announces Smallpox Vaccine Guidance for Blood Industry.** On December 30, 2002, the FDA issued a guidance for the blood industry regarding procedures for properly qualifying potential blood donors who have recently been inoculated with the smallpox vaccine (vaccinia virus) or those who may have had other direct exposure to smallpox vaccines. These recommendations were developed in consultation with experts on the vaccine virus (smallpox vaccine) at the US Centers for Disease Control and Prevention and the Department of Defense. They are preventive measures pertaining to non-emergency smallpox vaccination. In the event of widespread emergency vaccination due to an actual or impending smallpox outbreak, the procedures outlined in the guidance could be modified to adapt to changing risk/benefit assessments and other public health considerations.

The vaccine virus is closely related to smallpox (variola virus) and induces an immune response that is protective against smallpox. The vaccine virus has been used with great success for over 100 years to protect against smallpox. FDA is issuing this guidance as a precautionary measure to reduce the very slight risk of blood borne exposure to the smallpox vaccine among certain small patient populations that may develop adverse reactions to the vaccine. Those interested in the details of this guidance will find a copy at http://www.fda.gov/cber/guidelines.htm#smpox.

# International Regulatory Briefs

**Australian Code of Good Manufacturing Practice.** The Australia Therapeutic Goods Administration has issued a Questions & Answers document on the new Australian Code of Good Manufacturing Practice for Medicinal Products. The document contains 57 questions and answers covering the following topics:

**1.** Quality Management (Chapter 1); **2.** Personnel (Chapter 2); **3.** Premises and Equipment (Chapter 3); **4.** Documentation (Chapter 4); **5.** Production (Chapter 5); **6.** Quality Control (Chapter 6); **7.** Manufacture of Sterile Medicinal Products (Annex 1); **8.** Manufacture of Biological Medicinal Products (Annex 2); **9.** Manufacture of Herbal Products (Annex 7); **10.** Sampling of Starting and Packaging Materials (Annex 8); **11.** Computerized Systems (Annex 11); **12.** Use of Ionising Radiation in the Manufacture of Medicinal Products (Annex 12); **13.** Manufacture of Investigational Medicinal Products (Annex 13); **14.** Qualification and Validation (Annex 15); **15.** Auditing and Licensing; **16.** Active Pharmaceutical Ingredients; **17.** Mutual Recognition Agreements; **18.** Imports; **19.** Wholesale; and **20.** General.

This document can be found on the Australian Therapeutic Goods Administration (TGA) Web site at www.health.gov.au/tga. Those with questions not addressed in the document can e-mail questions to the GMP Auditing and Licensing Section at gmp@health.gov.au.

**Health Canada, Therapeutic Products Directorate Withdraws Toxicological Evaluation Guidelines.** The Health Canada Toxicological Evaluation guidances (revised 1996) are being withdrawn following an internal review by a Safety Expert Working Group which concluded that they no longer reflected current toxicological methodologies. The review revealed substantial areas of overlap and inconsistency between these guidances and their more recently adopted ICH counterparts.

The following Health Canada-adopted ICH Safety (nonclinical) guidances, previously available as part of the Toxicological Evaluation guidances, are being re-issued as stand alone documents:

1. S1A: Need for Carcinogenicity Studies of Pharmaceuticals;
2. S2A: Guidance on Specific Aspects Of Regulatory Genotoxicity Tests For Pharmaceuticals;
3. S3A: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies;
4. S3B: Pharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies; and
5. S5A: Detection of Toxicity to Reproduction for Medicinal Products.

These guidances can be found at www.hc-sc.gc.ca under Therapeutic Products.

**Health Canada to adopt Q7A.** Health Canada is adopting the ICH Q7A Guidance for Active Pharmaceutical Ingredients (APIs). A proposed regulatory framework will be developed in order to ensure the implementation of the ICH Q7A Guidance for APIs destined for human use. Over the past decade, the extension of Good Manufacturing Practices (GMP) to Active Pharmaceutical Ingredients (APIs) has been internationally recognized as a necessary element in ensuring the overall quality and consistency of marketed drug products. For this reason, the International Conference on Harmonization (ICH) formed a working group in 1997 to develop a GMP Guidance for APIs. A draft of this Guidance was published for comment by Health Canada in July 1999, followed by discussions with the pharmaceutical industry and associations as part of a workshop on selected ICH topics held in November of that year. The final consensus document entitled *Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients* (Q7A) was adopted by the ICH Steering Committee on November 10, 2000, and is currently being implemented by the three ICH regions (USA, Japan, and European Union).

You may view the *Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients* on the following Web site: http://www.hc-sc.gc.ca/hpfb-dgpsa/inspectorate/.

**Taiwan DOH English Web Site Officially Opens.** The Department of Health (DOH) has established a new English Web site, forging a stronger link with the world. The new Web site provides local and foreign institutions with the latest information on health and medical care, government health care policies, and DOH achievements in public health.

The DOH's new Web site is part of its effort to accelerate the internationalization of local healthcare, as Taiwan actively participates in the World Trade Organization (WTO) and World Health Organization (WHO), and drives forward with internationalization through the government's Challenge 2008 National Development Plan. A prominent feature of the Web site is its access to the latest information on global health care issues and trends. The DOH hopes that the construction and launch of its English Web site will fully convey Taiwan's concern and emphasis on its health-care environment, allowing the international community to better understand the DOH's policies, and the most current information on healthcare and other convenient services provided to the public in Taiwan. The Web site can be found at www.doh.gov.tw/dohenglish. ■

***—William Stoedter***

# International Calendar

## 2003

### February

February 24–28, 2003
**2003 PDA International Congress, Courses and Exhibition**
***Back to the Future—Ahead to the Past: Mastering the Fundamentals of GMPs to Manage the Challenges of Escalating Demands***
Congress: February 24–26
Courses: February 26–28
Exhibition: February 24–25
Hilton Prague, Prague, CZECH REPUBLIC

**PDA-TRI Lecture Courses:**
February 26–28
***Requirements and Preparation of Pharmaceutical Grade Waters***
February 27
***GMP for Investigational Medicinal Products—Draft GMP Annex 13 and the European Clinical Trials Directive Beyond the GMP/ISO Basics—Practical Strategies for Everyday Compliance***
February 28
***Aseptic Processing Validation—Trends and Issues***

February 27–28, 2003
**PDA/IABs Conference—*Scientific Considerations for Comparability of Biopharmaceuticals***
Hilton Prague, Prague, CZECH REPUBLIC

### March

March 31, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

### April

April 10–11, 2003
**2003 Taormina International Conference and Tabletop Exhibits for Senior Executives in the Pharmaceutical Industry—*Managing for Quality in a Cost-Focused Environment***
Conference: April 10–11
Tabletop Exhibits: April 10
Grand Hotel Timeo & Villa Flora, Taormina, Sicily
ITALY

### May

May 5–9, 2003
**2003 PDA International Congress, Courses and Tabletop Exhibits**
Congress: May 7–9
Courses: May 5–7
Tabletop Exhibits: May 7–8
The Ritz Carlton Millenia, Singapore, SINGAPORE

May 12–14, 2003
**ICH Q7A Training—*Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients***
Hotel TBD, Tokyo, JAPAN

### June

June 30, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

### September

September 29, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

### December

December 15, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

# Jesse Goodman, M.D., MPH, Named Director of CBER; Kathryn Zoon, Ph.D., Moves to NIH

Dr. Mark McClellan, Commissioner of the Food and Drug Administration, announced on December 16, 2002, that he has appointed Jesse Goodman, M.D., MPH, to replace Kathryn Zoon, Ph.D., as director of FDA's Center for Biologics Evaluation and Research (CBER). He also announced that he expects improvements in making effective new cancer treatments available as a result of Zoon's new appointment at the National Cancer Institute (NCI).

Zoon, who joined FDA in 1980 and has served as director of CBER since 1992, announced her pending resignation on December 13 in order to return to the National Institutes of Health, as Principal Deputy Director for Research, in the Center for Cancer Research, at NCI.

"As head of FDA's biologics center, Kathy Zoon has skillfully presided over a decade of dramatic change in the world of biotech, cellular, and gene therapies," said McClellan. "She has helped forge CBER into the world's premier biologic regulatory agency, the global leader in the development of vaccine, blood, and novel therapeutics. NCI Director Andrew von Eschenbach and I are convinced that the close FDA ties Dr. Zoon brings to her new post at NIH will enhance FDA's efforts to collaborate closely with NIH to bring safe and effective products to the market—one of my top priorities as FDA Commissioner."

Goodman, currently CBER's Deputy Director (Medicine), is a virologist who is board certified in internal medicine, oncology, and infectious diseases. Educated at Harvard, he earned an M.D. from Albert Einstein, and did residency and fellowship training at the University of Pennsylvania and UCLA.

Goodman joined FDA's Office of the Commissioner in 1998, where he directed the US government's Interagency Task Force on Antimicrobial Resistance. He later moved to CBER, where he has been active in a wide variety of clinical and public health issues including bioterrorism preparedness and response, product development, human subject protection, and blood and vaccine safety.

"Jesse Goodman possesses the ideal credentials and experience to serve the American public as an empowered director of FDA's biologics center," said McClellan. "This is a critical time for biologics, with technologies like cellular and gene therapies holding the promise of transforming medical care in the 21st century, and with new challenges including countering terrorism and protecting the blood supply from new threats. Dr. Goodman is absolutely committed, as am I, to meeting these challenges through sound regulation based on the best science and risk assessment models."

During Zoon's tenure at the helm, CBER licensed approximately 320 products, implemented the prescription drug user fee program for biological products, and met all performance goals under that program. The first woman to serve as director of an FDA center, she has served as an outspoken advocate for strong science, both in CBER and throughout the FDA.

Goodman will work closely with McClellan and the senior leadership of CBER in the coming days and weeks to seek new ideas and approaches to carrying out the FDA's public health mission. They will also work quickly to complete the transfer of certain product reviews formerly conducted in CBER to FDA's Center for Drug Evaluation and Research. Goodman is expected to assume his new duties as center director by mid-January. ■

*—FDA News Release*

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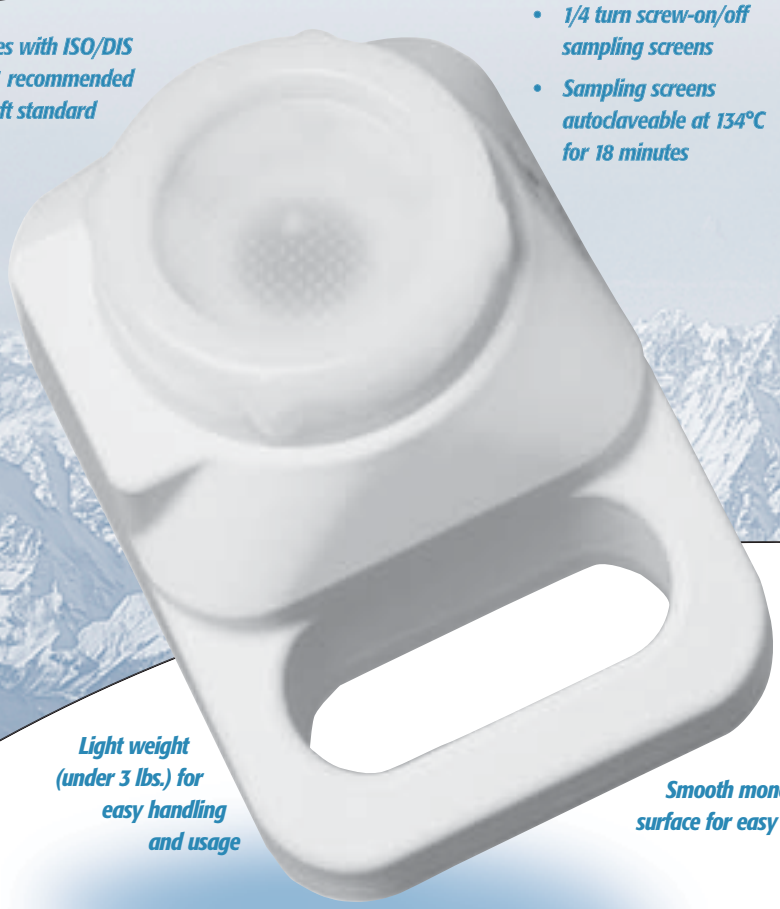

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# European Briefs

*by Esther Imboden, REGULIX Ltd; Bern, Switzerland and Gautam Maitra*

**European Community and Switzerland** Agreement between the European Community and Swiss confederation on mutual recognition in relation to conformity assessment entered into force on June 1, 2002. Chapter 15 of this agreement concerns medicinal products GMP inspection and batch certification and allows for the mutual recognition of the results of GMP inspections performed and manufacturing authorizations granted in the EU and Switzerland. As of June 1, 2002, imports of medicinal products into the EU from Switzerland are not required to be re-controlled at import provided they are imported in accordance with the provisions of Chapter 15. Official batch releases carried out by an authority of the exporting Party will be recognized by the other Party. The legal references of the "explanatory notes" on the operation of this chapter have been revised by the European Commission and the Swiss authorities in October 2002. Models for the Internationally Harmonized Requirements for Batch Certification and an EU Certificate of GMP Compliance of a manufacturer are also provided.

**Consultation on a New Proposal for a Revision of Annex 1 (Manufacture of Sterile Medicinal Products) to the EU GMP Guide (Volume 4)** The new proposal for a revision of Annex 1 to the EU GMP Guide has been adopted by GMP inspectors at their meeting on October 23, 2002. The amendments have primarily been introduced to harmonize the environmental standards for cleanrooms laid down in the GMP Guide with those laid down in international standards (e.g. EN/ISO 14644-1); (e.g. ranges of air speed have been defined, for open cleanroom applications as well as for closed isolators or glove boxes. It is also stated that maintenance of laminarity should be demonstrated and validated. Generally accepted guidance for temperature and relative humidity are given.) The Pharmaceutical Committee endorsed the proposal at its meeting on November 13, 2002. PDA has commented and the document can be found at www.pda.org.

**Updating the "Notice to Applicants" Volume 2A Chapter 3 "Community Referral"** DG Enterprises releases an up dated version of Chapter 3 "Community Referral" of the Notice to Applicants on Medicinal Products on the procedures for marketing authorization following the adoption of the Community Code relating to medicinal products for human use (2001/83/EC of the European Parliament and of the Council) in force since December 18, 2001. Legal references have been taken account of and no other changes have been introduced.

**Updating the "Notice to Applicants" Volume 2A Chapter 2 "Mutual Recognition"** DG Enterprises releases an up dated version of Chapter 2 "Mutual Recognition" of the Notice to Applicants on Medicinal Products on the procedures for marketing authorization following the adoption of the Community Code relating to medicinal products for human use (2001/83/EC of the European Parliament and of the Council) in force since December 18, 2001. Legal references have been taken account of and no other changes have been introduced.

**Updating the "Notice to Applicants" Volume 2A Chapter 1 "Marketing Authorization"** DG Enterprises releases an up dated version of Chapter 1 "Marketing Authorization" of the Notice to Applicants on Medicinal Products on the procedures for marketing authorization following the adoption of the Community Code relating to medicinal products for human use (2001/83/EC of the European Parliament and of the Council) in force since December 18, 2001. Legal references have been taken account of and no other changes have been introduced.

**Updated Version of Part 1A Administrative data in Part 1 of Volume 6B Notice to Applicants December 2002** An updated version of Part 1A Administrative data in Part 1 of Volume 6B Notice to Applicants has been produced with a possibility to use the tick-boxes in the form. A number of minor administrative changes (e.g. "future" European countries, line extensions, MRL status, List of proposed names and MA holders...) have also been introduced. This application format should be used for applications for marketing authorisations for veterinary medicinal products in the European Union.

**Updated Version of Chapter 6 Decision Making Procedure of Volume 6A Notice to Applicants December 2002** DG Enterprise is releasing a revised version of Chapter 6 dealing with the "Decision Making Procedure." The old version included additional information, which has been already published as guidelines in Volume 6C. This document is part of the "Notice to applicants—Volume 6A—Veterinary medicinal products—Procedures for marketing authorisation—Chapter 6: Decision Making Procedure" of "The Rules governing Medicinal Products in the European Union."

**The DG Enterprise Releases an Updated Version of Chapter 4 "Centralized Procedure" of the Notice to Applicants on Medicinal Products** This update is on the procedures for marketing authorization following the adoption of the Community Code relating to medicinal products for human use (2001/83/EC of the European Parliament and of the Council) in force since December 18, 2001. Legal references have been taken account of and no other changes have been

introduced.

**The Court of First Instance Supports that Centrally Authorized Medicines Should Generally Bear One Single Trade Name** In its judgement of December 10, 2002, the Court of First Instance annulled the decision of March 1, 2000, that had refused to vary the name and package layout of a centrally authorized medicine. The reason for the annulment is that the decision was not sufficiently motivated. On the merits, the Court states that the letter and spirit of Regulation 2309/93 suggests that a Community marketing authorization will contain as a general rule only one name. That name can be varied by adding another name only where the marketing authorization holder demonstrates that this is rendered necessary by exceptional circumstances which may adversely affect public health and where the Commission has ascertained that the variation applied for satisfies the criteria of the quality, safety and efficacy of the medicinal product.

**Review of the Pharmaceutical Legislation: Commission Modified Proposal for the Regulation** The Commission has adopted the modified proposal of the "regulation of the European Parliament and the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products." In general, four major objectives appear to be particularly relevant:

1. to assure a high level of public health protection, notably by making safe, innovative products available to patients as quickly as possible, and by an increased supervision of the market through the strengthening of inspection procedures and of pharmacovigilance;
2. to complete the single market for pharmaceutical products taking into account the stakes of globalization and to establish a regulatory and legislative framework that favors the competitiveness of European industry;
3. to respond to challenges of the future enlargement of the European Union;
4. to rationalise and simplify the system as well as to improve its overall coherence and visibility and the transparency of its procedures.

Finally with respect to veterinary medicines the proposals aim specifically to take into account the problem of the availability of medicinal products for veterinary use.

For further information on all of the above, please visit http://pharmacos.eudra.org.

* Notice to Applicants: The data requirements for registration of human medicinal products in EU Member States are detailed in Directive 75/318/EEC as amended and in guidelines which are known as the "Notice to Applicants". The Notice, issued by the Commission of the European Communities, was prepared to facilitate the compilation of the registration dossier required by Article 4 of the Directive 65/65/EEC. It has no legal force and provides the harmonized view of the EU Member States on how to meet the legal requirements of the relevant Directives as well as data requirements. The Notice details the format of the registration dossier and provides the guidance on the preparation of the expert reports. The Notice to Applicants was first published in 1986. ■

# Basel Pharmaceutical Forums

The PDA Europe Office is launching a series of Pharmaceutical Forums in 2003. The Forums will provide current technical and regulatory information to the Basel pharmaceutical community and foster direct interactions between the pharmaceutical industry and health authorities.

Dates are as follows:

- March 31, 2003;
- June 30, 2003;
- September 29, 2003; and
- December 15, 2003.

The Forums will be characterized by the following:

1. Held every three months, typically on a Monday;
2. Topics will be pharmaceutical and API manufacture/GMP/Regulatory issues;
3. Duration of one single day (from 09:00 to 16:00);
4. The morning session will generally consist of lectures by industry representatives and one invited guest from the health authorities;
5. The afternoon session will consist of discussion and Q&A sessions;
6. Materials will be e-mailed to participants at least one week prior to the Forum;
7. Hard copies of Forum materials will be available on-site and will be distributed if needed;
8. Forum working language will be English; and
9. Number of attendees will be limited.

PDA reserves the right to modify the structure of the Forums as necessary, without prior notice.

Preliminary Announcement about the First PDA Basel Pharmaceutical Forum:

**DATE:** March 31, 2003. From 09:00 to 15:00 (lunch 12:30 to 13:30).

**LOCATION:** UBS Ausbildungs-und Konferenzzentrum, Basel, Switzerland.

**TOPIC:** Common Technical Document (CTD and e-CTD) with additional emphasis on Sterile Manufacture and Biotech.

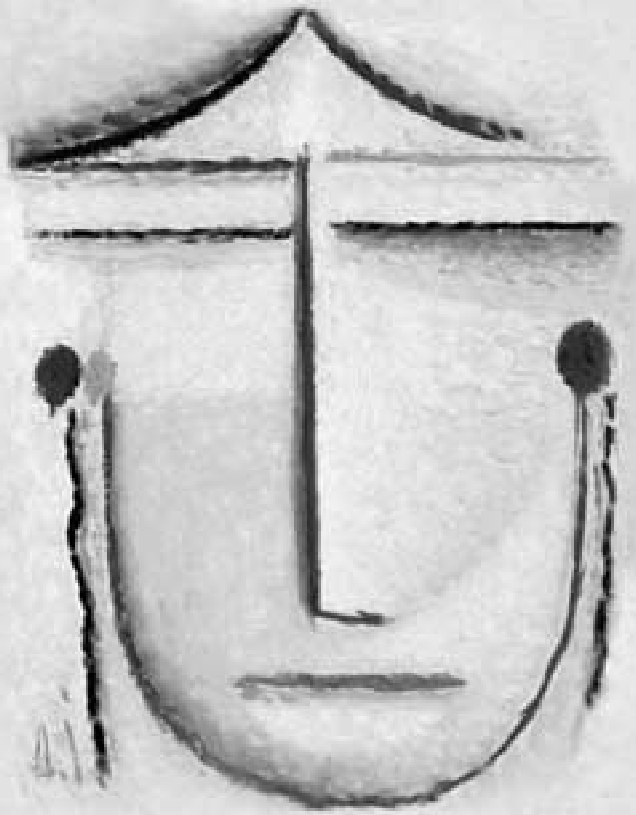
**SPEAKERS:** One/Two speakers from industry and one from a European Health Authority.

## Special Event

At 15:00 we will hold the Central European Chapter assembly to elect/nominate new chapter officers. This assembly will last until 17:00, and includes a half-hour apéro. ■

*—Gautam Maitra*

The Registration Form is included in the *PDA Letter* envelope to members in Europe. It is also found at www.pda.org.



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**QUALITY ASSURANCE SPECIALIST/MANAGER**
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**SCIENTISTS/RESEARCH ASSOCIATES, PHARMACEUTICAL SCIENCES**
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**DRUG SAFETY SPECIALIST**
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**PROCESS CONTROL ENGINEER**
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# TR-32 UPDATE

*by Harvey F. Greenawalt, ARC*

## Application of the PDA Process Model and ARC in the Subscriber Environment

Pharmaceutical Companies who are Subscribers have reported that using the PDA Process and membership to the repository has resulted in the enhancement of their System Life Cycle (SLC) practices.

Nearly all SLC practices in use today involve the acquisition of Commercial-Off-The-Shelf (COTS) products. The PDA program has established a standard way of performing organizational assessment of suppliers whose marketplace products are used in critical business operations that are either regulated or that impact the company's high risk computing base. The PDA Process has allowed subscribing companies to focus a handful of internal resources to be knowledge workers in analyzing supplier capability rather than high cost data collectors in executing audits. Data collector roles are fulfilled by PDA qualified, external, third-party services. The end result is the ability to manage multiple audits per year using qualified services strategically located around the world without leaving the comforts of home.

### Cost

Subscribers have reported that the average cost to self-perform an audit in the last three years has risen from $9,000 to approximately $11,000. The average cost of an audit for a Level VII or VI Subscriber to ARC is $5,000. Subscribers who subscribe to ARC at a Level V or higher-level recognize an average audit cost of $4,000 or less.

### Time

Subscribers have reported that the times required to self-perform an audit with a third party or internal resources averages seven weeks. This interprets into a lead-time of eight to 12 weeks to obtain and evaluate information on a particular supplier. Subscribers have reported that by using the PDA audit data available from ARC they can obtain audit data in one or two days and perform their evaluation within a week to 10 days. Subscribers report that the value of the immediate availability of audit data was an invaluable resource.

The quality of information contained in audits performed using the PDA Process allows the audit analysts to predict the likelihood of technology-use problems along with other risk factors and establish mitigation schemes that result in a win–win solution for both supplier and customer.

Subscribers have reported the following benefits:

- 400% increase in the number of audits that can be managed by a single individual;
- 80% Reduction in time required to obtain and evaluate audit data;
- Enterprise-wide sharing of audit information;
- Standardization of method for analysis and consistent look and feel to reports;
- Seamless integration with acquisition and SLC practices; and
- Fulfilling technical and regulatory expectations by being able to quantify some level of structural integrity of software internals required for computer products validation.

### Auditor Training & Qualification Benefits Recognized

One hundred and fifty auditors have been qualified under the purview of PDA to implement the process defined in TR-32. Representatives of pharmaceutical companies, suppliers, and third party consultant groups have attended auditor training. Roughly 17 percent of the auditors qualified reside in Europe and two auditors reside in Japan. Forty-eight percent of the auditors are from pharmaceutical industry companies with the remainder coming from consultancy groups.

Suppliers seeking to place their audit information in the repository for use by their pharmaceutical clients have found the information obtained from the auditor training to be extremely beneficial in expediting the audit process and in the internal benchmarking of their quality systems.

Pharmaceutical company personnel seeking qualification to perform audits using TR-32 as well as management personnel responsible for the implementation of validation, quality management, regulatory compliance, quality assurance and corporate computer systems implementation have attended the auditor training.

Information on applications for qualification and course registration is available on the PDA Web site at www.pda.org.

### Membership

Since the issue of TR-32 in January of 2000, 42 pharmaceutical, medical device, and biotechnology companies and 11 suppliers of computer technology and services have joined the PDA Process Repository.

### GAMP 4

Volume 1 Part 1 of the User Guide for Supplier Audits indicates that the PDA established repository for audit reports is available to pharmaceutical companies, as a vehicle for sharing audit reports

to meet their supplier audit needs.

The GAMP section for Shared Audit reports indicates that PDA has established a Standard Audit Process against which they have qualified Auditors to implement the process defined in PDA Technical Report No. 32.

ARC and PDA extend their deepest gratitude to the GAMP Forum for their support of the PDA Process and ARC.

## Availability of Audits

Currently 53 audits are either under consideration, in process, or available for distribution.

Table 1.0 provides a summary of the 27 audits that are currently available for distribution from the Repository.

For more information about the Audit Repository, audits and their availability, visit ARC's Web site at www.auditcenter.com. ■

**Table 1.0 Audits Currently Available from ARC**

| | Supplier | Product |
|---|---|---|
| 1 | Access 360, Inc. | EnRole 4.0 (Provisioning Software) |
| 2 | Alacris, Inc | IdNexus, Alacris products are designed to simplify identity management and maximize trust associated with Public Key Infrastructure (PKI) implementation and security technologies |
| 3 | Automation Tooling Systems, Inc. | Custom programming services for Process Control Software |
| 4 | Decision Management International, Inc. (DMI) | Regulus™ Document Authoring (DA) a member of the Regulus™ off-the-shelf solution set |
| 5 | Documentum, Inc. | Content Authentication Services (CAS), eContentServer, DocControlManager (DCM) and GMPharama |
| 6 | Entrust Technologies Ltd. | Public Key Infrastructure Technology (PKI). Digital Security technology for enterprise resource systems |
| 7 | Epicentric, Inc. | Foundation Enterprise Server 4.0, tool for coordinating information from disparate sources and for disparate users. |
| 8 | Fanuc Robotics North America | Robotic Controllers & Communications |
| 9 | Fisher Rosemount Systems, Inc. | Distributed Factory Automation, Delta V product Line |
| 10 | First Consulting Group, Inc. | Custom information based strategy software, operations improvements management and integration services |
| 11 | Foss NIRSystems, Inc. | SLE Near-infrared analysis of chemical and physical Properties |
| 12 | Infinity QS International (Lyle-Kearsley, Inc.) | Infinity QS Statistical Process Control Software |
| 13 | Inktomi Corporation | Enterprise Search Software (information retrieval solutions) |
| 14 | Interwoven, Inc. | Web Publication management |
| 15 | Lexign Corporation | Lexign Flow EPR Software |
| 16 | Loftware, Inc. | Loftware print server (LPS) Label printing system |
| 17 | MARC Global Systems | Warehouse Execution Systems |
| 18 | Merant, Inc. | PVCS Dimensions & PVCS Replicator Configuration Management Systems |
| 19 | Mercury Interactive | Test management Tools:<br>• QuickTest Professional<br>• Astra Fast Track<br>• Astra LoadTest<br>• Astra Quick Test<br>• Test Director<br>• LoadRunner<br>• LoadRunner TestCenter<br>• WinRunner |
| 20 | Propack Data GmbH | Enterprise production Management System, PMX 3.2 with Solutions MES and CTM |
| 21 | SAP AG | MySAP.com e-business platform, specifically aspects of Supply Chain management, Product Lifecycle Management and Business Intelligence relevant to manufacturing operations.(Includes Product Lines: SAP R/3 4.5B and SAP R/3 4.6B/C) |
| 22 | Schlumberger | Secure ID Card |
| 23 | SSA Global Technologies, Inc. | Mid range ERP software for manufacturing, supply chain and financial application domains |
| 24 | Serena Software, Inc. | Serena ChangeMan Automating the Software Lifecycle |
| 25 | Sparta Systems, Inc. | Track Wise Software |
| 26 | Supply Chain Logic, Inc. | General use COTS Asset Tracking/Delivery Systems |
| 27 | The Sycamore Group | Custom IT Solutions, Integration Suite of COTS products and services to bridge data across multiple internal computer systems, including e-Commerce, LIMS, ERP, enterprise database, mainframe and wireless portable devices |

# USP Update

*by Roger Dabbah, Ph.D., USP*

The January–February 2003, Pharmacopeial Forum (PF) has been published and contains a series of interesting developments.

The first Interim Revision Announcement includes a new chapter on Pharmacopeial Harmonization <1196>. It is intended to act as a guideline for its users. It includes the Pharmacopeial Discussion Group (PDG) Working Procedures, PDG Policy Statement. It also provides the Status of Harmonization for General Chapters and for Excipient monographs. The status of these chapters and monographs will be updated as they proceed through the PDG harmonization stages. It will also include the list of harmonized general chapters and monographs. The First IRA also includes revisions of a number of monographs as follows: Clavulanate Potassium (changes in the section on Limit of Clavam-2-Carboxylate Potassium); Dipyrimadole Tablets (changes in the Dissolution section); Etoposide (changes in the Assay and in the USP Reference Standards sections); Octisalate (changes in Chromatographic Purity section); Paclitaxel (changes in packaging and Storage and in Related Compounds sections); Propoxyphene Napsylate Oral Suspension (Changes in Assay); Propoxyphene Napsylate Tablets (changes in Dissolution and in Assay); and Propoxyphene Napsylate and Acetaminophen Tablets (changes in Dissolution, in Assay for propoxyphene napsylate, and Assay for acetaminophen). All the changes, unless otherwise indicated in the First IRA, are official February 3, 2003.

In the In-process revision section of the same PF, 16 new monographs are proposed in USP. In the NF section, eight new monographs are proposed. A number of general information chapters are being proposed in that section: <1010> Analytical Data-Interpretation and Treatment; <1118> Monitoring Devices-Time, Temperature, and Humidity; <1160> Pharmaceutical Calculations in Prescription Compounding; <1209> Sterilization-Chemical and Physicochemical Indicators and Integrators; <1222> Terminally Sterilized Pharmaceutical Products-Parametric Release; and <1223> Validation of Alternative Microbiological Methods. In the Nutritional Supplements section three chapters on microbiology are published: <2021> Microbial Limits-Nutritional and Dietary Articles; <2022> Microbial Procedures for Absence of Specified Microorganisms; and <2023> Microbiological Attributes of Non-sterile Nutritional and Dietary Supplements, with the last two chapters being new chapters.

In the Stimuli to the Revision Process, two articles are published. One article by Taborsky and McKinley on "Manufacturer's Market Containers and Closures: Proposed Revision to Containers-Permeation<671>"; the other article by Hofer and Gray on "Examination of Selection of Immediate-Release Dissolution Acceptance Criteria."

A USP Conference on "Biological and Biotechnological Drug Substances and Products" will be held April 1-4, 2003 at the Crystal Gateway Marriott in Crystal City, Virginia. The Conference Topics are" Equivalence of Biological and Biotechnological Drug Substances and Products with Presentations and Interactive Discussion by Expert Panelists"; "Blood and Blood Derived Products"; "Vaccines"; "Cell and Gene Therapy & Tissue Engineering"; "Bioassay"; and "Ancillary Products." Further information and registration materials will be available. For more information, contact Dr. Lokesh Bhattacharyya at (301) 816-8201 or lb@usp.org. ■

# Media Fills

The following remarks are taken from an exchange in the Pharmaceutical Sci-Tech Discussion Group, a PDA-sponsored Online Forum held on the Internet 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.

This month's posting…

## Question

**Could media fill be regarded as a test solely for aseptic processing routines?** Sterilization of stoppers, vials, overseals and process equipment is validated in separate autoclave cycles. During development it might happen that, for example, the stopper is changed (stopper shape and rubber formulation) after a media fill. Would it then be necessary to conduct a new media fill (or three?) or is it acceptable to demonstrate the sterility of the new stoppers by a validated autoclave cycle?

## Response 1

Media fills are a process validation test used to qualify the whole process carried out completely under validated aseptic processing in which the product is not subsequently terminally sterilized.

I think you have to conduct a new media fill test to verify the impact of such changes on the validated status.

## Response 2

If the physical dimensions of the stopper remain the same, and the stopper sterilization cycle, and the stopper handling routines (e.g., filling the hopper) remain the same, I would question what value another media fill would provide. In fact, I could make a good argument that in these situations, the change in the rubber formula is irrelevant, and another media fill is unnecessary.

## Response 3

In my opinion, media fill should be performed after any change/modification in primary packing material. Additionally long term stability studies are normally conducted after change in product contact packing materials.

## Response 4

The key is the process for insertion of the stopper into the vial. If the process of inserting the stopper in the vial does not change exposure, handling time, etc., then another media fill should be unnecessary. The media fill is an assessment largely of personnel and filling process. Individual component becomes critical when a change in component leads to change in handling procedures.

## Response 5

Referring to your first question, yes, media fill is a test to prove that an aseptic process is "really aseptic." Processes with terminal sterilization could be reviewed with other parameters like bioburden before sterilization. In the case of the stopper, if you change the design or material, you have to validate the sterilization cycle with the new stopper; if it is sterile and the handling of this material after autoclave is the same, with this study it will be enough. But, if this new stopper changes the way you put in the containers or the way you handle in the sterile core, you have to evaluate and "maybe" it would be necessary to run new media fills.

## Response 6

The substitution of any component which comes in direct contact with the product, particularly a packaging, will require validation. All components have extractables. The degree of extractability will depend on the nature of the product, e.g., lipohilic or lipophobic, pH, co-solvents, pretreatment procedures, etc. The perfect way to delay any application is to make changes. I have seen this approach really delay approvals. The bottom line is to do your development work early on so that you won't have to repeat it or have your approval process delayed. That's what GMPs are all about: validation. Done right the first time, it saves you lots of money and time, in the long haul.

*continues on page 20*

Join this lively online discussion group, where more than 2,000 of your colleagues from around the globe meet and find solutions to complex issues. Access is open to both PDA members and nonmembers, and discussions may be accessed via e-mail or the Web.

See the PDA Web site at **www.pda.org** to sign up via the Web or send an e-mail to *requests@www2.pharmweb.net* if you don't have Web access, with one of the following commands placed in the body of the message: "subscribe PharmTech" (to receive individual messages daily), or "subscribe digest PharmTech" (to receive one daily digest). Replace "subscribe" with "unsubscribe" to leave the list. For help topics, type "help PharmTech" in the body of the message and send.

*Media Fills from page 19*

## Response 7

The original aseptic process simulation qualified your filling equipment, processes and final container sterile integrity. The argument may be made that the stopper change you described (stopper shape and rubber formulation) may impact on the seal integrity of the final container. Some qualification of the new container closure system would be required. The level of qualification should be suitable for the intended use of the material (pre clinical vs. clinical). A risk/benefit analysis should include input from your QA compliance group. The justification of the final decision should be documented (change control), including appropriate approvals.

This addresses the sterile integrity of the container closure system only. In addition, the drug product container/closure interaction should be addressed so as not to alter the safety, identity, strength, quality or purity of the drug product. Samples should be set aside for the long-term stability program.

## Response 8

I agree that sterile media fills should be used to validate the entire process (not just your procedures or routines). This means you have to make room for the unknown. Though it may be unlikely that a change in your stopper's rubber formulation would impact your routines or procedures, a change in stopper shape could affect your process. For example, your filling equipment may prove to be unable to process the new stoppers (which are a different shape) as efficiently as the old stoppers. This could lead to longer fill times, an increase in the number of operator manipulations/interventions, etc. If these questions are not answered by some other study or qualification, your process (and state of control) could be compromised. Not all changes or differences warrant sterile media fills, but each should be scrutinized for its impact to the process.

## Response 9

The filling of a nutrient medium solution (media fill) alone does not constitute an acceptable aseptic process validation. The whole manufacturing cycle must be simulated, from the dispensing and reconstitution of the powdered medium under normal manufacturing conditions, to the filling and sealing process itself. Operators (and numbers of operators), numbers and types of filtrations, etc., shall all be "as normal," as shall holding times in any mixing vessels, interim-holding tanks etc. General activity shall be at a normal level, and

no attempt shall be made to take any "special" precautions to ensure that the test run is successful. If any deviation from the normal is permitted, it shall only be in the direction of presenting a greater, rather than a lesser, microbiological challenge to the process.

Before any meaningful aseptic process validating media fills can be carried out, all necessary equipment qualification and instrument calibration must be completed, together with the appropriate certification. The clean rooms used for all processing stages shall also have been confirmed and certified as complying with the required environmental standards.

Above are the in-built requirements of media fills and any deviations anywhere along these requirements after successful media fills are not acceptable, demanding fresh media fill runs and other associated studies.

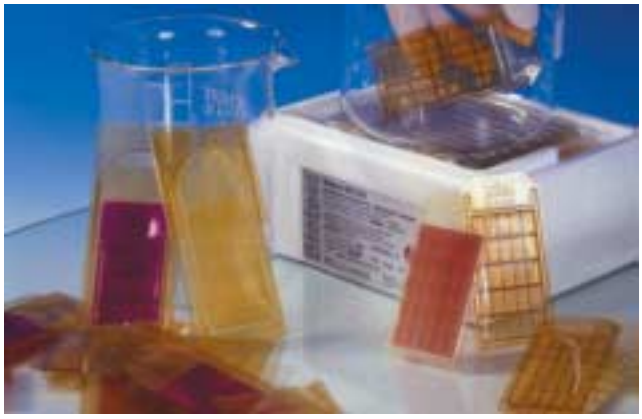
## Response 10

The most complete reference is PDA TR No. 22, available on the PDA Web site at www.pda.org.

## Response 11

It is necessary to define terms properly. Any change in the system requires the change to be "qualified" by appropriate studies. For closures, this will involve a range studies including compatibility, extractables, seal integrity, etc. In terms of "process validation" it would be necessary to validate steps of the "process" affected by the change. The media fill process validates the filling process. If the change in components has not resulted in change in the filling process, then you should not need to repeat media fill. You should place a report in your file explaining what you have done and your reasons for justification of the change. The best strategy and only strategy for regulatory compliance is good science, good technology and documented justifications and explanations. ■

**Join this lively online discussion group...access is open to both PDA members and nonmembers, and discussions may be accessed via e-mail or the Web. See the PDA Web site at www.pda.org to sign up via the Web or send an e-mail to *requests@www2.pharmweb.net*.**



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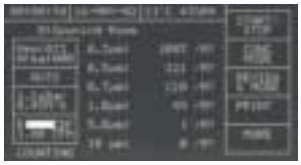

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# Interest Groups Report on Meetings in New Orleans

Most of PDA's Interest Groups were active at the Annual Meeting in New Orleans in December. The meeting summaries are published in the *PDA Letter* and in the IG sections of the PDA Web site as they become available. For additional information, please contact the appropriate IG leader.

**See future issues of the *PDA Letter* for more Interest Group Updates...**

## Filtration Interest Group

***Jack Cole, Jack Cole Associates LLC***

The Filtration Interest Group convened on Tuesday, December 10 during the PDA Annual Meeting in New Orleans. More than 50 industry representatives actively participated in the discussions.

Several potential tasks for the Group to undertake were discussed including the need to address pharmaceutical depth filter ratings, testing and general standards. There was general agreement that this should be pursued and a chairman is needed to initiate a proposal to PDA's Science Advisory Board.

A discussion also ensued on the subject of membrane ratings for sterility test, i.e., 0.1 $\mu$m, 0.2 $\mu$m and 0.45 $\mu$m, the latter being the current standard. Comments regarding the relative microorganism recoveries of these membranes would indicate that 0.45 $\mu$m will remain the standard.

A need for a filter challenge test standard for "0.1 $\mu$m" membranes was raised by the Chair and it was the Group's consensus that user input is needed prior to any action.

Jerry Martin, Pall Corp., presented a summary of the Viral Clearance Task Group progress and Frank Bing of Abbott gave a summary of the status of the Sterile Filtration of Gases Task Group.

The "FDA Preliminary Concept Paper, Sterile Drug Products Produced by Aseptic Processing," was the subject of a special plenary session on Monday, December 9. Maik Jornitz of Sartorius and Jerry Martin of Pall Corp. reviewed the comments relative to filtration therein and the presentation is available on the PDA Web site.

The Chair wishes to thank all who participated in the meeting, with special thanks to Maik Jornitz, Frank Bing, and Jerry Martin.

## Inspection Trends/Regulatory Affairs and QC/QA Interest Groups

***Robert L. Dana, Elkhorn Associates, Inc. and Don E. Elinski, Johnson & Johnson Merck***

At the 2002 Annual Meeting, the Inspection Trends/Regulatory Affairs and QC/QA Interest Groups held a joint meeting on December 11th. The meeting featured a panel of speakers who discussed FDA regulatory actions—types of enforcement actions available to FDA, ways to avoid them, and the implications should a company find themselves the subject of a regulatory sanction. Speakers included Alan Minsk, Partner and Leader of the Food and Drug Practice Team at Arnall Golden Gregory LLP; Don Elinski, QC/QA Interest Group Leader and Site Quality Manager, Johnson and Johnson-Merck, and Michael Gross, Vice-President, Worldwide Compliance, Aventis-Behring.

Mr. Minsk provided an overview of FDA's regulatory oversight function, including inspections, Warning Letters, Seizures, Injunctions, and Consent Decrees. He also discussed such related topics as FDA's criminal investigation activities, import/export powers, the Application Integrity Policy and criminal investigations, including personal liability. Relative to Warning Letters, he noted that these are typically issued if FDA considers a firm's response to an FDA-483 to be inadequate, if the deficiencies are sufficiently serious that FDA is prepared to proceed with further enforcement activity or if a firm demonstrates continued violative conduct. Trends he has seen in Warning Letter citations include senior management inattention, failure to provide adequate staff training, and weak corrective and preventive action programs.

He also discussed Consent Decrees in some detail, noting that they may be employed to resolve compliance issues when a firm has had some time to correct deficiencies, but has not done so to FDA's satisfaction. Consent Decrees are becoming more popular with FDA. They typically require the use of independent consultants to review a firm's facilities and operations, with these reviews being provided to FDA. They are costly in that they may require disgorgement of profits, and daily fines for failing to meet schedules for completion of agreed upon corrective actions. They have serious impact beyond their monetary penalties, in that they may result in delays in product approvals and shipments. They result in a loss of credibility with FDA, which can result in greater scrutiny in the future.

Recommendations for ways to avoid regulatory sanctions include prompt attention to resolve issues, including working with the District and/or Center, understanding FDA's concerns, and focusing on the right issues, determining and fixing the root cause of problems, having proactive timelines for corrective action, and keeping FDA informed of progress and ensuring that senior management is aware of and active in problem resolution.

Utilizing the FDA's System Approach to the conduct of drug product inspections, Mr. Elinski described ways that a firm can proactively help ensure that compliance issues are promptly iden-

*continues on page 24*

*Interest Group Meetings from page 23*

tified and addressed internally, before they become the subject of FDA sanctions. For the Quality System, which is considered the most critical of all the systems, he noted that firms should ensure that adequate resources and an appropriate structure exist. He also noted that independent oversight of a firm's operations, including the Quality System, is important for success. For the Facilities and Equipment, Production, and Materials Systems; validation, calibration, process knowledge and definition, change control and preventive maintenance are all areas requiring attention. Label control and issuance remain areas requiring attention to avoid potential mislabeling and mix-up. Finally, the system for Laboratory Controls deserves attention, to ensure that adequate, well-trained, staff exists; that methods are validated and adequate for their use and that equipment is properly calibrated and maintained. Handling of Out Of Specification results, including well done and well-documented inspections, is of utmost importance.

Finally, Dr. Gross discussed the implications for a firm operating under a Consent Decree. He noted that there are several potentially negative impacts on such a firm not immediately apparent in just reviewing the decree. As Mr. Minsk had also noted, these include a loss of credibility with regulators, but also include potential loss of key employees and difficulty recruiting replacements. There will likely be a loss of market shares and significant operational issues, including increased operational spending, extended production cycle times, reduced product yields, increased inventory due to increased work in process, and increased interest cost. Companies may become more risk averse and develop overlaying SOP's to "be sure they are covered."

The importance of understanding what lead to the Consent Decree so that preventive measures to prevent their reoccurrence may be implemented, the need to change mindsets of a company and its employees and the need to fully understand the issues and identify their root causes prior to implementing corrective actions were all identified as lessons learned in the process of developing one company's response to a Consent Decree. A key challenge for management is to convince the regulators that a company is committed to compliance, that they have developed a clear strategy to systematically address the root causes and have implemented a realistic action plan to deliver on their commitments. Finally, he noted the importance of continuing to update the regulatory authorities on the implementation progress.

Shifting topics, the joint Interest Group meeting concluded with a brief presentation describing a survey being conducted to benchmark current practices impacting the Cost of Quality. Details of the survey will be posted on the PDA Website (www.pda.org) as they become available.

## Stability Interest Group

***Rafik Bishara, Eli Lilly and Company***

The PDA Stability Interest Group benefited from the participation of the panel of speakers from the Stability Session on the main meeting program where the theme was "International Stability Regulation: The Next Steps." The session was moderated by Rafik Bishara, Ph.D., Director, Quality Knowledge Management and Technical Support, Eli Lilly And Company.

Carol Easter, Director, Pharmaceutical Analysis Control, Merck & Co., Inc. updated the 70- plus attendees on the latest harmonization efforts for Q1D, Q1E, and Q1F; Richard C. Adams, Chair, CDER Stability Technical Committee, Office of Generic Drugs, CDER, FDA, presented on the status of FDA Stability Guidance and Impact of the ICH process; Andrew Sopirak, Director, QA Analytical Services, AstraZeneca Pharmaceuticals, discussed a Global Stability Program and reaction to guidances; Rafik Bishara proposed a Stability Stewardship Program from discovery through legacy status. The presentation was coauthored by Robert H. Seevers, Senior Technical Advisor, Quality Knowledge Management and Technical Support, Eli Lilly and Company.

The final part of the session was allocated for clarifications, questions, and answers. For additional details the reader is encouraged to check the PDA Web site (www.pda.org).

During the Stability IG meeting, the participants discussed several topics including:

1. Adequate Justification for Stability Data to be Submitted if not ICH Data (e.g. Line Extension or Combination Products);
2. Statistical Analysis for Extending Dating;
3. Stability Data for IND (a) API, (b) Products;
4. Proper Use of Thermal Cycling Studies;
5. Harmonized Shipping Stability Studies;
6. Container Integrity Test vs. Sterility Testing;
7. ICH Q5C for Biotech Products;
8. Stability on Bulk Containers (See container/closure guidance); and
9. Container Closure Guidance Clarification. Hold Time: GMP vs. Registration Requirement.

## Sterilization/Aseptic Processing and Microbiology Interest Groups; Combined Meeting

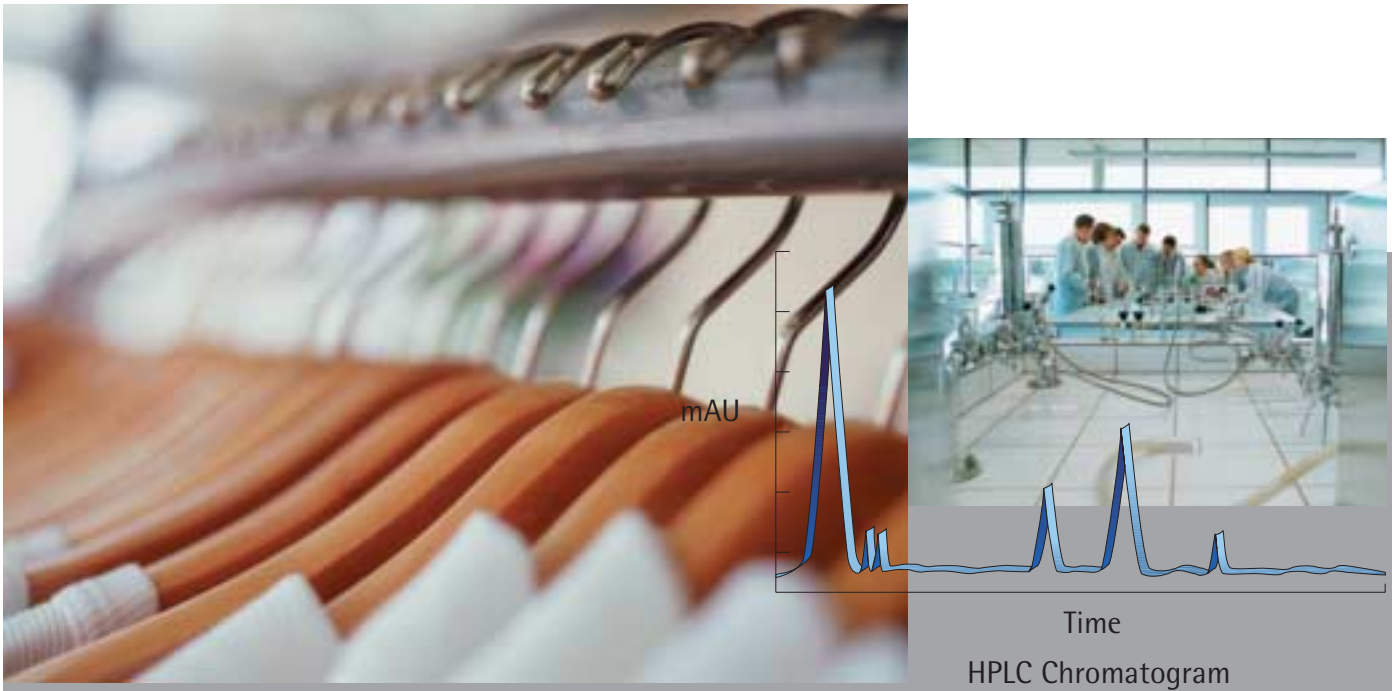
***James P. Agalloco, Agalloco & Associates***

The combined IGs discussed the following topics:

- Proposal for PDA Guidance on Aseptic Processing of Biologically-derived Materials;
- Update on Micro OOS Effort;
- Half-cycle for Steam Sterilization (Is FDA still pressing for this?);
- Is it Reasonable to Expect Product Contact

*continues on page 26*

sartorius

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*Interest Group Meetings from page 24*

Surfaces to be Sterile at the Completion of an Aseptic Process?
- Use of Multiple Substrates for BI's–VHP, Steam & Other Sterilization Methods;
- Freezing of Microbial Samples;
- Pending Revision of EU Annex 1–Sterile Medicinal Products;
- Evolving PDA petition to FDA/USP to Eliminate Sterility Testing for Terminally Sterilized Products; and
- Update on PDA Scientific Activities Impacting Sterilization/Microbiology/Aseptic Processing.

### Aseptic Processing of Biologically Derived Materials

This task force will develop a PDA document addressing the necessary controls for aseptic processing of sterile products using biological processes. Typical processes/products where this type of guidance might prove beneficial include cell culture, gene therapy, etc. where the process is predominantly aseptic and susceptible to adventitious contamination. It will draw upon PDA's existing guidance on aseptic processing of finished dosage forms (TR No. 22) and bulk sterile materials (TR No. 28) where possible.

### Microbiology OOS

**Half-cycle for steam sterilization**
- FDA inspectors have raised this in numerous inspections;
- Part of the new FDA aseptic processing draft; and
- To what extent is the half-cycle approach being utilized for steam sterilization validation?

**Half-cycles/PNSU & D-values**

Half-Cycle Applications
- ETO and other gas sterilization processes (but not isolators) where the relationship between the resistance of the bioindicator (and bioburden) at slightly different conditions is unknown;
- Radiation for extremely stable materials; and
- In an emergency where no validation had been performed.

**Monitoring Product Contact Surfaces**
- Is product at risk if the count is not zero?
- Can we expect EM never to contaminate a sample?
- What type of results should we expect?
- How can we change FDA's expectation?

**PDA Scientific Activities/Aseptic Processing**
- PTC in Validation of Aseptic Processing;
- FDA Aseptic Processing Guidance;
- Incubation and Intervention Practices;
- Process Simulation for Sterile Bulks;
- Aseptic Processing White Paper; and
- Aseptic Processing of Biologically-derived Materials.

**PDA Scientific Activities/Sterilization**
- *Technical Report No.1: Validation of Steam Sterilization Revision*;
- Filtration of Gases;
- Selection and Use of Bioindicators for Monitoring Sterilization Processes;
- Steam Quality;
- Petition to Eliminate the Sterility Test for Terminally Sterilized Products;
- DOP Testing of HEPA Filters in Ovens/Tunnels;
- ISO draft on Dry Heat Sterilization and Depyrogenation; and
- Packaged Pharmaceutical Water.

**PDA Scientific Activities/Microbiology**
- Microbial OOS Issues;
- In-process Bioburden Concerns for Biologics;
- Guidance on Freezing of Microbial Samples;
- Standardized Integrity Test and Labeling for Virus Removal Filters; and
- Container-Closure Integrity.

**PDA Scientific Activities/Related Subjects**
- Filter Manufacturing Vendor Audit Repository;
- Revision to Annex 1 of EU GMPs;
- Pharmaceutical Water Systems; and
- Survey on Environmental Control/Facility Design for Tablet and Capsule Operations. ■

**Additional Interest Group Reports may be found at www.pda.org, as well as future issues of the *PDA Letter*...**

# PDA Forms Pharmaceutical Cold Chain Discussion Group

PDA is pleased to announce the formation of a Pharmaceutical Cold Chain Discussion Group that will exchange current industry practices, ideas, and information on global shipping and distribution of temperature sensitive medicinal products (including active pharmaceutical ingredients, final product, clinical product, and reference standards). The group will also develop and be involved in training and education for shipping and distribution of temperature sensitive medicinal products through appropriate scientific, trade, and regulatory organizations and will develop harmonized guidelines for validation of shipping and distribution of these products. Finally, the group will propose standards to be published for industry through working with appropriate organizations including global regulators.

**The group will also develop and be involved in training and education for shipping and distribution of temperature sensitive medicinal products...**

## Goals

1. Develop "Cold Chain 101" educational presentation for our use and education of others (to include What, How and Why)
2. Develop Harmonized standards for shipping and distribution of temperature sensitive medicinal products
   a. PDA Technical Report
   b. USP Stimuli Article and/or General Chapter
   c. FDA Guidance
3. Publish technical reviews on current practices for the Cold Chain Management.
   a. Literature review
   b. Collaborative studies, e.g. thermal validation of shipping containers.
   c. Peer reviews
4. Participate in the PDA 2003 Spring Meeting on "Pharmaceutical Cold Chain Management"

Rafik H. Bishara, Ph.D., Eli Lilly and Company is chairing the group. Bishara can be contacted by phone at (317) 276-4116 or by e-mail at rhb@lilly.com.

For additional details, please contact Dan Colton, Genentech, (650) 225-2136, or colton.dan@gene.com. ■

*—Russell E. Madsen*


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Quality
On-Line

**April 10–11, 2003**

## 2003 Taormina International Conference and Tabletop Exhibits for Senior Executives in the Pharmaceutical Industry

# Managing for Quality in a Cost-Focused Environment

**Conference:** April 10–11
**Tabletop Exhibits:** April 10

Grand Hotel Timeo & Villa Flora • Taormina, Sicily ITALY

The objective of this important conference is to present practical information from world-renown experts relevant to effective compliance and quality management. Attendees will hear presentations from key officials in industry and regulatory agencies, in an outstanding Sicilian location. The design of the conference, including formal presentations, informal discussions, and social events, is specifically designed to enhance interactions among attendees and speakers.

Highlights include:

- Expert executives from Astra Zeneca, Abbott, Alcon, GlaxoSmithKline, Eli Lilly, Pfizer, SIFI, and other leading firms, presenting industry experiences, perspectives, and solutions;
- Outside technical expert Ronald Tetzlaff of KMI/Parexel, presenting perspectives on how the industry can improve managing for quality and avoid regulatory pitfalls;
- Perspectives on consent decrees and other consequences, and how to avoid them, presented by Eric Blumberg, FDA's Deputy Associate General Counsel, and William Vodra of Arnold and Porter; and
- Douglas Dean of PriceWaterhouse Coopers presenting cost trade-offs associated with quality management.


## Who Should Attend

Senior level pharmaceutical company representatives responsible for overseeing global quality, manufacturing, compliance, and regulatory affairs are encouraged to attend this important international conference.

## Learning Objectives

Participants in the conference will:

- Discuss the Development, Implementation, and Execution of a New Quality Management System;
- Define Quality Metrics;
- Identify Key Elements of Building an Effective Quality System;
- Discuss the Complexity of Managing Quality: Outside Views;
- Identify Legal Strategies for Consent Decree; and
- Discuss Supply Chain Management and Strategic Contracting.

## About Taormina

Since the end of the nineteenth century, Taormina has become a world-famous international resort whose visitors are, time and time again, enraptured by its charming atmosphere and its natural unspoiled beauty. Taormina has become a destination where visitors enjoy relaxing walks through old town pedestrian areas amid a climate that is mild year-round. In fact, many who have visited Taormina describe it as their "escape place" from chaotic city life.

PDA members are encouraged to share information about this important conference with industry management. Roundtable and panel discussions will provide attendees with opportunities for high-level interaction and information exchange.

The official brochure and registration information for this conference are now available online at www.pda.org. ■

*—Leslie Zeck*

# GMP Guidance for APIs Training to be Offered in Japan

## International Conference on Harmonization Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients

### Tokyo, Japan • May 12–14, 2003

PDA will offer a training workshop on ICH Q7A Guidance in Japan. The training was developed in collaboration with the Pharmaceutical Research and Manufacturers of America (PhRMA), the Generic Pharmaceutical Association (GPhA), the European Agency for the Evaluation of Medicinal Products (EMEA), the UK Medicines Control Agency (MCA), the US Food and Drug Administration (FDA), Pharmaceutical Inspection Convention/Cooperation Scheme (PIC/S), European Chemical Industry Council (CEFIC), European Federation of Pharmaceutical Industries and Associations (EFPIA), Irish Pharmaceutical and Chemical Manufacturers Federation (IPCMF), and International Generic Pharmaceutical Alliance (IGPA).

The International Conference on Harmonization (ICH) Q7A document, the first Good Manufacturing Practice (GMP) Guidance jointly developed between regulators and industry is intended for use worldwide. It impacts any manufacturer who manufactures in, or intends to supply into, the ICH regions (USA, Europe, and Japan).

This three-day workshop will provide training of regulatory personnel alongside industry participants. The faculty is comprised of both regulators and industry representatives who served as members of the ICH Expert Working Group that developed the document. Substantial time has been allotted for question and answer sessions.

Highlights:

- This Q7A Training is being conducted by members of the Expert Working Group that developed the guidance; and
- The joint industry/regulatory/faculty participation will facilitate a mutual exchange of discussion issues on the Q7A document.

Training will be presented by members of the ICH Q7A Expert Working Group.

The Q7A Guidance Document can be found on the following Web sites:

http://www.fda.gov/cder/guidance/index.htm;

http://www.emea.eu.int/pdfs/human/ich/410600en.pdf; and

www.ifpma.org/ich5q.html#gmp.

In addition, question/answers from the Chicago, Princeton, Newport Beach, and Puerto Rico Q7A training workshops, held in 2002, may be found on PDA's homepage at www.pda.org.

### Who Should Attend

This document covers all aspects of the manufacturing, controlling, and regulating of APIs. The following professionals will benefit from this training:

- Auditors of API Manufacturing Operations;
- Agents, Brokers, Traders, Distributors, Repackers and Relabellers of APIs;
- GMP Compliance Officials;
- Process Engineers;
- Production Engineers;
- Regulatory Investigators and Compliance Officers;
- Reviewing Chemists;
- Quality Assurance/Quality Control and Regulatory Affairs Professionals; and
- Consultants to the Pharmaceutical Industry.

### Learning Objectives

- Understand the intent of the Expert Working Group that developed the Q7A Guidance Document;
- Minimize variation in interpretation among industry and regulatory bodies worldwide;
- Address how the concepts of the Q7A guidance should be applied;
- Understand inspectional issues through side-by-side training of industry and regulators; and
- Understand how to interpret all 19 chapters of Q7A guidance, including special sections on APIs manufactured by cell culture/fermentation, and APIs for use in clinical trials.

**Working language will be English.**

To register, visit PDA's Web site at www.pda.org. ■

*—Leslie Zeck*

Tokyo, Japan

**May 5–9, 2003 • The Ritz Carlton Millenia Singapore**

# 2003 PDA International Congress, Courses and Tabletop Exhibits—Singapore

**Congress:** May 7–9
**Courses:** May 5–7
**Tabletop Exhibits:** May 7–8

PDA is finalizing plans for the 2003 Singapore Congress. An impressive listing of topics and speakers is being planned.

Dr. Clarence Tan, CEO, Health Science Authority Singapore, will deliver the regulatory keynote presentation. Other featured speakers include:

Bob Johnson, GlaxoSmithKline, USA
Susanne Keitel, BfaRM, Germany
Theodore Meltzer, Ph.D., Capitola Consulting Company, USA
David Rohrbach, Ph.D., Baxter Healthcare Corporation, USA
John Shabushnig, Ph.D., Pharmacia, USA
Eric Sheinin, Ph.D., USP, USA
Nick Turner, GlaxoSmithKline, UK
Michael Ward, Health Canada
John Westbrook, Pall Corporation, India
Manuel Zahn, Astra Zeneca, Sweden
Representative from Toyama Chemical Company, Ltd., Japan

Sessions at the conference will include discussions on such topics as:

- FDA Systems Based Inspections;
- Regulatory Procedure in the EU;
- Biotechnology Issues;
- Outsourcing;
- Aseptic Processing Issues;
- ICH Issues;
- Pharmacopeial Issues; and
- Process Analytical Technologies.

Opportunities for a limited number of tabletop exhibits are being offered. Please contact Nahid Kiani at (301) 986-0293 or via e-mail at kiani@pda.org for details.

Additional information is forthcoming and will be available on PDA's Web site, www.pda.org. ■

*—Leslie Zeck*

## PDA-TRI Courses

May 5–6, 2003
**A Practical Approach to Aseptic Processing and Contamination Control**
**Basic Concepts in Cleaning and Cleaning Validation**
**Active Pharmaceutical Ingredients: Manufacture & Validation**

May 5–7, 2003
**Requirements and Preparation of Pharmaceutical Grade Waters**

**September 8–12, 2003**

# 2003 PDA/FDA Joint Regulatory Conference, Courses and Tabletop Exhibits

**Conference:** September 8–10
**Courses:** September 11–12
**Tabletop Exhibits:** September 8–9

**Omni Shoreham Hotel • Washington, DC**

**Bigger Hotel! Better Networking Opportunities! More Exhibits!**

The 2003 PDA/FDA Joint Regulatory Conference in Washington, DC, PDA's preeminent conference, will deliver new opportunities for PDA members to interact with key FDA and international regulatory representatives.

Join your colleagues in the nation's capital for this important, annual, two-and-one-half day conference focusing on regulatory issues and cutting-edge topics that impact our industry.

- Extensive FDA Participation;
- Interactive Forums Addressing Technical and Regulatory Issues;
- Optional Breakfast Educational Programs;
- "Meet the Regulator" Roundtable Lunches with FDA and International Health Authorities;
- Networking Reception; and
- Informative Tabletop Exhibits.

Examples of topics to be discussed include:

- Revisions to the CGMPs;
- CDER/CBER Reorganization;
- Draft Concept Paper on the Aseptic Processing Guidance Document;
- Risk Management;
- Process Analytical Technologies;
- Designing and Effective Quality Unit;
- New Inspections guidelines for CBER;
- 21 CFR Part 11 Compliance;
- 21 CFR Part 11, BSE/TSE;
- Training, Integration Issues;
- Internal Audits;
- Laboratory Controls;
- GMPs in Drug Development;
- Water System Validation;
- Rapid Methods;
- System Based Inspections;
- Sterile API Facilities; and
- Change Control.

Submit your request for topics or technical and regulatory questions for the FDA and industry panelists and your colleagues in advance to info@pda.org

**DEADLINE FOR QUESTIONS**
August 1, 2003.

## Who Should Attend?

Individuals involved in pharmaceutical/biopharmaceutical product development, regulatory approval, production and quality assurance including those associated with drug product manufacture, service providers, contract services and USA and international regulatory authorities.

Registration information and a detailed brochure will soon be posted to the PDA Web site at www.pda.org. ■

*—Leslie Zeck*

**PDA-TRI Courses**

September 11–12, 2003
- Cleanroom Management
- CGMP & Compliance

September 11, 2003
- Biopharmaceutical QA/QC for Senior Management
- A Risk Based Approach to CGMPS

September 12, 2003
- Preparing for an FDA Pre-Approval Inspection
- Failures/Deviations and Change Control

PDA
An International Association For Pharmaceutical Science And Technology

FDA

**November 10–14, 2003**

# 2003 PDA Annual Meeting, Courses and Exhibition

**Annual Meeting:** November 10–12
**Courses:** November 13–14
**Exhibition:** November 10–11

## Hilton Atlanta • Atlanta, Georgia

Save the date now for the 2003 PDA Annual Meeting in Atlanta. A multi-track format for the conference will enable participants to select feature presentations from industry experts and regulatory representatives on a variety of cutting-edge issues related to pharmaceutical manufacturing.

Interactive presentations will cover the following issues:

- Regulatory Compliance;
- Toxic Material Processing/Handling;
- Validations of Processes;
- FDA Organizational Issues;
- Interest Groups;
- Isolator Technology;
- QA/QC; and
- More…

Interested presenters should submit an abstract or case study to PDA by March 1, 2003 for review and consideration by the Program Planning Committee. Watch the *PDA Letter* for updated information on this important conference.

A copy of the Call for Papers may be found enclosed with this issue and also in the Calendar section of www.pda.org. ■

*—Leslie Zeck*

**PDA-TRI Courses at the PDA Annual Meeting:**

November 13–14, 2003
– Basic Concepts in Cleaning and Cleaning Validation
– Computer-Related Systems Validation
– A Practical Approach to Aseptic Processing and Contamination Control

November 13, 2003
– Designing, Monitoring & Validation of Pharmaceutical Manufacturing Ventilation Systems
– Auditing Techniques for CGMP Compliance

November 14, 2003
– Managing in a GMP Environment
– Change Control & Documentation

**Deadline: Call for Papers—March 1st.**

*See enclosed flyer for details!*

**For Exhibiting Information**

*Contact Nahid Kiani*

*(301) 986-0293 x128*

*kiani@pda.org*

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*PDA Spring Conference from cover*

ing company bringing biopharmaceuticals from mind to market. He has approximately 15 years of experience in the biopharmaceutical industry.

## Deadlines

**Hotel reservations at the Paradise Point Resort and Spa will be accepted at the PDA discounted rate through February 17 or until the room block is full, whichever comes first**. Reservations made after February 17 can only be accepted at the prevailing rate, if space is available. Call reservations today at (800) 344-2626.

Avoid the onsite registration line by mailing/faxing your registration or by registering online at www.pda.org. Remember, you must have written confirmation to be considered registered for the Spring Conference. Online registrants will receive an e-mail confirmation in addition to a receipt. Questions? Call (301) 986-0293.

See you in San Diego! ■

*—Lisa Wade*

# Company, Colleague & Product Announcements

**Eisai Inc.**, a U.S. pharmaceutical subsidiary of Tokyo-based Eisai Co. Ltd., recently announced plans to strengthen its national sales force by adding an additional 150 sales representatives. The expansion is part of a two-year plan to increase Eisai's sales force to more than 500 sales representatives from its current number of about 250. The move supports Eisai Inc.'s plan to play a greater role in the promotion of its products and become a pharmaceutical company capable of promoting future products without relying on outside partners, when desired. Eisai Inc. also announced that the company has assumed USA distribution of Aricept® (donepezil hydrochloride tablets) from Pfizer Inc. Aricept®, a treatment for mild to moderate Alzheimer's disease, is co-promoted by Eisai Inc. and Pfizer Inc in the United States. Effective January 2, 2003, Eisai began fulfilling purchase orders for Aricept®, the number-one prescribed Alzheimer's medication worldwide, from a contract distribution center in Memphis, Tenn. Aricept® was discovered and developed by Eisai and is manufactured and packaged in its Research Triangle Park, N.C., facility. For more information, contact Judee Shuler at (201) 287-2241 or visit www.eisai.com.

**Patheon** recently announced that it has completed its agreement with Aventis Pharmaceuticals Inc. to provide long-term manufacturing and supply services to Aventis and to purchase Aventis' pharmaceutical manufacturing and development site located in Cincinnati, Ohio, USA. "The completion of this site acquisition—our first in the United States—marks an important milestone in the execution of Patheon's growth strategy," said Robert Tedford, CEO, Patheon Inc. "The FDA-approved facility gives us an operating presence in the world's largest pharmaceutical market and additional manufacturing capacity with which to serve our U.S. pharmaceutical and biotech clients. In addition, the Cincinnati site gives us a platform to expand our successful pharmaceutical development services in the United States." For more information, contact Robert C. Tedford at (905) 812-6760 or visit www.patheon.com.

Early this year, **Millipore** made available its Milliflex PLUS vacuum pump, a high-throughput filtration system for bioburden and water quality testing. The Milliflex pump uses pre-sterilized and ready-to-use filter units, offering an integrated solution for efficient and accurate process validation. The Milliflex filter units eliminate time-consuming washing, bagging, autoclaving and equipment handling for clean operation and optimal performance. By removing sterlilization steps, the Milliflex solution facilitates consistent workflow. The Milliflex pump includes built-in electronics to ensure high productivity and reduced testing time. For routine sampling, pre-loaded testing programs automatically control the pump through each filtration step. A manual mode also enables users to customize pump cycles to suit each standard operating procedure. Milliflex pumps are available in single, double, and triple head kits. For more information, contact Tara Hamre at (978) 715-1338 or visit www.millipore.com. ■

***—compiled by Joseph G. Bury***

**Send announcements on personnel changes and new products . . .**

. . . to Joe Bury via e-mail at bury@pda.org or mail hard copy to PDA headquarters in Bethesda, MD.

# PDA-TRI Director's Message

Editorial and publication deadlines being what they are, this is the first opportunity I have had to pen a few thoughts about news, events, and the future direction of PDA-TRI. First, though, I would like to take a moment to thank the PDA Board and staff as well as my friends and colleagues, for their good wishes and expressions of support as I assume my new role here at PDA-TRI.

In 2003 we will be offering five, off-site standalone training opportunities throughout the USA and Canada. Multi-day course offerings will be held in Puerto Rico (February 5–7), Baltimore, MD (May 14–16), Toronto (June 23–25), San Francisco, CA (August 19–21), and Boston, MA (October 20–22). We will also be offering course training opportunities in conjunction with PDA national and international meetings such as the International Congress in Prague, Czech Republic (February 24–28), PDA Spring Conference in San Diego (March 17–21), the International Congress in Singapore (May 5–9), PDA/FDA Conference in Washington DC (September 8–12) and the Annual Meeting in Atlanta, GA (November 10–14).

We will, of course, still be providing a series of laboratory course offerings throughout the year at the PDA-TRI facility outside of Baltimore. We are the only association that has such a hands-on laboratory program that is truly invaluable in linking theory and practice. Courses on high purity water systems, cleaning validation, and environmental mycology are being offered in February and March. The Aseptic Processing course series will be offered again in 2003 with four series dates on the schedule. This extremely informative course remains one of the industry's most popular hands-on courses. As of this writing the first two series dates are completely sold out. Space remains in the Series #3 and #4 offerings in the August–November time period.

So review the complete schedule and mark your calendars to take advantage of the opportunity to learn from some of our industry's most respected experts as well as to network with your fellow attendees. Remember, your learning need not stop when the class bell rings!

**We are the only association that has ... a hands-on laboratory program that is truly invaluable in linking theory and practice.**

In addition to these established lab and lecture offerings, we plan to seek out new, relevant course content and other "hot topics" of interest to our industry and our membership. Keep tuned into the PDA Web site and emails throughout the year as some of these offerings may occur rapidly.

Finally, we want to take full advantage of the unique facilities we have at PDA-TRI. We are already known for our outstanding lecture and laboratory courses. With your help, ideas, and support we will be establishing plans to put more "R" into "TRI" by initiating short term, practical research studies of particular interest to the pharmaceutical industry. By offering to conduct such studies on "neutral ground," it is hoped that mutual agreement and acceptance of the science-based results will be facilitated between industry and regulators.

All this will take time to develop, of course, so stay tuned in. We are in for some exciting new times here at PDA-TRI. Join us! ■

*—Robert Mello*

# Upcoming PDA-TRI Education Courses

Courses listed in alphabetical order

**Aseptic Processing 2003 Training Program—Lab** **Option 1**: January 27–31, 2003 and March 3–7, 2003; **Option 2**: April 7–11, 2003 and May 5–9, 2003; **Option 3**: August 25–29, 2003 and September 22–26, 2003; **Option 4**: October 27–31, 2003 and November 17–21, 2003; $7,500 members/$7,695 nonmembers; *Faculty:* John Lindsay and David Matsuhiro

SOLD OUT

SOLD OUT

**Cleaning Validation—Lab** February 19–21, 2003; May 19–21, 2003; October 13–15, 2003; $3,000 members/$3,195 nonmembers; *Faculty:* Jon Voss and Bob O'Brien

**Designing, Operating and Controlling High Purity Water Systems for Regulatory Compliance—Lab** February 12–14, 2003; $2,500 members/$2,695 nonmembers; *Faculty:* Bob Livingston and Gilbert J. Paul

**Ensuring Measurement Integrity in the Validation of Thermal Processes—Lab** April 28–29, 2003; November 6–7, 2003; $2,000 members/$2,195 nonmembers; *Faculty:* Göran Bringert

**Environmental Mycology Identification Workshop** March 13–14, 2003; May 15–16, 2003; October 2–3, 2003; December 4–5, 2003; $2,000 members/$2,195 nonmembers; *Faculty:* John Brecker ■

**These courses will be held at PDA-TRI in Baltimore, MD** unless otherwise noted.

**For course content information**, call PDA-TRI directly at **(410) 455-5800**.

**For registration information**, call PDA headquarters in Bethesda, MD at **(301) 986-0293**.

# PDA-TRI Location/Lodging Information

**Unless otherwise noted, PDA Institute courses are held at: PDA Training and Research Institute, 1450 South Rolling Road, Baltimore, MD 21227, Tel: (410) 455-5800; Fax: (410) 455-5802.**

PDA has not secured any specific room blocks for participants attending courses at the Training and Research Institute. There are several hotels in the Inner Harbor (downtown Baltimore) and BWI airport areas. These include, but are not limited to:

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(410) 625-1060 - fax

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(410) 859-5068 – fax

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(410) 850-0747
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**Homewood Suites BWI***
(410) 684-6100
(410) 684-6810 – fax

**Holiday Inn Inner Harbor****
(*Special Rates for our courses Attendees*)
(410) 685-3500
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**Hyatt Regency Baltimore Inner Harbor**
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(410) 605-2870 – fax

**Sheraton International Hotel BWI**
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**Courtyard Baltimore Downtown/Inner Harbor**
(443) 923-4000
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* no on-site restaurant

** **A discounted rate** is available for **Holiday Inn Inner Harbor of $99**, to receive this rate call the number above and mention the PDA-TRI Corporate Rate (ID# 100196574) when making your reservations, **rooms based on availability**.

*** **A discounted room rate** is also available from the **Holiday Inn—BWI**. You must call the number above and mention the PDA Corporate Rate (3-PDA) when making your reservations.

For additional hotel information, please visit ww.baltconvstr.com, the Baltimore Convention and Visitors Bureau's Web site.

**Transportation to PDA-TRI:** All listed hotels are no more than a 15–20 minute taxi ride to the Training and Research Institute. All hotels can assist you with taxi arrangements. Registrants may prefer to rent a car for easier access to and from the Institute.

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***Event Cancellation****: PDA reserves the right to modify the material or instructors without notice or to cancel an event. If the event must be canceled, registrants will be notified as soon as possible and will receive a full refund of fees paid. PDA will not be responsible for discount airfare penalties or other costs incurred due to a cancellation.*

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## PDA Books

### Good Practice and Compliance for Electronic Records

***published jointly with ISPE***


**Part 1—Good Electronic Records Management (GERM): Electronic Information Assurance for the Regulated Industry—Guide to Current Good Practice for Electronic Records and Signatures** What you need to know about positioning regulated establishments for achieving electronic information assurance—the concepts and principles that need to be considered when building, maintaining, managing and transitioning electronic environments—can be found in Good Electronic Records Management (GERM), Part 1 of the PDA–ISPE series on Good Practice and Compliance for Electronic Records and Electronic Signatures. Focusing on requirements and concepts rather than technical implementation details, this resource document is a valuable tool for the architects of electronic records environments. Whether your mission is to define the requirements, policies and procedures or to construct the physical environment, you will find that Good Electronic Records Management (GERM) is a must for your bookshelf. Key elements of the document include: prerequisites; electronic records; organizational controls; operations and infrastructure; transactions; records retention; personnel qualification and training; hybrid systems and controls; legal; glossary; and further reading.

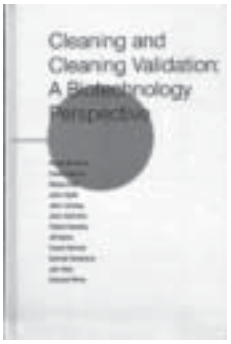
This document was produced through the collaboration of several industry groups (FDA regulated companies, system suppliers, legal experts, and consultants). It represents a compendium of current thinking on good electronic record management from an FDA regulated industry perspective. GERM attempts to present these practices at an abstraction level that is descriptive. The stated practices and concepts are meant to educate the reader when considering options for electronic records management. No endorsement of specific technologies is made, nor are there any specifics that direct a standard for the implementation of concepts. Current thinking on the topics presented means that this compendium is intended to evolve as experience with electronic recordkeeping grows. Application of concepts may require a paradigm shift in some organizations with regard to the treatment of electronic records. Such changes are a conscious business decision and not an intentional prerequisite for implementation of any of the concepts presented. 2002; 104 pages; $95 PDA members/$190 nonmembers **Item No. 19003**


**Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures** This document has been produced by a Special Interest Group of the GAMP Forum (pharmaceutical companies, suppliers, consultants and the Medicines Control Agency in the UK) in order to promote a better understanding of 21 CFR Part 11. It aims to provide industry and its suppliers with practical guidance on how to comply with the rule, while highlighting and addressing common issues of concern. The manuscript provides a management process for achieving and maintaining compliance with 21 CFR Part 11 in manufacturing environments. Specific guidance is provided for both new and existing systems in addition to the role of suppliers in supporting this approach. Appendices provide information, examples, templates, checklists, and a lifecycle for the management of electronic documents that are useful when implementing 21 CFR Part 11 compliance programs. A Glossary and References List are also included.

Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures; 80 pages; $95 members/$190 nonmembers
**Item 19001 (English)**

Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures; 80 pages, $95 PDA members/$190 nonmembers
**Item 19002 (German)**

Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures; 80 pages, $95 PDA members/$190 nonmembers
**(Spanish)**—*The Spanish version must be ordered directly from:* Ediciones VR, Av. Belgrano 3786, Of. #2, (1210) Buenos Aires, Argentina, Attn: Ms. Florencia Viscaino; E-mail: subscripciones@edicionesvr.com; Fax: 54 11 4931 4861 ext. 36




**Cleaning & Cleaning Validation: A Biotechnology Perspective** Authors: Roger Brunkow, David DeLucia, George Green, Shane Haft, John Hyde, John Lindsay, Jill Myers, Robert Murphy, John McEntire, Karen Nichols, Ray Prasad, Brenda Terranova, Jon Voss, Caroline Weil, Edward White; This book is intended to serve as a source of practical technical information for those persons in the biotechnology industry. Case studies and/or actual industry examples are used to support the text wherever possible. While much of the material contained within this text is equally applicable to non-biopharmaceutical processes, the emphasis has been focused directly upon biopharmaceutical manufacturing. Section I provides an in-depth analysis of the design concepts that lead to cleanable equipment. Also covered are cleaning mechanisms and cleaning systems. The first section is particularly useful to those persons faced with the task of designing systems that will be cleaned and also provides the biochemical background of the mechanisms associated with the removal of common biotechnology soils. Section II focuses on cleaning validation concepts. While the material is equally useful for single product cleaning, emphasis is placed upon multi-product cleaning validation. Included are general validation principles as they apply to cleaning validation, detailed analysis of cleaning process validation, sampling techniques, analytical methods and acceptance criteria. The material in Section II will be useful to anyone responsible for the development of a cleaning validation program. Section III provides an overview of multi-product biotechnology manufacturing procedures. Included an analysis of the risk to benefit scenarios associated with the various forms of product manufacturing, analysis of changeover programs, equipment considerations and material transport as they are affected by multi-product manufacturing strategies. 1995; 190 pages; $125 members/$145 nonmembers **Item 13002**

## Books from PDA-DHI Press

**Change Control** Soren Schwartz; This manual provides a well-organized, practical process for the management of changes to the Information and Control Systems used in GxP-related operations. 25 pp; $90members/$109 nonmembers **Item 17189**

**Electronic Records and Electronic Signatures Compliance Assessment** Chris Reid and Barbara Mullendore; *ERES* provides practical guidance on the interpretation of 21CFR Part 11 and the steps you need to take to address current and future compliance issues. 58 pp; $90 members/$109 nonmembers **Item 17177**

**External Quality Audit, The** Janet Gough and Monica Grimaldi; Will help you to effectively evaluate suppliers to determine reliability, quality and value. 100 pp; $120 members/$149 nonmembers **Item 17180**

**Filtration Handbook—Integrity Testing** Maik W. Jornitz and Theodore H. Meltzer; This complete guide explains the proper performance of filter integrity testing by clarifying its relationship to bioburden concerns and assessing its role in filter validation. It offers practical approaches to appropriate use of integrity testing, wetting and temperature requirements, the Bubble Point test, diffusive airflow testing and much more. Numerous regulatory citations and references complete this invaluable book. 150 pp; $185 members/$229 nonmembers **Item 17197**

**GMP in Practice: Regulatory Expectations for the Pharmaceutical Industry, 3rd edition** James Vesper; A quick guide to GMP, designed to simplify and enhance understanding of most of the current GMP expectations and how they apply to ongoing tasks in any given pharmaceutical manufacturing situation. 224 pp; $100 members/$125 nonmembers **Item 17199**

**Hosting a Compliance Inspection** Janet Gough; This is the guidance you need to host a compliance inspection. 106 pp; $120 members/$149 nonmembers **Item 17192**

**Internal Quality Audit, The** Janet Gough and Monica Grimaldi; This book provides guidance for performing a systematic internal quality audit with guidelines and a common sense approach to an often difficult task. 100 pp; $120 members/$149 nonmembers **Item 17179**

**Introduction to Environmental Monitoring in Pharmaceutical Areas** Michael Jahnke; Topics discussed include all aspects of cleanrooms, air handling systems, HAACP and risk analysis along with numerous useful charts, tables and figures. 104 pages; $90 members/$109 nonmembers **Item 17182**

**Laboratory Systems Validation Testing and Practice** Paul Coombes; This book, based on more than 20 years of experience in the pharmaceutical industry, put the subject of systems validation in its rightful place in the quality assurance world from the author's perspective. First, the primary importance of valid analytical data is discussed together with a persuasive case study and novel definition. The term LSV (laboratory systems validation) is used to make a distinction from CSV (computer systems validation) and equipment qualification. The differences that exist in the world of laboratory systems are explored, followed by a mass of detailed advice and examples of the specific qualities of many types of laboratory system. This provides the reader (who could be from a computing, chemistry, engineering, or QA background) with proven approaches to the generation of requirements specifications, and thereby, the subsequent validation testing strategies and tactics for laboratory systems. 113 pp; $120 members/$149 nonmembers **Item 17196**

**Media Fill Validation Environmental Monitoring During Aseptic Processing** Michael Jahnke; The second in this series of four books. Provides current, practical techniques that focus on considerations in the preparation and monitoring of aseptic manufacturing, taking into account the national and international requirements, and guidelines concerning the validation of aseptic processing. Topics include: Risk analysis, HAACP, Documentation and qualification; Qualification and training of personnel; Scope of validation; Overall requirements; Release requirements; Documentation; Authorization. The guide also includes an excellent Manufacturing and Testing Master Batch Record, and 25 extremely valuable charts, graphs, and figures. 108 pp; $90 members/$109 nonmembers **Item 17181**

**Microbiological Monitoring of Pharmaceutical Process Water** Michael Jahnke; Following a discussion of the regulations to be followed in the microbiological control of water processing and distribution systems, this work focuses on practical aspects in the pharmaceutical environment and gives advice on the methodology to be used, e.g., for sampling, the selection of nutrient media, incubation conditions, and identification of contaminants. It also describes trend analysis strategies and quality assurance to help you ensure consistent validation of water processing and distribution systems. The practices here were developed in a pharmaceutical manufacturing facility that produces drugs for parenteral use. The design, installation, and operation of a system to produce Purified Water and Water for Injection is presented and the practical aspects of microbiological monitoring is discussed. 70 pp; $90 members/$109 nonmembers **Item 17193**

**Microbiological Risk Assessment in Pharmaceutical Clean Rooms** Bengt Ljungqvist and Berit Reinmuller; This monograph clearly explains the Limitation of Risk Method (LR-Method). 17 pp; $75 members/$90 nonmembers **Item 17175**

**Microbiology in Pharmaceutical Manufacturing** Richard Prince, Editor; Providing valuable knowledge for the novice and the expert alike, many of the world's greatest pharmaceutical microbiologists and engineers, as well as other thought leaders, have invested their considerable talents and prestige in developing this comprehensive collection of timely information on this critically important subject. This book encapsulates current

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## Books from PDA-DHI Press *(continued)*

knowledge in a truly wide array of microbiological applications for the reader. It is hoped that this book will demystify the field of microbiology by describing it plainly and systematically from various scientific, technical, and functional perspectives. 900 pp; $240 members/$299 nonmembers **Item 17185**

**Practical Change Control for Health Care Manufacturers** Angie Jamison; Quick Guide. 124 pp; $120 members/$149 nonmembers **Item 17173**

**Quality Control Systems for the Microbiology Laboratory: The Key to Successful Inspections** Lucia Clontz; Addresses the main quality control systems that should be implemented in a microbiology laboratory with a focus on current issues and inspection trends. 175 pp; $120 members/$149 nonmembers **Item 17176**


**Steam Sterilization—A Practitioner's Guide** Jeanne Moldenhauer, editor; Contains pragmatic details on how to accomplish the tasks necessary for a sterility assurance program for steam sterilization processes. Each chapter author is a subject matter expert and has a minimum of 10 years of hands-on experience in the topics discussed. The authors use this experience to identify practical ways to perform research, development, validation, and production activities associated with steam sterilization. Many of the chapters include sample standard procedures or protocols that may be used as templates to generate documents for your facility. Other chapters outline and explain the requirements. The book also provides guidance for those individuals who are responsible for the oversight of these processes or those who wish to update their knowledge. While written primarily for the pharmaceutical industry, much of the content may be applicable to the food and cosmetic industries as well. While this book does not specifically address the bulk drug industry, certain information may be applicable to bulk drug manufacture. Whether your organization is small or large, this book contains insights and techniques that will prove invaluable in your effort to develop and maintain a sterility assurance program for steam sterilization processes. 740 pp; $200 members/$249 nonmembers **Item 17183**

**Understanding Active Pharmaceutical Ingredients** Seigfried Schmitt; Written by a Chartered Chemist and Member of the Royal Society of Chemistry, and edited by Trevor Deeks, this succinct document provides an overview of API use, including regulatory and validation details. 44 pp; $80 members/$109 nonmembers **Item 17188**

**Understanding GMP: A Practical Guide** Martyn Becker; This ex-MCA inspector, now at Merck, shares his expertise and perspectives on GMP regulations, legislation, applications, and practical challenges and solutions to applying GMP to the manufacturing environment. 237 pp; $120 member/$149 nonmember **Item 17174**

## Selected PDA Technical Reports

**TR 36 Current Practices in the Validation of Aseptic Processing—2001;** The validation of aseptic processing continues to be a major area of interest within the pharmaceutical industry. Five years have passed since the last PDA survey on this subject. While there have been no new broadly applicable regulations or regulatory guidance since that time, there has been continued controversy over the details of aseptic processing and process simulation practice. Industry practices largely adhere to current regulations and guidelines on aseptic processing by the European Union, ISO, and FDA. The impact of PDA's TR 22: Process Simulation Testing for Aseptically Filled Products, is also apparent. Over time industry methods, practices and limits have been modified to adapt to the changing circumstances. The Pharmaceutical Manufacturers Association (now PhRMA) in 1979 and PDA in 1986, 1992 and 1996 conducted surveys on this subject that have provided a clearer understanding of contemporary industry practice. This survey addresses the continuing need to track industry practice in the validation of aseptic processing as it evolves. Questionnaires were sent to 88 firms that specifically agreed to participate with PDA in this effort. Forty-three responses were received representing both US and overseas locations. The results were tabulated to provide both raw numerical and percentage of total respondents. Where the respondents provided comments, whether solicited or voluntarily, these are provided after the question. Where more than one respondent provided essentially the same response selection and comment, they have been consolidated and a number appears next to the response indicating the number of comments of that type. The nature and extent of the comments received were extensive, and for this reason the authors have chosen to combine similar responses. One of the major benefits of surveying on a regular basis is the opportunity to follow the evolution of concepts and practices over time. To that end, this survey instrument used many questions that were nearly identical to those asked in 1992 and 1996. 2001; 34 pages; $75 members/$125 nonmembers. **Item No. 01036**

**TR 35 A Proposed Training Model for the Microbiological Function in the Pharmaceutical Industry;** Many firms today have separate departments with different training requirements. Employees associated with the Microbiological Function do not always receive consistent training. This can lead to varying microbiological control practices within a manufacturing facility. This Technical Report was produced by the PDA Subcommittee on Microbiology Training, formed in January 2001, to develop an industry vision and guidance for instituting a step-wise, competency-based training program for microbiologi-

## Selected PDA Technical Reports *(continued)*

cal training of individuals engaged in work activities connected to contamination control and microbiological testing of pharmaceutical articles. 2001; 24 pages; $75 members/$125 nonmembers. **Item No. 01035**

**TR 34 Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products;** This technical report addresses essential user requirements for the application of isolator technology to a broad range of manufacturing, development and testing applications in the health care product manufacturing industry. It covers not only product sterility assurance, but also the use of isolators for the containment of hazardous materials. 2001; 25 pages; $75 member/$125 nonmember. **Item No. 01034**

**TR 13 Revised Fundamentals of an Environmental Monitoring Program;** The purpose of this document is to identify microbiological and particulate control concepts and principles as they relate to the manufacture of sterile pharmaceutical products. It expands substantially upon the first edition of Technical Report No. 13 (Revised), *Fundamentals of a Microbiological Environmental Monitoring Program*, published by PDA in 1990. While this publication cannot possibly supplant the wealth of information published on this subject, it provides summary information and appropriate references for the reader to consult, if necessary. The objective was to contemporize the first edition through the utilization of current definitions, recognition of improved environmental monitoring procedures, and equipment. This document serves as a source on clean room environmental test methods, and although some non-viable particulate and endotoxin testing data are included, its primary focus is microbiological control. The concepts for sterile product manufacturing are the most stringent application, but these concepts can also be applied to non-sterile product manufacture. The focus is environmental monitoring as it relates to facility control and compliance. This document was compiled to aid in setting up a program that is meaningful, manageable, and defendable. 2001; 37 pages; $75 member/$125 nonmember. **Item No. 01013**

**TR 33 Evaluation, Validation and Implementation of New Microbiological Testing Methods;** This report is intended to provide a general approach to the introduction of new microbiology methods in a government-regulated environment. It is also intended to provide guidance for the successful evaluation, validation and implementation of new microbiological methods needed by the pharmaceutical, biotechnology and medical device industries to assure product quality. These new methodologies offer significant improvements in terms of the speed, accuracy, precision and specificity with which testing can be performed. 2000; 37 pp; $75 members/$125 nonmembers. **Item No. 01033**

**TR 32 Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations;** Developed in response to an FDA challenge to develop a standard way to assess the structural integrity of acquired software, TR 32 was written by the PDA Supplier Auditing and Qualification Task Group (SA&Q), which included pharmaceutical companies, suppliers, auditors and FDA members who used their experiences with supplier audits and performed research to draft a common practice to satisfy industry needs. The scope of the project included audits of computer products and services and describes how the SA&Q Task Group, led by George J. Grigonis, Jr., Merck and Co., Inc., developed and tested a Process Model and Data Collection Tool. Use of these tools will provide consistent audit information that can be shared within the industry. December 1999; 277 pp; $90 members/$140 nonmembers (paper copy; **Item No. 01032**); **CD**—$50 members/$75 nonmembers (CD-ROM format; **Item No. 01132**).

## PDA Technical Archive on CD-ROM

**PDA Technical Archive on CD-ROM—PDA Archive Retrieval System;** The PDA Archive will give you easy access to more than 50 years of research papers written by highly qualified research scientists in the pharmaceutical industry. All PDA Journal articles, Technical Reports and Monographs, and selected Meeting Proceedings are available on this fully searchable CD-ROM. The archive is updated each year adding six issues of the PDA Journal, all PDA Technical Reports and Monographs, and selected PDA Meeting Proceedings. The archive is a 4-CD set.

**Archive** (2002 Release)
Price: $395 members/$495 nonmembers.
**Item No: 01101**

**2001 Update**
Price: $95 members/$195 nonmembers.
**Item No: 01002**

**See Page 27 for information on the "Orange Guide"...**

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- ❑ Engineering and Construction
- ❑ Government Regulatory Agency
- ❑ Industry Supplier
- ❑ Medical Device Manufacturing
- ❑ Pharmaceutical Manufacturing
- ❑ Pharmacy
- ❑ Recruiter
- ❑ Other

**Professional Interest (check all that apply)**

- ❑ Aerosols
- ❑ Analytical Chemistry
- ❑ Biologicals
- ❑ Biotechnology
- ❑ Computers
- ❑ Engineering
- ❑ Formulation Development
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- ❑ Liquids
- ❑ Maintenance
- ❑ Manufacturing/Production
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*2003 Calendar from back cover*

May 12–14, 2003
**ICH Q7A Training**
***Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients***
Hotel TBD, Tokyo, JAPAN

May 14–16, 2003
**PDA-TRI Baltimore Course Series**
Wyndham Inner Harbor, Baltimore, MD

May 15–16, 2003
**PDA-TRI Laboratory Course:**
***Environmental Mycology Identification Workshop***
PDA-TRI Baltimore, MD

May 19–21, 2003
**PDA-TRI Laboratory Course:**
***Cleaning Validation***
PDA-TRI Baltimore, MD

May 22, 2003
**UK & Ireland Chapter Meeting**
***Directive 2001//20/EC and Annex 13***
Britannia International, Canary Wharf, London, UK

**JUNE**

June 6, 2003
**PDA Southeast Chapter Golf Outing**
Location TBA

June 23–25, 2003
**PDA-TRI Toronto Course Series**
Westin Harbour Castle, Toronto, CANADA

June 30, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

**AUGUST**

August 19–21, 2003
**PDA-TRI San Francisco Course Series**
The Fairmont, San Francisco, CA

August 25–29, 2003
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 1***
PDA-TRI Baltimore, MD

**SEPTEMBER**

September 3, 2003
**UK & Ireland Chapter Meeting**
***Training Strategies***
Royal Pharmaceutical Society, UK

September 8–12, 2003
**2003 PDA/FDA Joint Regulatory Conference, Courses and Tabletop Exhibits**
Conference: September 8–10
Courses: September 11–12
Tabletop Exhibits: September 8–9
Omni Shoreham Hotel, Washington, DC

September 22–26, 2003
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 2***
PDA-TRI Baltimore, MD

September 24–25, 2003
**UK & Ireland Chapter Meeting**
***What to Do When Things Go Wrong***
Britannia International, Canary Wharf, London, UK

September 29, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

**OCTOBER**

October 2–3, 2003
**PDA-TRI Laboratory Course:**
***Environmental Mycology Identification Workshop***
PDA-TRI Baltimore, MD

October 13–15, 2003
**PDA-TRI Laboratory Course:**
***Cleaning Validation***
PDA-TRI Baltimore, MD

October 20–22, 2003
**PDA-TRI Boston Course Series**
Radisson Hotel Boston, Boston, MA

October 27–31, 2003
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 1***
PDA-TRI Baltimore, MD

**NOVEMBER**

November 6–7, 2003
**PDA-TRI Laboratory Course:**
***Ensuring Measurement Integrity in the Validation of Thermal Processes***
PDA-TRI Baltimore, MD

November 10–14, 2003
**2003 PDA Annual Meeting, Courses and Exhibition**
Annual Meeting: November 10–12
Courses: November 13–14
Exhibition: November 10–11
Hilton Atlanta, Atlanta, GA

November 17–21, 2003
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 2***
PDA-TRI Baltimore, MD

November 20, 2003
**UK & Ireland Chapter Meeting**
***Impact of FDA's Revised Guidelines on Aseptic Manufacture***
Keele University Management Centre, UK

**DECEMBER**

December 4–5, 2003
**PDA-TRI Laboratory Course:**
***Environmental Mycology Identification Workshop***
PDA-TRI Baltimore, MD

December 15, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

**Information on these conferences and courses will be posted on the PDA Web site as they become available.**

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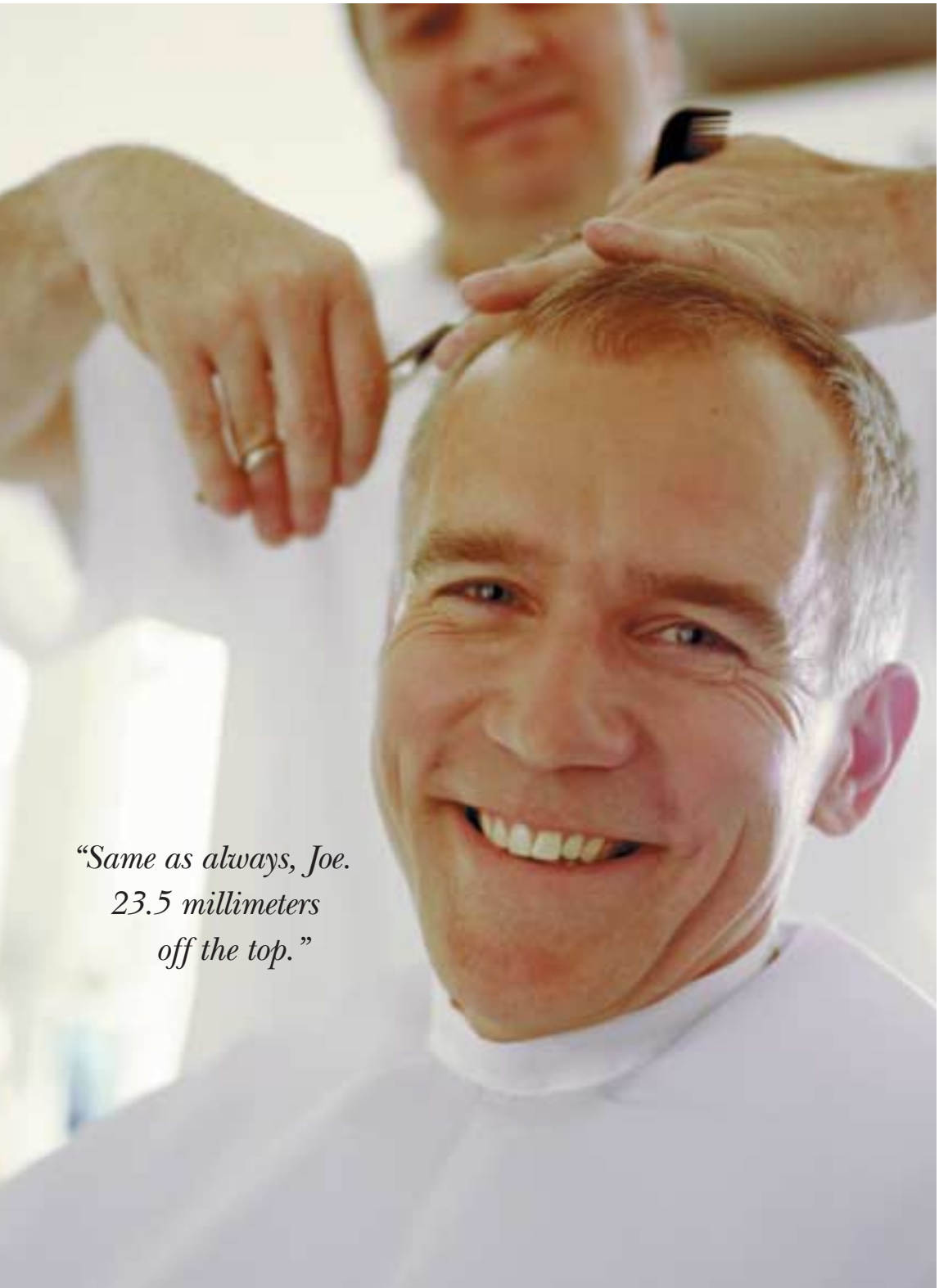

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# Calendar of Events

## 2003

### February

February 6, 2003
**UK & Ireland Chapter Meeting**
***BSE/TSE***
Crowne Plaza, Heathrow, UK

February 12–14, 2003
**PDA-TRI Laboratory Course:**
***Designing, Operating and Controlling High Purity Water Systems for Regulatory Compliance***
PDA-TRI Baltimore, MD

February 19–21, 2003
**PDA-TRI Laboratory Course:**
***Cleaning Validation***
PDA-TRI Baltimore, MD

February 24–28, 2003
**2003 PDA International Congress, Courses and Exhibition**
***Back to the Future—Ahead to the Past: Mastering the Fundamentals of GMPs to Manage the Challenges of Escalating Demands***
Congress: February 24–26
Courses: February 26–28
Exhibition: February 24–25
Hilton Prague, Prague, CZECH REPUBLIC

**PDA-TRI Lecture Courses:**
February 26–28
***Requirements and Preparation of Pharmaceutical Grade Waters***
February 27
***GMP for Investigational Medicinal Products—Draft GMP Annex 13 and the European Clinical Trials Directive***
***Beyond the GMP/ISO Basics—Practical Strategies for Everyday Compliance***
February 28
***Aseptic Processing Validation—Trends and Issues***

February 27–28, 2003
**PDA/IABs Conference**
***Scientific Considerations for Comparability of Biopharmaceuticals***
Hilton Prague, Prague, CZECH REPUBLIC

### March

March 3–7, 2003—**SOLD OUT!**
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 2***
PDA-TRI Baltimore, MD

March 6, 2003
**UK & Ireland Chapter Meeting**
***Validation & Operation of Aseptic Processes***
Manchester Airport Hilton, UK

March 13–14, 2003
**PDA-TRI Laboratory Course:**
***Environmental Mycology Identification Workshop***
PDA-TRI Baltimore, MD

March 17–21, 2003
**2003 PDA Spring Conference, Courses and Tabletop Exhibits**
***Bridging the Gap between Science and Compliance: The Impact of Today's Regulatory Environment on Biopharmaceutical Development and Approval***
Conference: March 17–19
Courses: March 20–21
Tabletop Exhibits: March 17–18
Paradise Point Resort, San Diego, CA

**PDA-TRI Lecture Courses:**
March 20
***Achieving a CGMP Compliance during Development of a Biotechnology Product***
***Good Documentation Practices in the Pharmaceutical Industry***
March 20–21
***A Practical Approach to Aseptic Processing and Contamination Control***
***Assessing Packaging and Processing Extractables/Leachables***
***Preparing for a FDA Pre-Approval Inspection***
***Validation: An Introduction***
March 21
***Conducting Compliant Deviation Investigations for Pharmaceutical Industry***

March 31, 2003
**PDA Presents**
***Basel Pharmaceutical Forums***
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

### April

April 7–11, 2003—**SOLD OUT!**
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 1***
PDA-TRI Baltimore, MD

April 10–11, 2003
**2003 Taormina International Conference and Tabletop Exhibits for Senior Executives in the Pharmaceutical Industry**
***Managing for Quality in a Cost-Focused Environment***
Conference: April 10–11
Tabletop Exhibits: April 10
Grand Hotel Timeo & Villa Flora, Taormina, Sicily ITALY

April 17, 2003
**PDA Southeast Chapter Spring Meeting**
Sheraton Imperial, Research Triangle Park, NC

April 28–29, 2003
**PDA-TRI Laboratory Course:**
***Ensuring Measurement Integrity in the Validation of Thermal Processes***
PDA-TRI Baltimore, MD

### May

May 5–9, 2003
**2003 PDA International Congress, Courses and Tabletop Exhibits**
Congress: May 7–9
Courses: May 5–7
Tabletop Exhibits: May 7–8
The Ritz Carlton Millenia, Singapore, SINGAPORE

May 5–9, 2003—**SOLD OUT!**
**PDA-TRI Laboratory Course:**
***Aseptic Processing Training Program—Week 2***
PDA-TRI Baltimore, MD

*continues on page 46*

Be sure to watch
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