Volume XL, No. 6

PDA Letter

June 2004

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

PDA's new event calendars appear on pages 28, 35 and 36

# IG Reports From the 2004 PDA SciTech Summit

## MEMIG Discusses FDA Guidance & PSIG Reviews USP <381> Comments

At the 2004 PDA SciTech Summit and Annual Meeting, most of PDA's Interest Groups (IGs) assembled to review current issues and/or report their progress.

In this edition of the *PDA Letter*, reports from the U.S. branches of the PDA Microbiology/ Environmental Monitoring IG (MEMIG) and Packaging Science IG (PSIG) are provided.

Participants in the MEMIG discussion focused on the FDA draft guidance on aseptic processing for pharmaceutical products, published in 2003. The PSIG discussion primarily covered the group's written comments on recently proposed revisions to the U.S. Pharmacopeia's (USP) General Chapter <381> *Elastomeric Closures for Injections.*

Additional IG Reports from the 2004 PDA SciTech Summit appeared in last month's issue.

*continues on page 10*

# PDA Chapter Events Tackle Regulatory Issues

## Spain Chapter Hosts March 15 EuroForum in Barcelona

The beautiful city of Barcelona was the host city for the first meeting of the PDA Spain Chapter in 2004: a PDA Euroforum titled, "Experiences and Challenges with the Implementation of CTD in Europe." The Spain Chapter also held its elections during the meeting and discussed how best to become more involved with PDA, how to increase membership in Spain and what kind of PDA events are needed in the future to help professionals in the pharmaceutical and biopharmaceutical communities in Europe become more efficient and better informed at work.

Attending the event were 23 members to hear experts from various European health authorities talk about the Common Technical Document (CTD). Health authority speakers were Christa Withumer-Hoche, Austrian Health Authority, Mª Luisa Gª Vaquero Donaire, Spanish Medicines Agency, and Hilde Boone, EMEA. Experts from industry also spoke: Karin Sewerin, Biologics Consulting Group, Sweden, and Andrew Marr, from GlaxoSmithKline in the UK.

*continues on page 30*

## Israel Chapter Sponsors Event on PIC/S in Tel Aviv

Following a one-day course in March (see the *PDA Letter*, April 2004, p. 24), the PDA Israel Chapter held a course on the Pharmaceutical Inspection Convention Scheme (PIC/S) on April 22.

The Israel Chapter invited Robert Tribe, Senior GMP Advisor, GMP Audit and Licensing Section, Therapeutic Goods Administration (TGA), Australia to Tel Aviv to give a course on PIC/S.

Over 20 professionals heard Mr. Tribe discuss the following topics:

- History of PIC/S,
- Role and functions of PIC/S,
- PIC/S accession procedure,
- PIC/S GMP guide and guidance documents,
- PIC/S seminars and expert circles,
- PIC/S plant approval inspections, and
- The IMID.

*continues on page 30*


If you created a company with unparalleled expertise in .....

....a solutions company that could keep pace with problems of your pharmaceutical, medical device, biotech, biologics or generic drug company -

PSI would be that company.

PSI SM

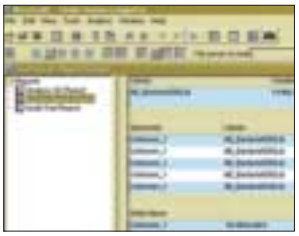
*Pharmaceutical Systems, Inc.*

909 Orchard Street • Mundelein IL 60060
Tel: 847.566.9229 • Fax: 847.566.4960
www.pharmsystems.com

# "When other groups have a tough bug they can't identify, they bring it to us."

**JOHN BARTELL**
**SENIOR SCIENTIST, R&D MICROBIOLOGY**
**AND MICROSEQ SYSTEM CUSTOMER SINCE 1997**

**MicroSeq offers an accurate and precise genotypic solution, the method recommended by the FDA.**
"Rapid genotypic methods are recommended for purposes of identification... shown to be more accurate and precise than biochemical and phenotypic techniques."
*—Pharmaceutical Current Good Manufacturing Practices*
(FDA Draft Guidelines 8/03)
**Read the FDA report on genotypic analysis.**
**Visit www.microseq.com**



**MicroSeq® Analysis Software**
Simplifies identification, taxonomy, and reporting with Windows® OS convenience, easy to use wizards, and a powerful, automated toolset.

"Our microbial lab supports clinical studies, so it's critically important to accurately identify organisms. **DNA-based MicroSeq® methodology is based on a constant characteristic and the results are extremely reproducible, even when microbiological conditions change—a luxury you often don't get with phenotypic analysis.** Basically, when those systems get it wrong, we get it right.

If you can't identify an organism correctly, you won't know if you're seeing it again. For good microbiology, you should have the right name and know how species are related. The MicroSeq® software really helps. It's easy to use, and extremely flexible. In addition to the built-in library, it lets us quickly compare results against other databases and add new sequences. It also makes it easy to draw phylogenetic trees and share results.

People are discovering new bacteria species with growing frequency. The MicroSeq® system is a powerful tool for characterizing these new organisms, as well as unculturable samples we wouldn't be able to classify using any other method."

**To learn more about reliable, reproducible bacterial and fungal identification using the MicroSeq® system, please visit: www.appliedbiosystems.com/microseq1**

**Visit us at ASM, Booth 929**

**Convenient MicroSeq® Application Kits**
Together with regularly-updated bacterial and fungal sequence libraries, plus proven Applied Biosystems instrumentation—a complete, integrated system for fast, reliable microbial identification.

iScience. Applied Biosystems provides the innovative products, services, and knowledge resources that are enabling new, integrated approaches to scientific discovery.

Applied Biosystems

## Important Dates...

- **July 1**—EMEA Note for Guidance on Minimising Risk of TSE becomes applicable
- **July 5**—Deadline for public comment on FDA CDER Draft Guidance on CMC submissions for drug substances
- **July 6**—Deadline for public comment on CDER/CBER draft guidances on risk management.
- **July 6**—Deadline for public comment on FDA combination products rule changes.
- **August 31**—EMEA API Master File guideline becomes effective
- **September 7-8**—PDA/BFS Inter'l. Operators Association Joint Workshop on Blow/Fill/Seal Processing Holopack Verpackungstechnick GmbH, Germany
- **September 20-24**—2004 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits: The New Guidances Omni Shoreham Hotel, Washington, D.C.



## IN THIS ISSUE...

**IG Reports From the 2004 PDA SciTech Summit** ..... **cover**

**PDA Chapter Events Tackle Regulatory Issues** ..... **cover**

**PDA News and Notes** ..... **6**
The President's Message ..... 6
New Faces at PDA ..... 7
PDA Volunteer Opportunities ..... 8

**Science and Technology** ..... **10**
Recent Sci-Tech Discussions ..... 14
Call for Papers ..... 16

**Regulatory News** ..... **20**
PDA Interviews USP's Roger Williams, Pt. 2 ..... 20
Regulatory Briefs (U.S. FDA, EMEA, EU) ..... 22

**Programs and Meetings** ..... **28**
More 2004 PDA SciTech Summit & Annual Meeting Photos ..... 28
Programs And Meetings Calendar ..... 28

**Membership and Chapters** ..... **30**
2004 CHAPTER EVENTS CALENDAR ..... 35

**PDA Training and Research Institute** ..... **35**
2004 Training And Research Institute Calendar ..... 36

**Audit Repository Center/TR-32** ..... **38**
Documentum extends its membership with the Audit Repository Center ..... 38

**Technical and Regulatory Resources Available** ..... **42**

The *PDA Letter* is published monthly by PDA, exclusively for PDA members. Subscriptions are not available. Articles in the *PDA Letter* may be reproduced with permission—contact the Senior Editor for details. 

**Production Staff**
Walter Morris, Senior Editor
Peter Marinovich, Manager, Web and Production
Matt Clark, Director, Marketing, Membership & Chapters

**Executive Staff**
Neal G. Koller, President

Vice Presidents
Vicki Dedrick, Quality and Regulatory Affairs
Lance Hoboy, Finance and Strategic Planning
Robert J. Mello, Ph.D., Education and Director of PDA Training and Research Institute
George A. Robertson, Ph.D., Science and Technology

Directors
Gautam Maitra, *Europe*
Wanda Neal, Programs and Meetings

**PDA Global Headquarters**
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900 Fax: +1 (301) 986-0296
E-mail: *info@pda.org*
Web site: **www.pda.org**

**PDA European Headquarters**
287 Avenue Louise
BE-1050 Brussels
Belgium
Tel: +32-2-643-2045 Fax: +32-2-645-2671

**PDA Office of European Director**
R-1059.747 Postfach
Schwarzwaldalle 215
CH-4002 Basel
Switzerland
Tel: +41 61 321 56 30 Fax: +41 61 321 83 48
E-mail: *maitra@pda.org*

**PDA Training and Research Institute**
c/o UMBC Technology Center
1450 S. Rolling Road
Baltimore, MD 21227 USA
Tel: +1 (410) 455-5800 Fax: +1 (410) 455-5802
E-mail: *info-tri@pda.org*

PDA
An International Association For Pharmaceutical Science And Technology

# The *New* PDA Publications E-store is here!

PDA is pleased to announce that its Publications E-store is now available online at https://www.pda.org/pubs. The fully-interactive E-store is a one-stop shop of the largest selection of scientific, technical, and regulatory resources PDA has offered in its 57-year history.

✓ **"Search the E-store"** using advanced search features to find select PDA publications by author, title, publication type, keyword(s), item number, or publication category (i.e. "Microbiology" and "Computer Validation").

**or**

✓ Browse the **"Table of Contents"** by publication type (for PDA Technical Reports, PDA Proceedings, Training Videos, and more) much like you would a hard-copy of the PDA Publications Catalog.

Visit the E-Store today and check out PDA's expansive new offerings.

**Ordering your publications from PDA has never been easier!**

Neal G. Koller
PDA President

## President's Message

# New Office in Brussels Preparing PDA for Challenges of the Future

I am very pleased to announce that PDA has increased our ability to serve PDA European members and the PDA European community as a whole by opening a new office in Brussels, Belgium. The new Brussels office will now be home for the PDA European Headquarters. This move will better position PDA to expand our level of service to PDA European members. For more information, please see the announcement of personnel, responsibilities and contact information on the next page.

Establishing a full-service Brussels office is a significant advance for PDA and will make it easier, more convenient and less costly for the members located in Europe and the pharmaceutical and biopharmaceutical communities there to interact with PDA.

Gautam Maitra, PDA European Director, will continue to work out of his office in Basel Switzerland. Basel is a major center for the pharmaceutical and biopharmaceutical industries. Maintaining Gautam's presence in Basel will serve as additional support and provide additional advantages for the European membership and the community.

The new Brussels headquarters will provide PDA European members and community with direct European access and support for:

- Membership Services
- Registrations
- Meeting Planning
- Exhibition Management
- Sponsorships Management
- Publications Management

In the past year, PDA has considerably increased membership activities in Europe. For instance, new European Branches of five PDA Interest Groups were established (Biotechnology, Drug-Device Delivery Systems, Filtration, Visual Inspection for Parenterals and Nanotechnology) along with three new Chapters (France, Prague and Spain). In collaboration with the European Federation of Pharmaceutical Industries and Associations (EFPIA), PDA recently submitted case studies to the EMEA concerning Annex 1 revisions. Moreover, PDA now provides science based comments on World Health Organization (WHO) guidance documents. Opening the office in Brussels considerably supports these groups and activities.

The new Brussels office will afford more capability and opportunity for PDA at a time of significant change in the European industry and regulatory environments. I refer specifically to the action plan by the European Commission (EC) on industrial innovation and the new road map for the European Agency for the Evaluation of Medicinal Products (EMEA) and the national health authorities, both published in April.

The EC's "Innovate for a Competitive Europe" action plan outlines a course of action that will have foundational effects on the pharmaceutical and biopharmaceutical industries and the way they are regulated. The plan outlines six objectives to help all the major industries in Europe get new and innovative technologies on the market:

- Innovate everywhere;
- Get innovation on the market;
- Knowledge everywhere;
- Invest in innovation;
- Skills for innovation; and efficient Innovation governance.

While each aspect of the plan is applicable to the pharmaceutical industry, objective two, "Get Innovation to the Market," will be of particular interest to PDA and its members. Here, the European Commission calls for technology-neutral regulation, leaving room for innovative solutions, ensuring stability and legal certainty, while taking into account the size and speed of development of new markets. The plan also points to the "proper use" of "voluntary standards." In the context of better regulation, the EU will assess the impact of regulations and standards on innovation. To meet this objective, the action plan calls for dialogue among stakeholders in the impact assessment and in the regulatory and standardization processes. PDA and its members can and will play a role in this process.

*continues on next page*

# New Faces at PDA

PDA is pleased to introduce the following new staff members:

PDA European Headquarters

Robert Jenks, PDA's new European Business Development Coordinator, will work on a variety of projects relating to marketing and communications for PDA. Previously, Mr. Jenks work at the European Commission in the Directorate General Enterprise. Mr. Jenks is from Ireland, but was raised in Brussels. Fluent in French, he also speaks English and Swedish. He holds a BSc Honours in Production & Operations Management from the University of Nottingham, UK, and an MSc in Business Administration—Strategy & Culture from Linköping University in Sweden.

Adline Lewuillon, PDA's new European Membership and Registration Coordinator, will support PDA's meetings and events planning in Europe. She is a graduate in Roman Philology, and holds a post-graduate programme in Multilingual Business Communication from the Université Catholique de Louvain (UCL), Belgium. A native of Belgium, she speaks French, English and has a working knowledge of Dutch and Italian.

Marianne Marti joins PDA's new European Headquaters as Assistant European Director. Ms. Marti will assist in the organization of all PDA events in Europe. She has extensive experience in this area, having worked previously for the European Nursing Association and Janssen-Cilag, a Johnson and Johnson company. Ms. Marti is a native of Switzerland and is a fluent speaker of English, German and French.

Mr. Jenks, Ms. Lewuillon and Ms. Marti, can be contacted at the new PDA European Headquarters:

PDA European Headquarters
287 Avenue Louise
BE-1050 Brussels
Belgium
Telephone: +32 2 643 20 45
Fax: +32 2 645 26 71
E-mail: jenks @pda.org; lewuillon@pda.org; marti@pda.org.

PDA Headquarters

Peter Marinovich joins PDA as the new Web and Production Manager. He has extensive experience in the pharmaceutical industry, having worked for 14 years at F-D-C Reports, Inc., publisher of the pharmaceutical trade publications *"The Pink Sheet"*, *"The Gold Sheet"*, and others. Mr. Marinovich graduated from Louisiana State University with a BA in Fine Arts.

Takiyah Jefferson joins PDA as Programs and Meetings Manager. She has more than seven years of volunteer and professional experience in meeting, conference and event planning. Prior to joining PDA, Takiyah worked as a meeting planner for the National Society of Black Engineers (NSBE), where she was responsible for planning over 30 meetings, conferences and events and assisting with its Annual Convention of over 10,000 attendees. Ms. Jefferson is a Certified Meeting Professional and a 2003 graduate of the New York University Professional Certificate Program in Meeting, Conference and Event Management. She also is a member of several meeting planning professional associations. ■

***President's Message**, from page 6*

"The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future," published by the EMEA, is a related plan. It outlines a twofold approach to improving the way medicines are regulated in Europe: "Provide better protected and informed patients and users of medicines, whilst encouraging and facilitating innovation and research in an enlarged EU." New European legislation has recently been passed that expands the responsibilities of the EMEA (see "Regulatory Briefs," pp. 22-26).

For more information on both of these European initiatives and PDA activities please contact Gautam Maitra, European Director, or Vicki Dedrick, Vice President Quality and Regulatory Affairs.

Industry involvement in these European initiatives is preferable and advisable to ensure success. PDA, as it always has, will be here to help our members, the industries and the regulatory authorities come together and to allow the best science and technology to guide their decisions. By opening the Brussels office, PDA has strengthened our ability to facilitate this all-important dialogue. ■

# Call for Volunteers

## New PDA Task Force—Putting GERM To Work

by George Grigonis, Consultant, QAEdge

**PDA Task Force:** Putting GERM To Work

**Who:** Managers and corporate leaders in:

- regulatory affairs,
- records management,
- information technology, and
- compliance.

**When:**

- 8 hours every month
- meet every 4-6 weeks
- total project time 12-18 months

PDA is initiating a new task force to work on a compliant activity set for electronic records management (ERM) that will put the Good Electronic Records Management (GERM) concepts to work for corporations. On March 8, 2004, a press conference at the Javits Center in New York City, announced the results of a research study conducted by jointly by ARMA, AIIM and Cohasset Associates on the state of ERM. The study, based on ERM practices of 2,200 participants, highlighted the electronic records crisis faced by Corporate America today, that is quickly reaching an out of control situation in all companies. The conclusions reached were that:

- Most organizations have serious operational problems regarding the processes by which they manage electronic records, one of their most important assets;
- Baseline studies conducted four years earlier, suggests there has been essentially no improvement in managing record assets. In fact certain earlier shortcomings have deteriorated substantially to the point where some are now alarmingly worse;
- The root cause of deficient practices is suggestive of the proverbial management "silos" relating to business functions that are key to successful management of electronic records;
- The number and magnitude of organizational and operational problems collectively create stunning business risks from both a legal and regulatory perspective; and
- ERM issues should be the focus of immediate corrective action and elevated to a high corporate priority

It is clear from this study that no level of risk management, advocated buy the FDA regulated industry for record compliance, will offset the weak foundation of institutionalized practices used to manage electronic records for business and regulatory needs.

The objective of this new task force will be to define an activity set framework for a compliant ERM program which implements PDA GERM principles and a corporate self-assessment guide that uses the Framework as a maturity metric. In addition to defining a framework the task force will also work on the necessary PDA training and industry advisory board infrastructure needed to deploy and sustain the framework.

PDA is looking for industry volunteers who are decision makers in their respective institutions and who are the managers and corporate *leaders* in the functional areas of legal, records management, information technology, and compliance. Service providers with expertise in ERM consulting services are also welcome. PDA is inviting U.S. FDA management with experience in this area to participate as advisors to ensure task force deliverables are in line with current Agency thinking on the subject. The team of representatives will meet on a regular basis in Bethesda, Maryland. Team members will be expected to put in at least eight hours per month, non-meeting time, to work on assignments. The Task Force is expected to meet every four to six weeks. Work effort is estimated to be 12 to 18 months.

Interested volunteers are asked to submit names and contact information to:

George A. Robertson, Ph.D.
Vice President, Science & Technology
PDA
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900, ext. 139
Fax: +1 (301) 986-0296
E-mail: robertson@pda.org

## New PDA Task Force—Computer Compliance

by George Grigonis, Consultant, QAEdge

PDA is initiating a new task force to align computer compliance with the modern realities of information technology (IT) concepts and related emerging technologies. Compliance expectations that formed the basis for computer validation practices are not suited for implementing computing solutions acquired and assembled from the marketplace. Nor are they suited for sourcing to computing service providers who are rapidly becoming a viable option to many companies. As corporations continue to depend on computing solutions to stay competitive, there is an increased business need for agility and speed. Current with this is the need to be compliant in the context of existing regulations and with emerging laws resulting from the various corporate scandals that are now requiring companies to show how technical choices are made in the course of business and to prove the trustworthiness of electronic information submitted to regulators and to the courts.

The objective of this new task force will be to research suitable modern practices that concentrate on process and testify to corporate maturity in the selection, implementation and use of computing solutions and then to endorse these practices in the form of education for practitioners, managers and executives. The scope will define:

- current Good System Practices (cGSP) curriculum for the PDA Training and Research Institute that utilizes currently available bodies of knowledge and courseware available from academic institutions devoted to implementing, servicing and evolving computing solutions,
- a outline for courseware development that places cGSP in a regulatory context and as a primer to a cGSP curriculum, and
- the necessary PDA infrastructure needed to deploy and sustain the curriculum in support of mature and compliant computing practices for regulated operations and trustworthy Part 11 records.

PDA is looking for industry volunteers who are managers and *leaders* in their corporate decision making process regarding computer compliance. Service providers whose computing services are predicated on modern computing practices are also welcome. PDA is inviting U.S. FDA with experience in this area management, to participate as advisors to ensure task force deliverables are in line with current thinking regarding expectations for compliant computing environments and Agency initiatives for risk and process oriented thinking. The team of representatives will meet on a regular basis in Bethesda, Maryland. Team members will be expected to put in at least eight hours per month, non-meeting time, to work on assignments. The Task Force is expected to meet every four to six weeks. Work effort is estimated to be 8 to 12 months.

Interested volunteers are asked to submit names and contact information to:

George A. Robertson, Ph.D.
Vice President Science & Technology
PDA
An International Association for Pharmaceutical and Biopharmaceutical Science and Technology
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900, ext. 139
Fax: +1 (301) 986-0296
E-mail: robertson@pda.org
www.pda.org

**PDA Task Force:**
Computer Compliance

**Who:** Managers and leaders in:

- computer compliance and
- service providers.

**When:**

- 8 hours every month
- meet every 4-6 weeks
- total project time 8-12 months

*continues on page 10*

*IG Reports, from cover*

## Microbiology/Environmental Monitoring—U.S. Branch

Leader: **Jeanne Moldehauer, PhD, VecTech Pharmaceutical Company**

E-mail: **jeannemoldenhauer@yahoo.com**

The topic under discussion for this IG meeting was issues in Environmental Monitoring. Jim Quebbeman of Pfizer and Victoria Galliani of Compliance Software Solutions Corp. served on the panel moderating this topic.

The following is an overview of some of the issues discussed:

**Advanced Aseptic Processing:**

As an industry we tend to assume that all Blow-Fill-Seal operations should be considered advanced aseptic processing. However, many of the older systems have not been upgraded to current standards and should not automatically be considered advanced processing.

**What is the "right" way to set EM limits?**

This was a lively discussion starting with a consideration of what is a limit versus level (process control parameter). Central to the discussion was whether ICH Q6A considers environmental monitoring (EM) values to be specifications.

The next part of the discussion focused on **whether one should be concerned with the number of organisms present, or the type of organism, e.g., are some objectionable?**

In considering objectionable organisms the group discussed the presence of mold in a cleanroom. Specifically, there was concern on whether each occurrence of mold should be considered objectionable or should trends be the issue. Since molds can be indigenous on people, the question was whether it really is unexpected to find occasional mold contamination.

Another consideration was **should limits specified in standards be automatically used?** The merits of selecting ISO Standards versus Grades from EU GMPs Annex 1 were discussed.

**In setting limits, what should be considered among an adverse trend?** There is not one consistent definition of what should be an adverse trend. The draft aseptic processing guidance from FDA (2003) provides recommendations on how to define an adverse trend, and the number of alert levels that can be exceeded before triggering an action level. An interesting example presented was whether one count of 50 is not as bad as counts of five in several areas over time.

**Do you really need a selective media and/or bi-phasic temperature incubation to grow mold?**

No consensus was achieved on this issue. Concerns voiced in the discussion were the limit of detection for the method, and the statistical tools used to evaluate the data.

**What kind of statistics should be applied to EM data?**

Some companies rely heavily on statistics. One should be sure that the statistics used are appropriate for their intended use.

There are some inherent problems in applying statistics to rooms with levels of 0/1. One method discussed was cumulative frequency evaluations to determine how often you might expect to find contamination in your facility.

The bottom line here is that we need to know our facilities.

**The merits of using control charts for evaluating environmental monitoring data were discussed.** Using this method several advocated use of $\pm 3\sigma$, daily plotting of data, and evaluation of patterns generated.

**Risk assessment was advocated in establishing sample sites and methods to be used.**

A concern voiced regarding risk assessment is that there is not much published guidance that describes how to use these techniques for microbiological data. Another hindrance to performing risk assessment is the reluctance to change in our facilities.

The FDA draft guidance on aseptic processing (2003) indicated that microorganisms should be identified to genus and species, with nucleic acid methods preferred. **The group discussed what various companies are doing, e.g., are you purchasing equipment to perform genetic identification or sending samples out to a contract laboratory for identification?** Responses were mixed on this topic. There was also diversity on whether the cost for genetic methods was comparable to traditional methods. The discussion segued to comparing the cost for these methods and whether the difference in cost was justified.

**Finally the group was surveyed to determine how many companies have already implemented using genetic identification methods as a result of the FDA draft guidance.** The survey revealed about 90% of the group had implemented these procedures based on the draft guidance.

*continues on page 12*


**The TexShield product line includes Sterile 70% Isopropyl Alcohol, Sterile 70% Isopropyl Alcohol with WFI, Isolator Cleaning Tools and Sterile Pens.**

The TexShield product line was developed to address the **contamination control** concerns of sterile product manufacturers. We realize you need products that offer **assured sterility** and **uncompromised quality.** We understand the importance of the documentation you receive with every sterile product you buy. We know you are looking to improve safety and reduce waste when using sterile alcohol products.

Packaged in the unique **SteriShield Delivery System™,** TexShield sterile alcohol contents remain sterile three months after first operating the trigger mechanism. The contents can be completely dispensed, **eliminating waste.** The innovative, lightweight Isolator Cleaning System is shaped to clean both flat surfaces and hard-to-reach corners. Each TexShield product is designed to make your job easier. For more information, call 1-800-839-9473, ext. 120 or visit our website.

TW Texwipe®

**Better solutions, together.**

**North America**
Tel 201 327 9100
Fax 201 327 5945
E-mail info@texwipe.com

**www.texwipe.com**

*IG Reports, from page 10*

## Packaging Science Interest Group—U.S. Branch

Leader: **Edward J. Smith, PhD, Manager, Packing and Testing, Wyeth Pharmaceuticals**
E-mail: **smithej@wyeth.com**

The PSIG met on March 9th in Orlando at the PDA SciTech Summit and Annual Meeting. Thirty attendees participated in the meeting, which was chaired by Diane Paskiet of Monarch Analytical Laboratories.

Participants listened to two presentations—one on a new laminated plastic vial and the other on anticounterfeiting. Brian McCarthy of Owens-Illinois described a new type of multilayer plastic vial that has many advantages over conventional homogeneous plastic vials and glass. Michael Eakins, PhD, Eakins & Associates, discussed some of the anticounterfeiting initiatives discussed at a recent meeting held by the U.S. FDA. Copies of both presentations have been distributed to all those on the PSIG distribution list and also may be found on PDA's Web site.

A key subject of discussion at the Packaging Science IG (PSIG) meeting was the latest proposed revision of the U.S. Pharmacopeia (USP) General Chapter <381> *Elastomeric Closures for Injections,* which appeared in the USP *Pharmacopeial Forum*, Vol. 30 [Jan.-Feb. 2004]. Several comments and recommendations on the proposal were discussed during the PSIG's meeting at the PDA SciTech Summit and Annual Meeting and many more were received by the PSIG following the meeting. A summary of these comments, shown below, will be sent to the USP by PSIG through the PDA office. The following are the PSIG comments on USP <381>, organized by the chapter's headings:

### INTRODUCTION

Remove reference to "identification tests". Specified identification tests have been removed from the "Identification Tests" section.

The USP 381 rev. states that the physicochemical tests apply only to the base elastomer and not to the laminated coating and that the functionality tests apply to the entire coated closure. The European Pharmacopeia (EP) test protocol states that the specification does not apply to laminated or coated closures. To harmonize this point, it is suggested that the EP protocol be followed until a meeting between the USP and the EP can resolve this issue.

In the second paragraph of the Introduction, the USP 381 rev. defines what types of closures fall under the type I and type II specification. Both the USP and the EP describe type II closures as closures used for multi-dose containers for injections: "single dose or multi-dose containers for injections containing vegetable oils, including emulsions and liposomal formulations or other non-aqueous vehicles…." It is PDA's position that the first sentence in the stopper classification referencing multi-dose stoppers as part of the class II specification is too open ended since most closure systems in the industry hold water based drugs for multi-dose application. Class II requirements typically fall under the umbrella for closures, packaging drugs with non-aqueous vehicles. In some cases, where special physical requirements are also an issue, as in IV set connectors and injection sites, the class II designation would also be correct. With the present definition of what falls into the class II specification, it would allow most closures made in the industry today, to be able to fall into this lower specification requirement. We suspect that this was not the intent of the EP Monograph. Perhaps the EP could shed some light on this matter.

After "…and not to the laminated coat.", add "Uncoated/non-laminated closures made from the same rubber compound may be tested to obtain USP <381> test results."

Change the phrase "…apply to the base elastomer, and not to the laminate coat." to "…apply to the base rubber compound and not to the laminated coating."

### CHARACTERISTICS

1. Rubber closures are elastic; they are translucent or opaque and have no characteristic color, the latter depending on the additives used. They are homogeneous and practically free from flash and adventitious materials (e.g., fibers, foreign particles and waste rubber).

### IDENTIFICATION TESTS

1. Closures made of a wide variety of elastomeric materials and optional polymeric coatings. For this reason, it is beyond the scope of this chapter to specify identification tests that encompass all possible closure presentations. However, it is the responsibility of the closure supplier and the pharmaceutical manufacturer to verify the identity of the elastomeric closure formulation and any coating or laminate materials used according to suitable, identification tests.

Examples of some of the analytical test methodologies that may be used include Specific Gravity, % ash analysis, sulfur content determination, thin layer chromatography of an extract, ultraviolet (UV) spectrophotometry of an extract, or infrared (IR) absorption spectrophotometry of a pyrolyzate. (A parallel test of the pyrolyzate analysis would be an Foirier Transform IR-ATR test, which eliminates the need for pyrolysis.)

**TEST PROCEDURES**

1. The USP 381 rev. states that before performing biological, physicochemical, or functionality tests, it is advisable to pretreat and process closures in a manner simulating actual conditions of use. (e.g., referencing the impact that radiation sterilization could have on the performance of a closure).

This protocol would be wise for any pharmaceutical firm to follow when carrying out initial packaging trials with the chosen closure. However, the physicochemical test protocol carried out by the closure manufacturers (to establish an elastomer profile) and the initial evaluation of the closures by the drug packaging firm should remain simple and without the added burden of whether the formulation would or would not sustain further heat or radiation stability. It would in fact, double the time to carry out a normal EP extractables protocol.

Trials on new formulations are normally carried out by the closure manufacturers, who can advise their clients on the ability of their closure to withstand specific types of sterilization cycles. The direct interpretation of the EP requirement reads, "The closures are washed and may be sterilized before use." This has always been interpreted in the past to mean, for normal (initial) study of the extractables, no pre-sterilization was necessary. Pre-sterilization was only necessary as a second and more in depth step in the evaluation of closures by the pharmaceutical manufacturer. It must also be realized that pre-sterilization of the closures, prior to physicochemical testing, would lower the extractables profile of a rubber formulation below it's typical or "as is" profile. Until there can be a resolution to this matter in discussions with the USP and the EP, it is recommended by the PDA that no pre-sterilization take place before evaluation of the extractable profile of a rubber formulation.

Biological Tests

1. The biological test protocol as outlined in the USP 381 rev., should be incorporated into the newly harmonized EP test protocol.

Physicochemical Tests – Preparation of Solutions

1. The Pharmacopeia Europa (Ph. Eur.) prescribes the preparation of a blank solution in parallel with the preparation of the Solution S. The blank is required in some of the tests, such as the UV analysis of the solution. The USP 381 rev. does not require a blank. This should be corrected.

Physicochemical Tests – Appearance of Solution

1. We recommend that the instructions for the Reference Solution preparations, described under the Appearance of Solution test, read as follows in order to match the concentrations of their EP counterparts and that the color requirements for Solution S be changed to match the EP requirement as well (change from water reference to Matching Fluid Reference). Change the last 10 lines of the Requirement section to read: "For visual inspection Solution S is not more opalescent than Reference Suspension B for Type I closures and not more opalescent than Reference Solution C for Type II closures. Solution S is not more intensely colored than an equal quantity of a mixture of 3ml of Matching Fluid O (see Color and Achromicity <631>) and 97ml of diluted hydrochloric acid, examined through identical, colorless, transparent and neutral glass containers, viewed vertically against a white background in diffuse daylight."

Physicochemical Tests – Acidity or Alkalinity

1. Change from " Continue using this same solution to test for alkalinity…", to: "Transfer a second 20ml portion of Solution S to a suitable container, and add 0.1ml of Bromothymol Blue Solution."

Physicochemical Tests – UV Absorbance

1. Change from reading in the range of 200-360 nm to the original 220-360 nm.

Physicochemical Tests – Reducing Substances

1. To correspond with Ph. Eur., it would be necessary to change the USP 381 rev. to state that the tests would need to be run within 4 rather than 5 hours of preparation.

Physicochemical Tests – Heavy Metals

1. The USP 381 rev. specifies to test according to USP <231> Method I, however this does not duplicate the procedure specified in Ph. Eur. (Section 2.4.8 Method A). The two methods should yield equivalent results, therefore, for consistency purposes it is requested that the Ph. Eur. method be reprinted in the new USP <381> so that two separate methods need not be carried out to assure compliance with both compendia.

Physicochemical Tests – Soluble Zinc Content

1. The USP 381 rev. states to transfer 10ml of Solution S to a 100ml volumetric, then to "add 0.5ml of 0.1 N hydrochloric acid to volume and mix." The addition of 0.5ml should be deleted, because it is redundant.

*continues on page 17*

# Recent Sci-Tech Discussions

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

## Question 1

For storing bulk product to be packaged at a later date for clinical supplies, does your organization:

A. Place a portion of the bulk on stability? or
B. Retest the actual bulk material (e.g. grab a sample from the actual bulk container in the warehouse & retest at defined intervals)?

### Response 1

Developing the holding period (bulk to packaging) should be part of the development program and should be part of the Quality Standard. Retesting the actual bulk material would be the best approach. It is critical that the bulk material is stored in appropriate storage conditions.

### Response 2

You should consider doing the following (I am presuming that you already have good data base and background info to know that you do not have stability problems with formulation and package):

Package sufficient amount of product in the proposed clinical package to initiate stability studies as per your stability protocol. You should develop a stability protocol for your clinical study products.

Bulk product should be stored in a container equivalent or better than the proposed clinical package in terms of protecting the product (moisture, gas, light permeation).
It should be stored under same conditions as per label storage conditions for packaged clinical product.

Hopefully, you will not be storing the bulk product for ever. It would be good idea to have a RT testing schedule for bulk stored product if it is stored for a long time. It would be a good idea to test the product at each time of packaging and shipment.

Keep in mind that the cost the clinical study, and its impact on FDA approval, and adhering to your project and market schedule, is probably thousand or many thousand times more costly than the cost of stability testing.

### Response 3

We normally perform the In-process Hold up stability study during R&D scale-up of the product. The preliminary study is done by complete analysis of sample withdrawn at regular interval from the bulk container stored at intended temperature and relative humidity. This study gives an indication of hold up time and storage conditions required for in-process materials. This study is extended to first validation batch.

### Response 4

In general first three commercial lots must be placed under stability studies at both real time and accelerated conditions as defined in ICH guidelines. The minimum intervals for each condition are defined clearly in the guideline.

The retest date should be fixed based on real time stability data. If the data obtained from accelerated data do not show significant variation, the retest date can be fixed 1.5 times of available real time data but not exceeding 12 months of available real time data.

When initially no stability data available, it would be good idea to conduct the stress studies and sees the intrinsic stability profile of the API. In that case, it would be preferable to test the API prior to consumption for formulation.

## Question 2

We are a medical device/biotech company. We currently do in-house endotoxin testing using both the gel-clot and the turbidometric methods. Both are USP compendia methods, therefore, are there really a need to validate the assays in-house, or are the qualification for USP sufficient? If validation is required, to what extent should it be done? Should we do accuracy and reproducibility, or do we just qualify the operator? Also, any suggestions for a validation test plan would be greatly appreciated. Thanks in advance for your response.

### Response 1

The suitability of a compendial analytical procedure must be verified under actual conditions of use (21 CFR 211.194(a)(2)). Information on the specificity, intermediate precision and stability of the sample solution should be included.

*continues on page 18*

# A PDA Audio Conference

## Will FDA Revise Part 11 Regulations?

### FDA Public Meeting on 21 CFR Part 11: Recap and Insight

## Wednesday, June 23, 2004

1:00 p.m. – 2:30 p.m., EDT

Unable to attend FDA's public meeting on 21 CFR Part 11 on June 11? Want a recap of key elements of the meeting with expert commentary? If yes, join **John F. Murray, Jr.**, and **John C. McKenney**—two widely recognized Part 11 experts—who will discuss FDA's June 11 public meeting on 21 CFR Part 11, live from PDA Global Headquarters in Bethesda, Maryland. Participate in this audio conference for an insightful review and summary of salient points raised during the public meeting. The presentation will be followed by an interactive question-and-answer session to address your questions regarding the Public Meeting on Part 11.

**Gain insight into critical issues concerning Part 11 that were raised during the FDA public meeting and hear answers to important questions, such as:**

- Which Part 11 controls are viewed as helpful and important and, which are viewed as impediments to innovation and technological advance?
- Is additional clarity needed regarding which records are required by predicate rules and are therefore required to be Part 11-compliant?
- In re-examining Part 11, how should FDA address issues such as scope, risk-based approaches, validation, audit trails, record retention, record copying and legacy systems?
- Should FDA revise Part 11 to be less prescriptive or more prescriptive?

**Sign up for this audio conference if you are a stakeholder impacted by possible revisions to Part 11, including:**

- Manufacturers of products regulated by the FDA
- Suppliers of software products
- Consultants to FDA-regulated industries

**Presenters:**

**John F. Murray, Jr.**, Software and Electronic Records expert for the Office of Compliance, CDRH, FDA, develops and interprets compliance policies, and advises manufacturers and FDA field and headquarters staff regarding regulatory and compliance requirements for software and electronic records. Mr. Murray represents CDRH as a member of the FDA Part 11 Committee.

**John C. McKenney**, President and CEO, SEC Associates, Inc., a regulatory compliance consulting and computer validation services firm, is the lead author of *The "New" Part 11 and Drug Development: A Q&A Reference Guide*. In addition, Mr. McKenney served as an active core team member of the PDA Part 11 Task Group that produced the Good Electronic Records Management (GERM) guidance document for industry and FDA.

For more information, go to **www.pda.org/audio**

Conference April 4–6

Exhibition April 4–6

PDA-TRI Courses April 7–8

# Call for Papers

## 2005 PDA Annual Meeting

### Chicago, Illinois

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

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

**Abstracts Must Be Received By August 30, 2004 For Consideration.**

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

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

Commercial abstracts promoting of products and/or services will not be considered.

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

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

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

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

***IG Reports**, from page 13*

Physicochemical Tests – Ammonium

1. It is recommended that the concentration of the sodium hydroxide solution used to adjust pH, and the concentration of the alkaline mercuric potassium iodide solution, be changed to correspond with that used in the Ph. Eur. This should help in the standardization of the two protocols.

Physicochemical Tests – Total Solids

1. Although it is expected that in future meetings between the USP and the Ph. Eur., the issue of the validity and accuracy of the Total Solids test may be broached, it is recommended that in the immediate future, the test be carried out as outlined in the existing USP 381 rev.

Physicochemical Tests – Volatile Sulfides

1. From: "Separately prepare a control solution by placing 0.154mg of sodium sulfide in a 100ml flask, and dissolving in 50ml of a 2% citric acid solution" change to: "Prepare a control solution containing 3.08mcg/ml of sodium sulfide in 2% citric acid solution and place 50ml of this solution in a 100 ml flask."

Functionality Tests

1. To eliminate the need for duplicate testing, it is requested that the pretreatment specified in the Ph. Eur. also be included in USP <381>.

Functionality Tests - Penetrability

1. The draft states, "Using a new hypodermic needle for each sample, pierce the closures…." For clarity, it is requested that this be changed to read: "Using a new hypodermic needle for each closure…." The way it is currently written, it may be interpreted that a sample is the group of ten closures.

Functionality Tests - Fragmentation

1. The USP 2004 proposed revision prescribes that fragmentation testing for type I closures be performed with water while fragmentation for type II closures be done with sesame oil. The remainder of the procedure as well as the limit for the number of fragments however is the same. Since this constitutes a change from the EP protocol, it is recommended that this difference be eliminated for the time being, from the USP revision. As in several other test protocols, this would be a good issue for review in upcoming USP/EP harmonization discussions.

Functionality Tests – Self-Sealing Capacity

1. Not noticed in the previous revision, there effectively is still a difference with Pharm. Eur. 3.2.9. The latter uses a 1% methylene blue solution for this test, whereas the 2004 and 2003 proposed revisions to USP mention 0.5% methylene blue. Since there is no known rationale for this, it would be better to align with Pharm. Eur. 3.2.9. on this issue. ■

*Recent Sci-Tech Discussions, from page 14*

### Response 2

Carrying out complete control curve by the analyst to check whether he/she achieves the lysate sensitivity within two fold of labeled sensitivity is sufficient to demonstrate analyst qualification.

In case of endotoxins assays you need to confirm that product itself neither inhibits nor enhances the reaction when tested at different MVD levels. For new product you can do the screening at MVC, 2MVC, 4MVC, etc., and decide the maximum concentration which does not show inhibition or enhancement.

### Response 3

There is on the FDA web site (www. fda.gov) a guideline about LAL test validation and its name is "Guideline on validation of the Limulus Ameobocyte lysate test as an end-product endotoxin test for human and animal parenteral drugs, biological products & medical devices." In this guideline it is stated that (Validation of the LAL test as an endotoxin test for release of human & animal drugs includes the followings:

1. Initial qualification of the laboratory (i.e., confirming the labeled LAL Reagent sensitivity);
2. Inhibition & enhancement tests (i.e., the degree of product inhibition or enhancement of the LAL procedure in assisting of endotoxin content of any drug).

## Question 3

It's stated in the General ICH Stability Guideline that examples of semi-permeable containers are plastic bags, semi-rigid LDPE pouches and LDPE ampoules, bottles and vials. Nevertheless, I would like to receive some feed-back in relation to Polypropylene packaging classification.

According to your experience, should it be also included as a semi-permeable container?

Can "Normal" climatic conditions (25ºC 60% and 40ºC 75%) be applied to products packaged in those PP containers? or 25ºC 40% and 40ºC 25% is a must?

### Response 1

Polypropylene bottles are permeable for water (increase of concentration of drug, may compensate for loss by decomposition or precipitation) and are permeable for oxygen and carbon dioxide (no need for vacuum or inert gas blanket or for antioxidants). Take it from here if you want to define it as semi permeable or not. (I consider it as permeable).

### Response 2

Please notice that Dye Bath Test has, between others, next disadvantages, unsuited for highly colored solutions, contamination by undetected dye, and as has been mentioned, ampoules need subsequent cleaning. I you need the test for QC purposes, well, if not, consider other alternatives.

### Response 3

The answer is yes. Polypropylene permeability to oxygen, carbon dioxide and water vapor is somewhat less than that of low density polyethylene, but greater than that of high density polyethylene. ■

# PDA Interest Groups & Leaders

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

### Biotechnology
U.S. Branch
**Frank Matarrese**
Chiron Corporation
*E-mail:* frank_matarrese@chiron.com
European Branch
**Roland Günther**
Novartis
*E-mail:* roland.guenther@pharma.novartis.com

### Computer Systems
U.S. Branch
**Barbara L. Meserve**
Acculogix, Inc.
*E-mail:* bmeserve@acculogix-usa.com

### Contract Manufacturing
U.S. Branch
**Thomas Handel**
Meridian Medical Technology
*E-mail:* Tom.Handel@meridianmt.com

### Drug-Device Delivery Systems
U.S. Branch
**Raymond A. Pritchard**
Alkermes, Inc.
*E-mail:* ray.pritchard@alkermes.com
European Branch
**Alexander Schlicker, Ph.D.**
Hoffmann La Roche Ltd;
E-mail: Alexandra.schlicker@roche.com
**Georgios Imanidis, Ph.D.**
Pharmaceutical Technology
E-mail: georgios.imanidis@unibas.ch

### Filtration
U.S. Branch
**Jack Cole**
Jack Cole Associates
*E-mail:* jvcole@aol.com
European Branch
**Roger Seiler**
Sartorius
*E-mail:* roger.seiler@sartorius.com

### GMP Purchasing
U.S. Branch
**Nancy M. Kochevar**
Amgen, Inc.
*E-mail:* nancyk@amgen.com

### Inspection Trends/ Regulatory Affairs
U.S. Branch
**Robert L. Dana**
Elkhorn Associates Inc.
*E-mail:* elkhornassoc1@aol.com

### Isolation Technology
U.S. Branch
**Dimitri P. Wirchansky**
Jacobs Engineering Group, Inc.
*E-mail:* dimitri.wirchansky@jacobs.com

### Lyophilization
U.S. Branch
**Edward H. Trappler**
Lyophilization Techology
*E-mail:* frzdry@lyo-t.com

### Microbiology/ Environmental Monitoring
U.S. Branch
**Jeanne E. Moldenhauer, Ph.D.**
Vectech Pharmaceutical Consulting, Inc.
*E-mail:* jeannemoldenhauer@yahoo.com

### Nanotechnology
European Branch
**D. F. Chowdhury**
Aphton Corporation
*E-mail:* fazc@aol.com

### Ophthalmics
U.S. Branch
**Chris Danford**
Alcon Laboratories Inc.
*E-mail:* chris.danford@alconlabs.com

### Packaging Science
U.S. Branch
**Edward J. Smith, Ph.D.**
Wyeth Pharmaceuticals
*E-mail:* smithej@wyeth.com

### Pharmaceutical Water
U.S. Branch
**Theodore H. Meltzer, Ph.D.**
Capitola Consulting Co.
*E-mail:* theodorehmeltzer@hotmail.com

### Production and Engineering
U.S. Branch
**Frank Bing**
Abbott Laboratories
*E-mail:* frank.bing@abbott.com

### Quality Assurance/ Quality Control
U.S. Branch
**Don E. Elinski**
Eli Lilly & Company
*E-mail:* elinski@aol.com

### Solid Dosage Forms
U.S. Branch
**Pedro J. Jimenez, Ph.D.**
Eli Lilly & Company
*E-mail:* jimenez_pedro_j@lilly.com

### Stability
U.S. Branch
**Rafik H. Bishara, Ph.D.**
Eli Lilly & Company
*E-mail:* rhb@lilly.com

### Training
U.S. Branch
**Thomas W. Wilkin, Ed.D.**
Schering-Plough Corp.
*E-mail:* thomas.wilkin@spcorp.com

### Vaccines
U.S. Branch
**Frank S. Kohn, Ph.D.**
FSK Associate
*E-mail:* fsk@lowatelecom.net

### Validation
U.S. Branch
**Bohdan M. Ferenc**
Qualification Services
*E-mail:* biferenc@aol.com

### Visual Inspection of Parenterals
U.S. Branch
**John G. Shabushnig, Ph.D.**
Pfizer Inc.
*E-mail:* john.g.shabushnig@pfizer.com
European Branch
**Markus Lankers, Ph.D.**
APSYS GmbH
*E-mail:* markus.lankers@apsys.de

# PDA Interviews USP's Roger Williams, Pt. 2

**USP activity with biologics:**
Monographs: 143, 28 proposed in PF and 20 in preparation.
General Chapters: 33, 12 proposed in PF and 22 in preparation.

Below is part two of a three-part interview that PDA Senior Editor Walter Morris conducted with U.S. Pharmacopeia (USP) CEO and Executive Vice President Roger Williams earlier this year. In the first installment, which appeared in the May 2004 *PDA Letter*, Dr. Williams talked about a number of the changes that have taken place at USP since he joined the pharmacopeia in 2000.

In part two of the interview, PDA asked Dr. Williams about the pharmacopeia's involvement in developing monographs and standards for biopharmaceutical products, the challenge USP faces in collecting from industry information on these products and the pharmacopeia's future should manufacturers turn away from public standards.

**Editor:** You are well aware of the evolution of drug therapies over the last ten years. The industry is moving away from traditional chemical therapies to those based on biological, cell, tissue and genetic sources. USP started focusing on this market segment two cycles ago and sharpened the focus last time. Two resolutions in particular targeted this market segment: equivalence for products containing complex active ingredients, and applied genomics—USP policy and strategy. Over the last four years, what do you see as the most important contributions made by USP in these areas?

**Dr. Williams:** Many biologics regulated in the United States under the Food, Drug and Cosmetic Act are also regulated under the Public Health Service Act (PHSA). The PHSA is an older piece of legislation that is outdated in many ways, for example, the definition of a 'biologic' in the Act [Editor's note: see sidebar for the definition of "biologic."]. The PHSA didn't explicitly mention USP when it was created because it was thought at the time that compendial standards wouldn't be important for parenteral dosage forms. This has unfortunate consequences—for example, there is little public collaborative testing of biologic reference standards and, in many cases, public standards aren't readily available. All manufacturers and the US public at large would benefit from public standards. Fortunately, these are sometimes made available through the World Health Organization.

The term "biologic" was first defined by the U.S. government in the 1902 **Biologics Control Act**, which was later brought under the PHSA. The 1902 legislation defined biologic as: "any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man."

There might be an argument for USP not to do very much under the PHSA. However, USP's Council of Experts has not taken this view. We have been very vigorous with our approach to what I call complex active ingredients and dosage forms. We have four expert committees working on them:

- Biotechnology and Natural Therapeutics and Diagnostics,
- Blood and Blood Products,
- Cell and Gene Therapy and Tissue Engineering, and Vaccines, Virology and Immunology.

These committees have created a wealth of activity in developing monographs and general chapters, all of which has been extremely useful to manufacturers, practitioners and patients and the public at large.

One General Chapter receiving special attention recently is <111> *Design and Analysis of Biological Assays*. A biologic is distinguished from a small molecule in that it can't be completely characterized through physical or chemical means. A practical outcome of this is that the potency (strength) of the biologic is measured frequently in terms of units/mass, not mass alone. This is assessed through a biologic potency test. A biologic potency test assesses a dose- or exposure-response relationship. To allow comparisons, a preliminary test is termed parallelism. USP has formed an Advisory Panel to explore revisions to Chapter <111>, which needs important updating. I'm pleased to say that the Advisory Panel is comprised of some truly talented experts, and I expect that their deliberations will have important impact on how we think about the biologic potency test and a parallelism assessment.

A biologic potency test is critical in many ways, including assessing batch-to-batch consistency, comparability (pre- and post manufacturing changes), and equivalence between a dosage form from two difference manufacturers. The work on <111> is going to be very seminal and the experts involved in it are extremely excited about it. There is a need for continuing science dialogue and USP is pleased to be part of it.

The USP Convention in 2000 endorsed Resolution 2, which relates to equivalence of complex active ingredients. This focus has been science-based and has amplified our understanding of issues associated with determining consistency, comparability, and equivalence of biologics and biotechnology products. USP held an open conference on the topic in November 2003. A summary of the deliberations of the Expert Panel is in preparation and will conclude our work on this Resolution for this cycle. Again, our goal was to inform the public debate about assuring consistency, and, in the presence of change, comparability and equivalence. This is not a standards-setting activity, but can be used by the Council of Experts if they wish.

**Editor:** Seeing this from a very high level, when you listen to people discuss biologics and equivalences issues, do you get a sense about how far away we are from generic biologics. Do you think the hurdles will be overcome anytime soon?

*continues on page 46*

sartorius


HPLC Chromatogram

# Need a good analyst?

**Sartorius offers the most comprehensive, documented extractables analysis possible in just 30 days.**

**30 days**
*commitment*

You'll experience total peace of mind when you use Sartorius Extractables Testing Services.

Sartorius helps you validate with CONFIDENCE® by offering a completely documented analysis that meets or exceeds regulatory guidelines. We're talking about any cure, from 'model-solvent' to a comprehensive 'reality-stream' cure that uses **your** product, **your** process and **your** components – even from other manufacturers. We also offer complete Validation and Qualification testing that includes: Bacterial Challenge Tests, Integrity Tests, Long-term Stability studies plus adsorption and chemical and biocompatibility testing. For a complete analysis with the **30 days** option, make an appointment today.

For all the details, contact the Extractables Hotline at **1-800-368-7178, ext. 8373**, email **extractables@sartorius.com** or visit **www.sartorius.com**

Sartorius AG, Weender Landstrasse 94–108, 37075 Goettingen, Germany
Sartorius North America Inc., 131 Heartland Blvd., Edgewood, NY 11717, USA
www.sartorius.com

# Regulatory Briefs

## Important Dates

**July 1** **EMEA** Note for Guidance on Minimising Risk of TSE becomes applicable.

**July 5** Deadline for public comment on **FDA CDER** draft guidance on CMC submissions for drug substances.

**July 6** Deadline for public comment on **CDER/CBER** draft guidances on risk management.

**July 6** Deadline for public comment on **FDA** combination products rule changes.

**Aug. 31** **EMEA** API Master File guideline becomes effective

## U.S. FDA

**FDA Publishes "Critical Path" White Paper…**

Analyzing and offering solutions for the "pipeline problem," FDA has published a new report called, "Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products." The growing "pipeline problem"—the declining number of new drug applications (NDAs) being submitted for new molecular entities, new high-tech medical devices and other highly anticipated advanced therapies—is out of line with the increasing amounts of resources dedicated to product development.

The agency has identified three hurdles along the "critical path" from discovery to the market—assessment of safety testing, proof of efficacy and industrialization—each of which presents its own set of scientific and technological challenges.

To target appropriate initiatives, the agency is developing a National Critical Path Opportunities List and a public docket to get input on activities that could reduce existing hurdles in medical product design.

In a related news, the U.S. Department of Health and Human Services (HHS), the parent government agency for FDA, is creating a new task force to determine ways to help speed the development of new medical technologies and drug compounds, Secretary Tommy Thompson said in a speech at the Milken Institute Global Conference in April.

The task force will include Mark McClellan, Administrator of the Centers for Medicare & Medicaid Services; Lester Crawford, Acting FDA Commissioner; Julie Gerberding, head of the Centers for Disease Control and Prevention; and Elias Zerhouni, head of the National Institutes of Health.

**…Solicits Comment on Initiative**

The FDA is "seeking input on the most pressing scientific and/or technical hurdles causing major delays and other problems in the drug, device and/or biologic development process, as well as proposed approaches to their solution," the agency said in a document announcing creation of the public docket.

Links to the "Critical Path" report and the docket are available in the regulatory news archive at www.pda.org/regulatory/RegNewsArchive.html.

**FDA Publishes Risk Management Guidances**

In May, FDA published three draft guidances, written jointly by the Center for Drug Evaluation (CDER) and Research and the Center for Biologics Evaluation and Research (CBER) that utilize risk-based strategies for product development, application submission and post-approval. The draft guidances are called: "Premarketing Risk Assessment," "Development and Use of Risk Minimization Action Plans," and "Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment."

The draft guidances were published in 2003 as "concept papers" and were the subject of a public meeting. The comments submitted on the concept papers and at the public meeting were considered in developing these draft guidances.

These three draft guidances address risk management issues pertinent to the successive stages of a product's lifecycle, specifically:

- during medical product development,
- during product application review and approval, and
- during the postmarketing period.

The approaches recommended in the draft guidances should not be viewed as a new collection of generalized and discrete tools for risk minimization but rather as part of much broader, ongoing, and comprehensive efforts to provide additional guidance to industry on measures that can be employed to minimize the risks while preserving benefits of medical products.

The draft guidances recommend that sponsors consider specific risk minimization efforts beyond routine risk minimization measures for the few products presenting unusual types or levels of risk. In these circumstances, using strategies that go beyond routine risk assessment and minimization may further improve the product's benefit-risk balance. FDA is specifically soliciting public comment on how to best characterize the types and levels of risk that might suggest the need for a risk management plan.

FDA understands that risk management programs generate costs and place new burdens on product developers, health care practitioners, and patients. FDA recommends that, whenever possible, sponsors give every consideration to using the least burdensome method to achieve the desired public health outcome. For example, making increasing use of automatic reporting and future notification systems for adverse events will help the agency learn quickly of potential problems. Use of networks for electronic prescribing can enable the real-time, efficient collection of data on adverse events and even alert physicians to adverse events at the time of prescribing.

*continues on page 24*

# Eliminate Filter Sterilizing

## Disinfectants & Sporicides

# SIMPLE MIX®

### What is SimpleMIX?

The convenient, patent pending SimpleMIX System provides a sealed multi-chamber container that when activated mixes the two solutions. The top part contains the sterile concentrate disinfectant or sporicide and the bottom part contains the sterile USP WFI Quality Water. Just pull the tab and they instantly mix together.

### Features of SimpleMIX:

- All chemical agents and the WFI Quality Water are filtered at 0.2 microns and manufactured in a Class 100 filling operation.
- Eliminates regulatory concerns for mixing & sterility of the solution.
- No more concerns for mixing concentrate phenolics, quaternary ammoniums or peracetic acid & H2O2 with sterile water in aseptic manufacturing operations.
- The contents of the double bag package are sterilized through a validated gamma radiation cycle.
- Lot sterility tested per current USP compendium.
- The system assures the appropriate dilution is made each time in a closed, sterile system.
- Concentrate solutions are never handled.

**Now available!**
*16 ounce trigger spray*


US and Foreign Patents Pending

**Made for Veltek's DECON-PHENE®, DECON-PHASE®, DECON-CYCLE®, DECON-QUAT100®, DECON-Clean® and DECON-SPORE 200 Plus®**

vai
Veltek Associates, Inc.
15 Lee Blvd
Malvern, PA 19355-1234 USA
(610) 644-8335 • Fax (610) 644-8336
www.sterile.com

INNOVATIVE CLEAN ROOM PRODUCTS

*Regulatory Briefs, from page 23*

As new products are developed, FDA recommends that sponsors seek to identify risk signals as early as possible in a product's development cycle, to evaluate the risks, to communicate predictable risk and benefit information effectively and thoroughly, and to employ efforts to manage these risks as efficiently as possible.

The comment period for the drafts closes on July 6, 2004. Links to the draft guidances are available at www.pda.org/regulatory/RegNewsArchive.html.

**FDA Acts on Combo Product Rules**

In May, FDA released a draft guidance for combination product manufacturers entitled, "Combination Products, Timeliness of Premarket Reviews, Dispute Resolution Guidance." This guidance document provides information on how an applicant submitting an application(s) covering a combination can request that the FDA Office of Combination Products (OCP) help resolve disputes about the timeliness of reviews. A link to the draft guidance is available at www.pda.org/regulatory/RegNewsArchive.html. Comments on the draft are due by July 6.

A timeliness dispute arises when FDA does not review and act on an applicant's combination product application within the applicable performance goal set by the Prescription Drug User Fee Act (PDUFA) or the Medical Device User Fee and Modernization Act (MDUFMA). Under PDUFA and MDUFMA, it is not expected that every application will meet every performance goal. Applications covering combination products in particular often present challenging review and regulatory issues. Nevertheless, because the PDUFA and MDUFMA, performance goals reflect current review time expectations, it is appropriate to use them as guidelines.

The purpose of a timeliness dispute resolution request is to obtain the relevant review as quickly as possible, rather than to impose any sanction on the reviewing Center. In keeping with this perspective, upon receipt of a request for resolution of a timeliness dispute, OCP will contact the Center reviewing division and the Center Ombudsman to determine the current status of the review and what OCP can do to facilitate completion of the review as quickly as possible. If necessary and feasible, a plan for the completion of the review, including a target date for completion, will be developed.

FDA also proposes to amend its combination product regulations to create new definitions in Sec. 3.2 of "mode of action" and "primary mode of action" (PMOA). These definitions are used for assigning the FDA center to handle a combination product application.

This proposal also sets forth a two-tiered assignment algorithm in Sec. 3.4, which the agency would use to determine assignment when it cannot determine which mode of action of a combination product provides the most important therapeutic action of the product. Finally, the rule proposes to require that sponsors base their recommendation of the agency component with primary jurisdiction for regulatory oversight of its product in terms of the PMOA definition and, if appropriate, the assignment algorithm. A link to the proposal is available at www.pda.org/regulatory/RegNewsArchive.html. Comments on the proposal are due by July 6.

**Mode of action** would be defined as "the means by which a product achieves a therapeutic effect." For purposes of this definition, "therapeutic" effect or action includes any effect or action of the combination product intended to diagnose, cure, mitigate, treat, or prevent disease, or affect the structure or any function of the body. Products may have a drug, biological product, or device mode of action. Because combination products are comprised of more than one type of regulated article (biological product, device, or drug), and each constituent part contributes a biological product, device, or drug mode of action, combination products will typically have more than one mode of action.

1. A constituent part has a biological product mode of action if it acts by means of a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product applicable to the prevention, treatment, or cure of a disease or condition of human beings, as described in section 351(a) of the Public Health Service Act.

2. A constituent part has a device mode of action if it meets the definition of device contained in section 201(h)(1) to (h)(3) of the act (21 U.S.C.321(h)(1) to (h)(3)), it does not have a biological product mode of action, and it does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and is not dependent upon being metabolized for the achievement of its primary intended purposes.

3. A constituent part has a drug mode of action if it meets the definition of drug contained in section 201(g)(1) of the act and it does not have a biological product or device mode of action.

**Primary mode of action** would be defined as "the single mode of action of a combination product that provides the most important therapeutic action of the combination product." This would be the mode of action that is expected to make the greatest contribution to the overall therapeutic effects of the combination product. As with "mode of action," for purposes of PMOA, "therapeutic" effect or action includes any effect or action of the combination product intended to diagnose, cure, mitigate, treat, or prevent disease, or affect the structure or any function of the body.

**CBER Evaluates Product Review**

The Center for Biologics Evaluation and Research (CBER) plans to develop a template for reviewing proposed products, to implement a formal

training program for reviewers and to create more opportunities for biotech firms and other stakeholders to provide input on efforts to enhance the development of new products.

The review template will institutionalize best review practices and improve the consistency and efficiency of reviews, according to the report. The training program for reviewers will focus on the fundamentals of risk management, assessment and communication.

"We are fully committed to quality improvement and excellence in all of our review processes, including enhanced efficiency, management and consistency of review that incorporates best practices, such as the tradition of fostering early interactions during the review process," CBER Director Jesse Gordon said in an open letter accompanying the release of the center's fiscal 2003 annual report.

Despite this emphasis on improving the review process, CBER said it had met or exceeded most review performance goals under the Prescription Drug User Fee Act.

A link to the open letter and more information on this initiative are available in the regulatory news archive at www.pda.org/regulatory/RegNewsArchive.html.

## EMEA

**EU Overhauls EMEA**

In legislation passed in March, the EU revised a regulation and two directives regarding the EMEA. Once the legislation is fully in effect, the Agency will be given a stronger role in the provision of information to the patients and the public, including a mandate to develop a database of all medicines approved in the European Union ('EuroPharm'). There are also provisions for giving small and medium-sized companies administrative and scientific support. Some of these new capabilities became effective May 20.

Provisions that will enter into force in November 2005 include conditional approvals and fast-track reviews, in addition to an increase in the scope of the centralized procedure. The name of the Agency also changes to reflect its broader responsibilities, to the European Medicines Agency. The acronym 'EMEA' will continue to be used. Other changes include:

- Committee for Medicinal Products for Human Use replaces the Committee for Proprietary Medicinal Products. The new Committee will be known as the CHMP. Membership of the Committee changes from two to one member per Member State (following EU enlargement this means 25 members) and in addition one member from Iceland and Norway.
- Committee for Medicinal Products for Veterinary Use replaces the Committee for Veterinary Medicinal Products. The new Committee will continue to be known as the CVMP. Membership of the Committee is similar to the CHMP.
- There are no changes to the Committee for Orphan Medicinal Products (COMP).
- A new Committee for Herbal Medicinal Products is created and is expected to begin activity later in 2004. The new Committee will be known as the HMPC.
- Composition of the Management Board changes from two to one member per Member State, in addition to two representatives each of the European Parliament and the European Commission. They are joined by two representatives of patient organizations, one representative of doctors' organizations and one representative of veterinarians' organizations. There are a total of 33 members of the Board.

**EMEA's Consultation Exercise on Road Map**

On April 15, the EMEA announced the launch of a "consultation exercise" on the discussion paper "The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future." The paper outlines the Agency's strategy to further develop as one of the world's foremost regulatory authorities for medicinal products, which is public health oriented, science-driven and transparent in the way it operates. The road map takes a twofold approach: to provide for better protected and informed patients and users of medicines, whilst encouraging and facilitating innovation and research in an enlarged EU. Comments from the public and interested parties are welcome until June 30.

As a result of significant changes in the institutional, legislative and scientific environment, the EMEA will acquire new responsibilities with a greater focus on public and animal health. Particular attention will be given to the needs and expectations of patients and users of medicines. Support to small and medium sized companies will be further increased. The implementation of the EMEA vision requires the establishment of a network of excellence between all European regulatory authorities. Given the impact of an increasingly complicated network model, involving over 40 national agencies in the future, the road map also looks at how the existing partnership between all European regulatory authorities can be reinforced.

The discussion paper has identified six specific areas of the Agency's tasks relating to scientific advice, scientific assessment, post-authorization activities, transparency and communication, provision of information to patients and good manufacturing/clinical practices. The specific needs of veterinary medicines are also taken into account, as is the proposed role and functioning of the Agency's secretariat. A link to the "Road Map" can be found at www.pda.org/regulatory/RegNewsArchive.html.

## EU

**EC Releases New Innovation Action Plan**

In April, the European Commission (EC) published an action plan called "Innovate for a Competitive Europe." Initiatives launched under the umbrella of this plan could have foundational effects on the pharmaceutical and biopharmaceutical industries and the way they are regulated.

The plan outlines six objectives to help all the major industries in Europe get new and innovative technologies on the market:

Objective 1: Innovation everywhere: Promote innovation in all forms, technological or other. Improve innovation performance and competitiveness at enterprise level by disseminating excellence, learning from the best. Spread innovation in all sectors and in millions of SMEs and not only among a limited number of high-tech "happy few."

Objective 2: Get innovation on the market: Improve the regulatory and administrative environment for innovation, in particular technical regulations, standards and competition rules.

Objective 3: Knowledge for innovation: Stimulate the dissemination and the absorption of knowledge (including technologies), in particular by improving the use and management of intellectual property, by encouraging the opening of innovation systems and clusters to new ideas, technologies and players and by enhancing the R&D Framework Programme's impact on innovation.

Objective 4: Invest in innovation: Increase investment in innovation by exploiting the Community sources of finance (financial instruments, European Structural Funds) and by increased cooperation with the European Investment Bank. Ensure that state aid policy works to stimulate innovation.

Objective 5: Skills for innovation: Foster the development of "innovation skills" and creativity, while facilitating the mobility of "knowledge workers".

Objective 6: Efficient innovation governance: Mobilise Member States, regions, enterprises and other innovation actors. Promote and improve innovation governance.

The action plan is meant to target initiatives that will improve competitiveness, productivity, added value and growth in Europe by facilitating innovation. The EU's Enterprise Directorate-General is developing a new innovation action plan to address the main market deficiencies that currently hamper innovation in European enterprises. A major component of the plan is the consult with stakeholders across the EU.

The Plan will mobilize resources and rally the Member States around ambitious common objectives, while placing the enterprise at the centre of innovation policy. It emphasizes the importance of both technological and non-technological innovation, including new business concepts and organizational or presentational innovation. It targets services and traditional as well as high-tech sectors.

It also takes account of the all-embracing nature of innovation, aiming to create the basis for an efficient dialogue among all innovation stakeholders, policy-makers, regions, research, civil society and enterprises. ■

***—compiled from health authority press releases***

# Picky about particulates?


# Manic about microbes?

# Count on Biotest

The HYCON® System for Environmental Monitoring: RCS Air Samplers, APC Particle Counters and Contact Slides.

APC Airborne Particle Counters and RCS Microbial Air Samplers combine to give you a clear picture of airborne contamination. Biotest Diagnostics Corporation offers a full line of reliably accurate, technically-advanced, hand-held, air monitoring devices. When you're picky about maintaining air quality standards, count on Biotest. Call today or visit our website at www.BiotestUSA.com.

Biotest

CE

Biotest DIN EN ISO 9001 HYCON

**BIOTEST DIAGNOSTICS CORPORATION**
66 Ford Road, Suite 220, Denville, New Jersey 07834
Phone: 973.625.1300 • 800.522.0090 • Fax: 973.625.9454
www.BiotestUSA.com

## PROGRAMS AND MEETINGS CALENDAR

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

### 2004

**June**
**23** PDA Audio Conference: "Will FDA Revise Part 11 Regulations?"

**September**
**7-8** PDA/BFS Inter'l. Operators Association Joint Workshop on Blow/Fill/Seal Processing
Holopack Verpackungstechnick GmbH, Germany

**9** PDA Audio Conference: "GERM 3: Models Document

**20-24** 2004 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits: The New Guidances
Omni Shoreham Hotel, Washington, D.C.

**November**
**TBD** PDA Regulatory Summit
Brussels, Belgium

### 2005

**February/March**
**28-2** PDA International Congress, Courses & Exhibitions
Rome, Italy

**April**
**4-8** PDA Annual Meeting, Courses and Exhibitions
TBD

**May**
**16-18** PDA Viral Safety Conference
TBD

**September**
**12-16** 2005 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits
Washington, D.C.

**October**
**TBD** Taormina Conference
Taormina, Italy

# More 2004 PDA SciTech Summit & Annual Meeting Photos

**(Photo above)** The Blow, Fill and Seal Technology Panel: (from left to right) Berit Reinmuller, Bengt Lungqvist, Richard Friedman, Anders Lofgren, Eric Dewhurst, and Martin Haerer

**(Above)** PDA's Chapter Council

**(Left)** Attendees "Meet The PDA Author" Russel Madsen

# CLEAN & DISINFECT
# FLOORS, WALLS & CEILINGS


*Pro XL*

## Choose From More Than Seventeen Cleaning And Disinfecting Systems

We are the world's leading manufacturer, supplying a wide range of multi-bucket cleaning systems engineered to capture and isolate contaminants. Our TruCLEAN systems are designed to deliver uniform application of solutions to walls, floors and ceilings. Easy operator adaptability. Reliable performance. Consistent results. **GUARANTEED.**

*All TruCLEAN Systems compatible with Gamma, ETO and Autoclave Sterilization.*

**PERFEX CORPORATION**
***Experts in Clean Systems for Controlled Environments***

**800-848-8483 USA & Canada**
**315-826-3600**
**Fax: 315-826-7471**

**E-MAIL:**
**perfex@ntcnet.com**

**WEBSITE:**
**www.perfexonline.com**


***FREE*** *PROFESSIONAL REFERENCE GUIDE*
*FREE CD ROM AND VIDEO ALSO AVAILABLE*

***Israel Chapter Workshop,*** *from cover*

Mr. Tribe explained that the goal of PIC/S is to lead the international development, implementation and maintenance of harmonized GMP standards and quality systems of inspectorates in the field of medicinal products. He mentioned that when a country joins PIC/S, the results include:

- improvements and cost savings,
- alignment with international GMPs, and
- increased exports of medicines.

Mr. Tribe also noted that PIC/S member countries often have an easier time forming mutual recognition agreements (MRAs) with each other.

About the process of joining, Mr. Tribe noted that a general interest and commitment is a prerequisite to enter PIC/S. The candidate must submit a written application to the PIC/S secretary with supporting documents. This is followed by PIC/S appointing a rapporteur to evaluate the application. The applicant is then invited to a PIC/S committee meeting to answer questions. Afterwards the PIC/S delegation undertakes an assessment visit. Finally, the PIC/S committee decides on membership after issuing a delegation report. The whole process takes about two years. Each member authority is reassessed every three years.

**Regarding benefits of PIC/S membership to a health authority, Mr. Tribe stated that the EU and PIC/S usually adopt each other's GMP guides and guidance documents in the harmonized consultation procedure.**

Regarding benefits of PIC/S membership to a health authority, Mr. Tribe stated that the EU and PIC/S usually adopt each other's GMP guides and guidance documents in the harmonized consultation procedure. The International Medicinal Inspectorates Database (IMID) is a new

*continues on bottom of page 34*

***Spain Chapter Euroforums,*** *from cover*

Christa Wirthumer-Hoche, appointed by the European Commission as coordinator for the CTD implementation in Europe, stated that the CTD by definition is an agreed common format for applications that will be acceptable in all the three of the regions participating in the International Conference on Harmonisation—the U.S., EU and Japan. Dr. Wirthumer-Hoche noted that the CTD is a locator for data and is the common dossier format in the ICH region. She explained in detail the structure of the CTD and compared it to the "old" EU format according to the Notice to Applicants Vol. 2B (1998 edition). She also stated that the review process in the EU was a "from top to bottom" process—from the expert reports to the detailed documents where the file is normally not known to the reviewer before submission. In the U.S., the process is a "bottom to top" process, i.e., from the data analysis to the summaries. The CTD became mandatory in the EU on July 1, 2003, and at the national level on November 1, 2003. Since the CTD has gone into use, there has been improvements to assessment times, number of assessors and number of inquiries to some extent.

**Since the CTD has gone into use, there has been improvments to assessment times, number of assessors and number of inquiries to some extent.**

Hilde Boone from the EMEA provided a very good summary of the EMEA experience with the CTD. She stated that in the case of EMEA, most questions related to the application were dealt with during the pre-submission contacts with the applicants. She also stated that the EMEA is available to provide assistance to applicants at pre-submission stage. She said that, for the EMEA, the CTD has neither prolonged nor shortened the assessment time. She presented the EMEA's "performance indicators" for the CTD. The overall satisfaction level compared to the old format was positive. With respect to variations to marketed products, there

*continues on page 33*

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

## Asia Pacific

### Australia Chapter
Contact: Ken Dibble
Millipore Australia
Tel: +61-4-1835-0455
Fax: +61-3-9563-2605
E-mail: ken_dibble@millipore.com

### India Chapter
Contact: Darshan Makhey
Nicholas Piramal India Limited
Tel: +011 91 22 56 63 67 89
Fax: +011 91 22 24 16 37 87
E-mail: dmakhey@nicholaspiramal.co.in

### Japan Chapter
Contact: Hiroshi Harada
Tel: +81-3-3815-1681
Fax: +81-3-3815-1691
E-mail: hharada@bcasj.or.jp
Web site: http://www.j-pda.jp/index.html

### Korea Chapter
Contact: Jun Yeon Park
Tel: +82-2-560-7833
Fax: +82-2-560-7822
E-mail: jun_yeon_park@pall.com

### Southeast Asia Chapter
Contact: K. P. P. Prasad, Ph.D.
Pfizer Asia Pacific Pte Ltd
Tel: +65-6419-0250
Fax: +65-6419-0011
E-mail: prasad.kpp@pfizer.com

### Taiwan Chapter
Contact: Tuan-Tuan Su
Tel: +8862-2550-9301
Fax: +8862-2555-4707
E-mail: pdatc@ms17.hinet.net

## Europe

### Central Europe Chapter
Contact: Erich Sturzenegger, Ph.D.
Novartis Pharma AG
Tel: +41-61-324-5572
Fax: +41-61-324-2089
E-mail:
erich.sturzenegger@pharma.novartis.com

### France Chapter
Contact: Phillippe Gomez
Sartorius Corporation
Tel: +33-0607-453868
E-mail: philippe.gomez@sartorius.com

### Italy Chapter
Contact: Vincenzo Baselli
Pall Italia
Tel: +39-02-477-961
Fax: +39-02-423-6908
E-mail: vincenzo_baselli@europe.pall.com
Web site: http://www.pda-it.org

### Prague Chapter
Contact: Zdenka Mrvova
Léciva A.S.
Tel: +420-2-67242275
E-mail: zdenka.mrvova@zentiva.cz

### Spain Chapter
Contact: Jordi Botet
STE Compliance Services
Tel: +34-935-923150
Fax: +34-935-923152
E-mail: jbotet@stegroup.com

### United Kingdom and Ireland Chapter
Contact: John Moys
Sartorius
Tel: +44-1372-737-140
Fax: +44-1372-726-171
E-mail: john.moys@sartorius.com

## Middle East

### Israel Chapter
Contact: Karen S. Ginsbury
PCI-Pharmaceutical Consulting Israel Ltd.
Tel: +972-3-921-4261
Fax: +972-3-921-5127
E-mail: kstaylor@netvision.net.il

## North America

### Canada Chapter
Contact: Grace Chin
Pellemon, Inc.
Tel: +1 (416) 422-4056 x230
Fax: +1 (416) 422-4638
E-mail: grace.chin@snclavalin.com

### Capital Area Chapter
Areas Served: MD, DC, VA, WV
Contact: Barry A. Friedman, Ph.D.
Cambrex Bio Science Baltimore, Inc.
Tel: +1 (410) 563-9200 ext. 285
Fax: +1 (410) 563-9229
E-mail: barry.friedman@cambrex.com
Web site: www.pdacapitalchapter.org

### Delaware Valley Chapter
Areas Served: DE, NJ, PA
Contact: Art Vellutato, Jr.
Veltek Associates, Inc.
Tel: +1 (610) 983-4949 x110
Fax: +1 (610) 983-9494
E-mail: artjr@sterile.com
Web site: www.pdadv.org

### Metro Chapter
Areas Served: NJ, NY
Contact: Frank R. Settineri
Chiron Corporation
Tel: +1 (908) 730-1222
Fax: +1 (908) 730-1217
E-mail: frank_settineri@chiron.com

### Midwest Chapter
Areas Served: IL, IN, OH, WI, IA, MN
Contact: Amy Gotham
Northview Labs
Tel: +1 (773) 562-1451
E-mail: PDAMidwest@comcast.net

### Mountain States Chapter
Areas Served: CO, WY, UT, ID, NE, KS, OK, MT
Contact: Jeff Beste
Pendelton Resources
Tel: +1 (303) 832-8100
Fax: +1 (303) 832-9346
E-mail: cmdjeff@aol.com
Web site: www.mspda.org

### New England Chapter
Areas Served: MA, CT, RI, NH, VT, ME
Contact: Mark A. Staples, Ph.D.
MicroCHIPS
Tel: +1 (781) 275-1445 x223
E-mail: mstaples@mchips.com

### Puerto Rico Chapter
Contact: Silma Bladuell
Wyeth Lederle, Inc.
Tel: +1 (787) 776-4960
Fax: +1 (787) 776-4144
E-mail: bladues@wyeth.com

### Southeast Chapter
Areas Served: NC, SC, TN, VA, FL, GA
Contact: Mary Carver
Eisai, Inc.
Tel: +1 (919) 474-2149
Fax: +1 (919) 941-6934
E-mail: mary_carver@eisai.com
Web site: www.pdase.org

### Southern California Chapter
Areas Served: Southern California
Contact: John Spoden
Allergan
Tel: +1 (714) 246-5834
Fax: +1 (714) 246-4272
E-mail: spoden_john@allergan.com
Web site: http://www.pda.org/chapters/Website-SoCal/SoCal-index.html

### West Coast Chapter
Areas Served: Northern California
Contact: Randall Tedder
Tel: +1 (415) 841-0373
Fax: +1 (415) 841-1961
E-mail: randall@iconnova.com

# PDA Membership Application

M

LTR 06/04

Return your completed PDA membership application, with check or bank draft payment made to: PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA; **Fax Credit Card payments to: +1 (301) 986-1093**.

❑ Mr. ❑ Ms. ❑ Dr. Last Name _____

First Name _____ MI _____

Job Title _____

Company _____

Address _____

City _____ State/Province _____

Country _____ Zip+4/Postal Code _____

Business Phone: _____ Fax: _____

E-mail: _____

Were you referred by a PDA Chapter? ❑ Yes ❑ No If so, which Chapter? _____

**Join PDA today and save up to 50% on training courses, meetings, conferences!**

*Plus…*

- ✓ Gain access to expert, peer-reviewed information relevant to your career
- ✓ Connect to global and regional science and regulatory expertise
- ✓ Become a part of the world's leading international network of pharmaceutical and biopharmaceutical professionals

For more details on PDA and the benefits of becoming a member, visit www.pda.org today.

## Payment (*Membership fees are nonrefundable and nontransferable.*)

❑ Individual Membership: ❑ $195 U.S.

❑ Government Agency Employee Membership: ❑ $80 U.S. *(Must be an employee of a government agency or health authority.)*

**Business Environment (check only one)**

- ❑ Academic
- ❑ Consultant
- ❑ 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
- ❑ GMP Compliance/Inspection Trends
- ❑ Liquids
- ❑ Maintenance
- ❑ Manufacturing/Production
- ❑ Microbiology
- ❑ Ointments
- ❑ Ophthalmics
- ❑ Packaging
- ❑ Parenterals
- ❑ Quality Assurance/Quality Control
- ❑ Regulatory Affairs
- ❑ Research
- ❑ Solid Dosage Forms
- ❑ Sterilization/Aseptic Processing
- ❑ Training
- ❑ Validation

**Note for U.S. members:**
*PDA dues are not tax-deductible as charitable contributions under the Internal Revenue Code of the United States. However, the dues may be deductible as ordinary and necessary business expenses.*

3. **Payment Options** (please check one).

❑ A. By **Credit Card** (VISA, MasterCard/EuroCard, American Express, Diners Club), clearly indicating account number and expiration date and billing address. **Proceed to Item 4 below.**

❑ B. By **Bankers' Draft/Check** forwarded together with the application form PAYABLE IN US DOLLARS ONLY to:

PDA, Inc., P.O. Box 79465, Baltimore MD 21279-0465

Please mark here to request a **PROFORMA INVOICE** from PDA to process your company payment. ❑

❑ C. **Wire Transfer Payments**/By bank-to-bank transfer to: (required if paying in foreign currency; prevailing exchange rates at date of submission will apply.)

**UBS AG Basel** Swift Code: **UBSWCHZH40M**

Account number (please specify correct account number for currency being remitted):

- ❑ CHF: Account No. 292-568-280-01F
- ❑ EUR: Account No. 292-568-280-60Z
- ❑ GBP: Account No. 292-568-280-61W
- ❑ USD: Account No. 292-568-280-62Q
- ❑ YEN: Account No. 292-568-280-63Y

Please reference code: **DUES**

**Bank Address:**
UBS AG Basel
Postfach
Aeschenplatz 6
4002 Basel, Switzerland

Currency conversions available at: www.forex.com/forex_market_commentary.html

Wire Transfer Confirmation: _____
(insert your confirmation of receipt by UBS Bank here.)

4. **Please check the appropriate box:** Charge: ❑ MasterCard/EuroCard ❑ VISA ❑ AmEx ❑ Diners Club

Account Number: _____ Exp. Date: _____

Name *(exactly as on card)*: _____

Signature: _____ Date: _____

Billing Address: _____

**Federal Tax I.D. #52-1906152**

5. **RETURN COMPLETED FORM WITH CHECK OR BANK DRAFT MADE TO:** PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA **FAX CREDIT CARD PAYMENTS TO:** +1 (301) 986-1093 (credit cards only)

PDA USE:
Date: _____ Check: _____ Amount: _____ Account: _____

*Spain Chapter Euroforums, from page 30*

is generally no requirement to reformat the "old" dossier.

Mª Luisa Gª Vaquero, Head of Regulatory Affairs, Spanish Medicines Agency, gave a very useful perspective on the implementation of the CTD. Spain began a transitory period for CTD implementation in 2001, ending when the CTD became mandatory on November 1, 2003. The main objectives of this transitory period were to gather experience with the CTD, to identify possible problems and solutions, and to facilitate the switch to the new format. With some training, the assessors in general welcomed the CTD format for the Centralized Procedure. However, for the Spanish National Procedures, the pharmaceutical companies were reluctant to use the CTD format. The main reason was that most companies decided to wait till they were forced by national legislation. Regarding variations to marketed products, Spain follows the European Variations system. Ms. Vaquero mentioned that the CTD gave a more logical structure of the dossier and it was far easier to identify the technical content of the submission dossier.

Andrew Marr, GlaxoSmithKline, UK, is a "topic leader" on the CTD for the European Federation of Pharmaceutical Industries and Association. (EFPIA). He provided a comprehensive overview of the current status of the electronic submissions in the EU. He stated that in Europe there is no homogeneous position on the e-CTD, but there is a coordinated approach. The implementation is at an early stage. The EMEA has already experienced four e-CTD submissions, and the UK's Medicines and Healthcare products Regulatory Agency (MHRA ) two submissions. The U.S. FDA seems to be a bit ahead, with the e-CTD representing the preferred e-submission format. The FDA is promoting the e-CTD heavily. For Europe, submissions have been and are being made. The experience so far is positive.

An important presentation on the chemistry, manufacturing and control (CMC) requirements for products in development was given by Karin Sewerin, The Biologics Consulting Group, Sweden. She offered a very detailed analysis on the level of GMP required throughout the drug development process. Three important points were:

- GMP should be applied gradually throughout the clinical study,
- the amount of information depends on the novelty of the product, and
- the material in the license should be representative of the material used in the clinical trials.

In conclusion, this PDA EuroForum has been a learning experience for the new-born Chapter. With the few but very enthusiastic members, PDA has a very good chance of growing in Spain.

**Spain Chapter Election results**

The following persons were elected at the Chapter meeting after the forum:

- President – Jordi Botet,
- Vice-President – Carina E. Sonnega,
- Treasurer – Jordi Fabrega, and
- Secretary – José Mo Vilella Llebaria.

The Spain Chapter also selected Carina Sonnega to be the member representative on PDA's Regulatory Affairs and Quality Committee.

**What is a PDA EuroForum?**

A PDA EuroForum is a one-day symposia that is intended to address one relevant issue. At least one health authority expert is invited, along with industry experts. The session includes a panel discussion in an informal atmosphere. This venue also affords doctoral student candidates to present their thesis, time permitting. ■

***—Gautam Maitra, European Director***

*Israel Chapter Workshop, from page 30*

option for sharing of information on the GMP compliance status of manufacturing sites. This often results in cost reductions for participating health authorities by allowing inspection reports to be shared among all participating PIC/S authorities. This results in reduction of inspections by the participating PIC/S authorities.

Mr. Tribe also described the GMP requirements of Australia's Therapeutic Goods Administration (TGA) which are one of the best and strictest in the world.

A case study on the Pan Pharmaceutical crisis was described at length. The company faced serious noncompliance issues. The lessons learned from the case resulted in increased unannounced audits, a reduction in the time to notify on intended inspections, longer time on the site of inspections, product samples taken during audits and tested by TGA, and an increased focus on manufacture of complementary medicines.

Mr. Tribe also took time to meet with senior level experts in the Israel Ministry of Health to start the process of Israel application for a PIC/S membership. At the Ministry, Mr. Tribe heard a presentation by the Director, Rachel Karpel, PhD, on the status of GMP in Israel. On one of her slides, Dr. Karpel credited PDA for helping health authority inspector and specialists improve their skills. The slide read, "Inspectors and specialist undergo continuing professional development by attending courses and workshops organized by international training organizations such as PDA and others."

PDA thanks the Israel Chapter for organizing the workshop and facilitating Mr. Tribes' visit with the Israel Ministry of Health. PDA looks forward to working with the Israel Chapter to organize another valuable event and continuing to assist the Israeli inspectorate and product specialists improve their skills and knowledge. ■

***—Gautam Maitra, European Director***

# 2004 CHAPTER EVENTS CALENDAR

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

**June**

4 Southeast
4th Annual Golf Social
Raleigh, NC

7-10 Italy
Aseptic Processing: EU & US perspective
Bologna, Italy

9 Capital Area
Aseptic Processing Discussion
Gaithersburg, MD

9 Delaware Valley
Design & Validation of Pharm. Water Sys
Malvern, PA

10 Australia
Current Trends in Pharmaceutical & Biopharmaceutical Manf from PDA Congress
Mt. Waverly, Australia

14 Israel
Designing Pharmaceutical/Biotech Facilities for Regulatory Compliance Seminar
Tel Aviv, Israel

17 Metro
Disinfection/Sanitization
Clark, NJ

21-22 PDA EuroForum/PDA Central Europe
Common Tech. Document: Learning by Doing
UBS Ausbildungs-und Konferenzzentrum
Basel, Switzerland

25 Taiwan
Taiwan Chapter Annual Meeting
Taipei

**August**

5-6 Japan
Topics & Current Tendency of QA/QC & Reg. —Engineering Course for GMP
Tokyo, Japan

9 India
PDA Course on Pharmaceutical & Biopharmaceutical Inspections
Mumbai, India

**September**

2-3 Japan
Education & Training courses: "API GMP & Qualification/Validation," "How to prepare & receive FDA Inspection"
Tokyo, Japan

9 Southern California
Compliance with FDA Change Control Regulations & Validation Management
Irvine, CA

22 Delaware Valley
Aseptic Processing
Malvern, PA

27 PDA EuroForum/PDA Central Europe
Biotech Interest Grp—EU Section/Biosafety
UBS Ausbildungs-und Konferenzzentrum
Basel, Switzerland

**October**

1 New England
Workshop on Combination Product Development
Cambridge, MA

18-19 Italy
Biosafety Forum
ISPE/AFI/PDA Meeting
Rome, Italy

19 Israel
Seminar:Process Validation
Tel Aviv, Israel

20 Southeast
Annual Fall Meeting
Research Triangle Park, NC

25 Spain
Science/Risk Based Approach to Validation
Barcelona, Spain

**November**

9-10 Japan
Japan Chapter Annual Meeting
Tokyo, Japan

17-19 Central Europe
Aseptic Processing Course
Basel, Switzerland

17 Delaware Valley
Environmental Monitoring
Malvern, PA

19 Metro
Current Compliance Trends
Clark, NJ

19 Midwest
Rapid Methods
Northbrook, IL

**November/December**

30-1 France
PDA European Summit—Reg Compliance
Brussels, Belgium

**December**

7-8 France, Two-Day Summit
Brussels, Belgium

13 PDA EuroForum/PDA Central Europe
Pharma Economic: Challenges, Hurdles for Industry to Innovate
UBS Ausbildungs-und Konferenzzentrum
Basel, Switzerland

27 Israel
Annual Meeting
Tel Aviv, Israel

TBD New England
Dinner Seminar on PAT
Cambridge, MA

# 2004 TRAINING AND RESEARCH INSTITUTE CALENDAR

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

## Laboratory Courses

**June**

**14-18** Aseptic Processing Training Prgm: Week 2

**August**

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

**16-20** Aseptic Processing Training Prgm: Week 1

**September**

**1-3** Adv. Environmental Mycology Workshop

**13-17** Aseptic Processing Training Prgm: Week 2

**October**

**4-8** Aseptic Processing Training Prgm: Week 1

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

**18-22** Rapid Microbiological Methods

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

**November**

**1-5** Aseptic Processing Training Prgm: Week 2

**11-12** Developing and Validating Cleaning & Disinfection Prgms for Controlled Envn.

**15-17** Cleaning Validation

**18-19** Remediation of Existing Computer Sys

**December**

**2-3** Environmental Mycology Identification Workshop

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

## Lectures

**June**

**3-4** Computer Products Supplier Auditing Process Model: Auditor Training
PDA-TRI, Baltimore, MD

**August**

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

**September**

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

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

**October**

**4-5** Visual Inspection
Location TBA
Berlin, Germany

**December 2004**

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

## Course Series

**June**

**15-17** Toronto, Canada

Sterile Manf. with Blow/Fill/Seal Tech.
Basic Concepts in Cleaning & Cleaning Validation
Cleanroom Management
Computer & Network Infrastructure (CNI) Qualification Using C3Q™
Preparing for an FDA Pre-Approval Inspection
Qualification & Validation of API Manf. Ops.
Analytical Problem Solving for CAPA Sys
GMP Fundamentals
How to Develop Validation Protocols
Radiation Dosimetry & Calibration

**August-September**

**30-1** Chicago, Illinois

A Comprehensive Guide to OOS Regulations
A Practical Approach to Aseptic Processing & Contamination Control
Assessing Packaging & Processing Extractables/Leachables
Pharmaceutical Water Sys: A Practical Approach
Preparing for an FDA Pre-Approval Inspection
CGMP & Compliance
Application of Clean-In Place to the Pharmaceutical Industry
Environmental Monitoring in Pharmaceutical Manufacturing
Risk Management
Z1.4 Attribute Inspection Sampling in a GMP Environment

**September**

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

Change Control & Documentation
Auditing Pharmaceutical Microbiology Laboratories
Basic Concepts in Cleaning & Cleaning Validation
Compliance Auditing of Cleanrooms and Controlled Environments
Qualification and Validation of API Manufacturing Ops.
Auditing Techniques for CGMP Compliance

**18-20** Boston, Massachusetts

Analytical Problem Solving for CAPA Sys.
Design and Validation of a Cleaning & Disinfection Prgm
Intro. to Writing and Auditing CGMP Doc.
CGMPs for Bioprocesses
Pharmaceutical Water Sys. Design & Validation
Maximizing SOPs - An Untapped Resource of Trng. Solutions
Everything You Wanted to Know About Environmental Monitoring but Were Afraid to Ask
Qualification and Validation of API Manufacturing Ops.
Achieving CGMP Compliance During Development of a Biotechnology Product
Annual Product Reviews: How to Comply with FDA & ICH Req.

# PDA Training and Research Institute Registration Form

R
LTR 06/04

1. **Please type or print your name, address and affiliation.**

**Preferred Address:** ❑ **Business** ❑ **Home**

❑ Mr. ❑ Ms. ❑ Dr. First Name _____ Middle Initial _____ Last Name _____

Job Title _____ Membership Number _____

Company/Organization _____

Address _____

City _____ State/Province _____ ZIP+4/Postal Code _____

Business Phone _____ Fax _____ E-mail _____

❑ Substituting for _____
(Check only if you are substituting for a previously enrolled colleague; a nonmember substituting for member must pay the additional fee.)

Were you referred to this event by a PDA Chapter? ❑ Yes ❑ No If so, which Chapter? _____

## Not a current PDA member? Join today and save up to 50% on training courses!

*Plus…*

✓ Save on PDA meetings, conferences and publications

✓ Connect to global and regional science and regulatory expertise

✓ Gain access to expert, peer-reviewed information relevant to your career

✓ Become a part of the world's leading international network of pharmaceutical and biopharmaceutical professionals.

**Check below to become a PDA member:**

❑ **Individual membership fee: $195 U.S.** (one year)

❑ **Special discounted government/health authority fee: $80 U.S.** (one year)*

* Must be an employee of an official government agency or health authority

For more details on PDA and the benefits of becoming a member, visit www.pda.org today.

2.

| Course Title/Course No. | Date | Current Member | Join PDA and Attend Course | Attend Course Only; Do Not Join PDA | Government/Health Authority Employee * |
|---|---|---|---|---|---|
| | | | | | |
| | | | | | |

* *You must be an employee of an official government agency or health authority to qualify for this rate.*

TOTAL _____

**Deadline:** Enrollment is limited for the benefit of all attendees; this necessitates early registration. Paid registrations must be received one week prior to the event. **Confirmation:** Written confirmation will be sent to you once payment is received. You must have this written confirmation to be considered enrolled in a PDA event. Please allow one week for receipt of confirmation letter. **Substitutions:** If a registrant is unable to attend, substitutions are welcome and can be made at any time, even on-site up to the time of the course. If you are pre-registering as a substitute attendee, indicate this on the registration form. **Refunds:** Refund requests must be in writing. If received one month prior to the start of an event (course series, conference, etc.), a full refund, minus a $55 handling fee, will be made. If received two weeks prior to the event, one-half of the registration fee will be refunded. After that time, no refunds will be made. **Event Cancellation:** PDA reserves the right to modify the material or instructors without notice or to cancel an event. If an 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. **For more details, call PDA at (301) 656-5900.**

3. **Payment Options** (please check one).

❑ A. By **Credit Card** (VISA, MasterCard/EuroCard, American Express, Diners Club), clearly indicating account number and expiration date and billing address. **Proceed to Item 4 below.**

❑ B. By **Bankers' Draft/Check** forwarded together with the registration form PAYABLE IN US DOLLARS ONLY to:

PDA, Inc., P.O. Box 79465, Baltimore MD 21279-0465

Please mark here to request a **PROFORMA INVOICE** from PDA to process your company payment.[1] ❑

[1] You are not considered registered for a PDA course until payment is received and a confirmation letter is issued by PDA. Should you attend a course without a formal confirmation or receipt of payment you will be required to provide a credit card as guarantee of payment at the time of the course.

❑ C. **Wire Transfer Payments**/By bank-to-bank transfer to: (required if paying in foreign currency; prevailing exchange rates at date of submission will apply.)

**UBS AG Basel** Swift Code: **UBSWCHZH40M**

Account number (please specify correct account number for currency being remitted):

❑ CHF: Account No. 292-568-280-02T
❑ EUR: Account No. 292-568-280-64B
❑ GBP: Account No. 292-568-280-65E
❑ USD: Account No. 292-568-280-66M
❑ YEN: Account No. 292-568-280-67C

Please reference code: **2-2-2000**

**Bank Address:**
UBS AG Basel
Postfach
Aeschenplatz 6
4002 Basel, Switzerland

Currency conversions available at: www.forex.com/forex_market_commentary.html

Wire Transfer Confirmation: _____
(insert your confirmation of receipt by UBS Bank here.)

4. **Please check the appropriate box:** Charge: ❑ MasterCard/EuroCard ❑ VISA ❑ AmEx ❑ Diners Club

Account Number: _____ Exp. Date: _____

Name *(exactly as on card)*: _____

Signature: _____ Date: _____

Billing Address: _____

**Federal Tax I.D. #52-1906152**

5. **Return completed form with check or bank draft made to:** PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA **Fax Credit Card Registrations to:** +1 (301) 986-1093 (credit cards only)

PDA USE:
Date: _____ Check: _____ Amount: _____ Account: _____

## TR-32 Update

# Documentum extends its membership with the Audit Repository Center

*By: Paul Gray Documentum and Harvey F. Greenawalt, ARC*

One of the challenges facing companies in regulated industries, such as pharmaceutical, biotechnology and healthcare, is bringing new products to market as quickly as possible, while ensuring adherence to rigorous federal government requirements. Pharmaceutical companies have a monumental task in managing the documentation associated with new drug submissions. In the past decade, many of these companies have implemented content management technology to streamline this process and have reaped rewards by bringing drugs to market more quickly, allowing themselves more protected sales time before going off-patent.

The Documentum Enterprise Content Management (ECM) platform enables many companies to be compliant with the Food and Drug Administration's (FDA) prescribed regulatory requirements for electronic records and signatures (21 CFR Part 11). In fact, Documentum created its own 21 CFR Part 11 compliant Quality Manual using the Documentum ECM platform.

With more than 200 customers in the pharmaceutical industry, Documentum understands and meets federal government requirements for vendors supplying products and services to the pharmaceutical industry. Documentum has undergone an increasing number of audits from 1995 up until 2001 when they were successfully audited by 16 vendors. The number of customer audits has declined significantly since Documentum joined the Audit Repository Center. In 2002 and 2003 Documentum hosted 4 and 2 customer audits, respectively, in an environment where the demand for customer audits is still rapidly growing, so the company has first hand experience with quality audits, as well as the associated time, costs and savings.

When PDA developed the standardized Pharmaceutical Industry Software Supplier Quality Audit process model, Documentum was one of the first vendors to recognize the benefit of offering customers and prospective customers an economical alternative to costly on-site audits. In March 2001, Documentum successfully completed its first PDA audit. In 2002, Documentum underwent further audits at its Pleasanton site and in 2003 at its Toronto and Ottawa sites. Most recently, it has completed an audit at its Cambridge site. These evaluations were conducted by independent, PDA-sanctioned auditors. The audits verify Documentum's commitment to product, quality of service and acceptability to the pharmaceutical and related industries. Documentum's audit results are available through the PDA licensed Audit Repository Center, at a much lower cost than conducting an onsite audit.

For more information, contact Paul Gray, Director of Corporate Quality for Documentum, at (925) 660-5649 or email at paul.gray@docuemtnum.com.

## About Documentum

Documentum, a division of EMC Corporation, provides enterprise content management solutions that enable organizations to unite teams, content and associated business processes. Documentum's integrated set of content, compliance and collaboration solutions support the way people work, from initial discussion and planning through design, production, marketing, sales, service and corporate administration. With a single platform, Documentum enables people to collaboratively create, manage, deliver and archive the content that drives business operations, from documents and discussions to email, Web pages, records and rich media. The Documentum platform makes it possible for companies to distribute all of this content in multiple languages, across internal and external systems, applications and user communities. As a result, Documentum's customers, which include thousands of the world's most successful organizations, harness corporate knowledge, accelerate time to market, increase customer satisfaction, enhance supply chain efficiencies and reduce operating costs, improving their overall competitive advantage. For more information, visit Documentum on the Web at www.documentum.com.

## About ARC

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

# AVAILABILITY of AUDITS

Currently Sixty-two (62) audits are either under consideration, in process or available for distribution. Thirty audits are available for immediate distribution.

| Supplier Name | Supplier Product |
|---|---|
| Access360, Inc. | enRole 4.0 (provisioning software |
| **Agilent Technologies** | **Cerity for Pharmaceutical QA/QC. Network data system for analytical laboratories** |
| Alacris, Inc. | idNexus |
| **Applied Biosystems, Inc.** | **SQL*LIMS™ Software - Laboratory Information Management System** |
| Automation Tooling Systems, Inc. | Custom programming services for process control software |
| **Axalto, Inc** | **Cyberflex Palmer Smart Card and Cyberflex Access Intergration Kit** |
| Decision Management International, Inc. (DMI) | Regulus(tm) Document Authoring (DA) a member of the Regulus(tm) off-the-shelf solution set |
| **Docent** | **Docent Learning Management Server**<br>**Docent Content Delivery Server** |
| Documentum, Inc. | Administrator<br>Application Builder<br>Content Authentication Services (CAS)<br>Control Manager (DCM)<br>DeskTop<br>Desktop for Macintosh<br>Digital Asset Manager<br>DocApp Installer<br>eContent Server<br>GXPharma<br>Media Services<br>Records Manager (RM) Release 3.1 and 3.1.1<br>Web Development Kit<br>WebDAV Server<br>Website Manager<br>WebTop<br>Workflow Manager |
| **Epicentric, Inc.** | **Foundation Enterprise Server 4.0, which is a tool for coordinating information from disparate sources and for disparate uses.** |
| First Consulting Group, Inc. | Custom information based strategy software, operations improvements, management and integration services |
| **Fisher-Rosemount Systems, Inc.** | **Distributed factory automation, Delta V product line** |

| | |
|---|---|
| GE Kaye Instruments, Inc. | Thermal validation systems, monitoring systems, thermocouple references and turbine temperature monitoring equipment– LabWatch™, ValProbe™ and the Validator®2000 systems |
| **IBM** | **Content Manager (CM) v8.2** |
| Inktomi Corporation | Inktomi Enterprise Search. |
| **Innovatum, Inc.** | **DataThread™ - Data audit, workflow, 21 CFR Part 11 and E-signature solution for AS/400 applications, without programming changes** |
| Lexign Corporation | Lexign Flow™ EPR Software |
| **Merant** | **PVCS Dimensions & PVCS Replicator Software Configuration Management Tool** |
| Mercury Interactive<br>Test Management Tools | QuickTest Professional<br>Astra QuickTest<br>Astra LoadTest<br>Astra FastTrack<br>LoadRunner<br>LoadRunner TestCenter<br>TestDirector<br>WinRunner |
| **Propack Data GmbH** | **Enterprise Production Management System, PMX 3.2 with Solutions MES and CTM** |
| Rational Software Corporation | Rational Suite® Enterprise<br>Rational ClearQuest (for team-based change request and defect management) |
| **Rational ClearCase** | **(configuration management for smaller development teams)** |
| SAP- AG | mySAP.com e-business platform, includes Product Lines: SAP R/3 4.5B and SAP R/3 4.6B/C |
| **Serena Software, Inc.** | **ChangeMan (ZMF) (DS)**<br>**StarTool (STL)**<br>**TeamTrack (TT)** |
| Sparta Systems, Inc. | TrackWise®.<br>Training, Configuration, Installation and Support for TrackWise® |
| **SSA Global Technologies, Inc.** | **Mid Range ERP software for manufacturing, supply chain and financial application domains** |
| 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 databases, mainframes and wireless and portable devices |
| **Waters Corporation** | **Empower™ chromatography software and Connections AQT–HPLC System, System Components, Data Management** |

## New Technical Publications Available!

PDA is your source for technical publications produced jointly with industry experts and regulatory bodies, providing the most current scientific, technical and regulatory information you need for success.

# Pharmaceutical Quality

Edited by **Richard Prince**

How do you define quality?

***Pharmaceutical Quality*** offers examinations of quality from international, governmental, industrial, and individual perspectives. With 758 pages of useful information written by subject matter experts and expertly edited, this book takes a comprehensive and systematic look at the discipline of quality and provides a blueprint for the production and delivery of higher-quality products on a more consistent basis.

Is this publication for me?

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

- Quality control professionals
- Quality assurance professionals
- Quality management professionals
- Regulatory affairs professionals
- Regulatory Compliance professionals
- Trainers
- Legal professionals
- Validation professionals
- Manufacturing professionals


**Item No. 17207**
**Member: US $240**
**Nonmember: US $299**

## Two New Shep's Narrated System Audit Training CD-Roms

In response to many requests, Richard "Dick" Shepherd has added narration to his Shep's System Audit Training CD-Roms. Each enhanced CD-Rom now includes:

- Detailed explanation of systems audit training program
- Step-by-step procedures for conducting a system audit
- Observations to assist in the evaluation of audit findings

**Are these products right for me?**
**Shep's Narrated System Audit Training CD-Roms** are cost-effective training tools that will benefit pharmaceutical and biopharmaceutical managers and associates.

### JUST RELEASED!

**Technology Transfer**
(A 35-minute presentation, including 38 slides.)
**Item No. 11047**
**Member: US$350**
**Nonmember: US$1045**

**QC Laboratory Operations**
(A 50-minute presentation, including 66 slides.)
**Item No. 11048**
**Member: US$350**
**Nonmember: US$1045**

*For complete descriptions of these new PDA products and to order and pay online (U.S. Dollars only), just visit www.pda.org/estore.*

## PDA-DHI Press Books

| Item No. | Title | Author/Editor | Price (All US$) Member | Nonmember | Government |
|---|---|---|---|---|---|
| 17173 | Practical Change Control for Healthcare Manufacturers | Angie Jamison | $120 | $149 | $ 50 |
| 17174 | Understanding GMP: A Practical Guide | Martyn Becker | $170 | $209 | $ 70 |
| 17175 | Microbial Risk Assessment in Pharmaceutical Clean Rooms | Bengt Ljungquist/ Berit Reinmuller | $ 75 | $ 90 | $ 30 |
| 17176 | Quality Control Systems for the Microbiology Laboratory: The Key to Successful Inspections | Lucia Clontz | $170 | $209 | $ 70 |
| 17177 | Electronic Records and Electronic Signatures Compliance Assessment | Chris Reid/ Barbara Mullendore | $ 90 | $109 | $ 40 |
| 17179 | The Internal Quality Audit | Monica Grimaldi/ Janet Gough | $120 | $149 | $ 50 |
| 17180 | The External Quality Audit | Monica Grimaldi/ Janet Gough | $120 | $149 | $ 50 |
| 17181 | Media Fill Validation Environmental Monitoring During Aseptic Processing | Michael Jahnke | $ 90 | $109 | $ 40 |
| 17182 | Introduction to Environmental Monitoring in Pharmaceutical Areas | Michael Jahnke | $ 90 | $109 | $ 40 |
| 17183 | Steam Sterilization: A Practitioner's Guide | Jeanne Moldenhauer | $215 | $269 | $175 |
| 17184 | Rapid Analytical Microbiology: The Chemistry and Physics of Microbial Identification | Wayne P. Olson | $195 | $239 | $130 |
| 17185 | Microbiology In Pharmaceutical Manufacturing | Richard Prince | $240 | $299 | $160 |
| 17188 | Understanding Active Pharmaceutical Ingredients | Siegfried Schmitt | $ 80 | $109 | $ 35 |
| 17189 | Change Control | Soren Schwartze | $ 75 | $ 90 | $ 30 |
| 17199 | GMP in Practice: Regulatory Expectations For The Pharmaceutical Industry Third Edition | James Vesper | $105 | $129 | $ 75 |
| 17192 | Hosting a Compliance Inspection | Janet Gough | $120 | $149 | $ 50 |
| 17193 | Microbiological Monitoring of Pharmaceutical Process Water | Michael Jahnke | $ 90 | $109 | $ 65 |
| 17194 | Sorting Out the Critical Variables: A Worked Example for the Non-Statistician | Alfred Wachter | $ 90 | $109 | $ 40 |
| 17195 | Validation Master Plan, The Streetwise Downtown Guide | Trevor Deeks | $ 80 | $109 | $ 60 |
| 17196 | Laboratory Systems Validation Testing and Practice | Paul Coombes | $120 | $149 | $ 50 |
| 17197 | Filtration Handbook: Integrity Testing | Maik W. Jornitz/ Theodore H. Meltzer | $185 | $229 | $ 75 |
| 17198 | Quality and Safety of Gene Medicines: A Practical Guide | Anthony Meager | $155 | $189 | $ 65 |
| 17200 | Commercial Off-The Shelf Software Validation for 21 CFR Part 11 Compliance | David Nettleton/ Janet Gouch | $185 | $229 | $ 75 |
| 17201 | Laboratory Validation: A Practitioner's Guide | Jeanne Moldenhauer | $250 | $309 | $170 |
| 17203 | The Essence of GMPs: A Concise Practitioner's Guide | U. G. Barad | $185 | $229 | $ 75 |
| 17204 | Supply of Chemicals in the Pharmaceutical Industry: Regulatory Guidelines and Rulings | Mark Selby | $185 | $229 | $ 75 |
| 17205 | Excellence Through Validation: A Practitioner's Guide | U. G. Barad | $160 | $199 | $ 65 |

**For complete descriptions, visit our publications E-store at our Web site, www.pda.org.**

## PDA Technical Reports

Your library is incomplete without them!

Order Today!

*Note: Technical Report Nos. 2 and 6 have been superseded by Technical Report No. 22, and Technical Report No. 8 has been superseded by Technical Report No. 30. The superseded reports are no longer available. Technical Report No. 13 was reissued (2001) with the same number. All prices are US$.*

**PDA Technical Monograph No. 1:** Validation of Steam Sterilization Cycles [1978] 36 pp. $75 member/$550 nonmember **Item No. 01001**

**TR3:** Validation of Dry Heat Processes Used for Sterilization and Depyrogenation [1981] 55 pp. $75 member/$550 nonmember **Item No. 01003**

**TR4:** Design Concepts for the Validation of a Water-For-Injection System [1983] 12 pp. $75 member/$550 nonmember **Item No. 01004**

**TR5:** Sterile Pharmaceutical Packaging: Compatibility and Stability [1984] 137 pp. $75 member/)$550 nonmember **Item No. 01005**

**TR7:** Depyrogenation [1985] 116 pp. $75 member/$550 nonmember **Item No. 01007**

**TR9:** Review of Commercially Available Particulate Measurement Systems [1988] 30 pp. $75 member/$550 nonmember **Item No. 01009**

**TR10:** Parenteral Formulations of Proteins and Peptides: Stability and Stabilizers [1988] 26 pp. $75 member/$550 nonmember **Item No. 01010**

**TR11:** Sterilization of Parenterals by Gamma Radiation [1988] 10 pp. $75 member/$550 nonmember **Item No. 01011**

**TR12:** Siliconization of Parenteral Drug Packaging Components [1988] 14 pp. $75 member/$550 nonmember **Item No. 01012**

**TR13:** Revised: Fundamentals of an Environmental Monitoring Program [2001] 37 pp. $75 member/$550 nonmember **Item No. 01013**

**TR14:** Industry Perspective on the Validation of Column-Based Separation Processes for the Purification of Proteins [1992] 11 pp. $75 member/$550 nonmember **Item No. 01014**

**TR15:** Industrial Perspective on Validation of Tangential Flow Filtration in Bio-pharmaceutical Application [1992] 13 pp. $75 member/$550 nonmember **Item No. 01015**

**TR16:** Effect of Gamma Irradiation on Elastomeric Closures [1992] 12 pp. $75 member/$550 nonmember **Item No. 01016**

**TR17:** Current Practices in the Validation of Aseptic Processing—1992 [1993] 21 pp. $75 member/$550 nonmember **Item No. 01017**

**TR18:** PDA Report on the Validation of Computer-Related Systems [1995] 17 pp. $75 member/$550 nonmember **Item No. 01018**

**TR19:** Rapid/Automated ID Methods Survey [1990] 7 pp. $75 member/$550 nonmember **Item No. 01019**

**TR20:** Report on Survey of Current Industry Gowning Practices [1990] 5 pp. $75 member/$550 nonmember **Item No. 01020**

**TR21:** Bioburden Recovery Validation [1990] 8 pp. $75 member/$550 nonmember **Item No. 01021**

**TR22:** Process Simulation Testing for Aseptically Filled Products [1996] 16 pp. $75 member/$550 nonmember **Item No. 01022**

**TR23:** Industry Survey on Current Sterile Filtration Practices [1997] 13 pp. $75 member/$550 nonmember **Item No. 01023**

**TR24:** Current Practices in the Validation of Aseptic Processing [1997] 23 pp. $75 member/$550 nonmember **Item No. 01024**

**TR25:** Blend Uniformity Analysis: Validation and In-Process Testing [1997] 99 pp. $75 member/$550 nonmember **Item No. 01025**

**TR26:** Sterilizing Filtration of Liquids [1998] 31 pp. $75 member/$550 nonmember **Item No. 01026**

**TR27:** Pharmaceutical Package Integrity [1998] 48 pp. $75 member/$550 nonmember **Item No. 01027**

**TR28:** Process Simulation Testing for Sterile Bulk Pharmaceutical Chemicals [1998] 15 pp. $75 member/$550 nonmember **Item No. 01028**

**TR29:** Points to Consider for Cleaning Validation [1998] 23 pp. $75 member/$550 nonmember **Item No. 01029**

**TR30:** Parametric Release of Pharmaceuticals Terminally Sterilized by Moist Heat [1999] 6 pp. $75 member/$550 nonmember **Item No. 01030**

**TR31:** Validation and Qualification of Computerized Laboratory Data Acquisition Systems [1999] 12 pp. $75 member/$550 nonmember **Item No. 01031**

**TR32:** Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations [1999] 277 pp.

Print: $100 member/$575 nonmember **Item No. 01032**

CD-ROM: $75 member/$550 nonmember **Item No. 01132**

**TR33:** Evaluation, Validation and Implementation of New Microbiological Testing Methods [2000] 37 pp. $75 member/$550 nonmember **Item No. 01033**

**TR34:** Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products [2001] 25 pp. $75 member/$550 nonmember **Item No. 01034**

**TR35:** A Proposed Training Model for the Microbiological Function in the Pharmaceutical Industry [2001] 24 pp. $75 member/$550 nonmember **Item No. 01035**

**TR36:** Current Practices in the Validation of Aseptic Processing-2001 [2001] 34 pp. $75 member/$550 nonmember **Item No. 01036**

Points to Consider for Aseptic Processing, Volume 57 Number 2 Supplement [2003]. $75 member/$550 nonmember **Item No. 03004**

The easiest way to order a PDA book or other technical & regulatory resource is by logging on to PDA's new E-store.

Remember: You can search the E-store by author, title, publication type, key word(s), item number, or publication category.

Just go to: www.pda.org/estore

Order by phone with your credit card:
+1 (301) 656-5900
8:30 a.m.
to
5:00 p.m. ET.

# PDA Technical Resource Order Form

S

LTR 06/04

Use this form to order PDA Technical Resources. If ordering by mail, include a check payable to PDA to the address below. Be sure to include shipping and handling charges in the total. If ordering by fax, please include all credit card information. All orders must include payment. Prices are subject to change at any time.

❑ Mr. ❑ Ms. ❑ Dr.

Name _____ Member No. _____

Company _____

Address _____

City _____ State _____ Country _____ Zip+4/Postal Code _____

Tel: _____ Fax: _____ E-mail: _____

## Not a current PDA member? Join today and save up to 50% on training courses!

*Plus…*

✓ Save on PDA meetings, conferences and publications

✓ Gain access to expert, peer-reviewed information relevant to your career

✓ Connect to global and regional science and regulatory expertise

✓ Become a part of the world's leading international network of pharmaceutical and biopharmaceutical professionals.

**Check below to become a PDA member:**

❑ **Individual membership fee: $195 U.S.** (one year)

❑ **Special discounted government/health authority fee: $80 U.S.** (one year)*

* Must be an employee of an official government agency or health authority

For more details on PDA and the benefits of becoming a member, visit www.pda.org today.

| Item No. | Title | Qty. | Price | Total |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |

**Shipping & Handling Rates—**Domestic U.S. orders are shipped via UPS Ground. Second-day and next-day air service is available. Call or e-mail for prices.

**International orders**

Please add 20%, minimum $18.00, maximum $150.00. Items are sent priority air, with delivery in 3–8 weeks, but express service is available for some countries; please call for details.

**U.S., Puerto Rico & Canada**

| *If your order totals:* | *Add:* |
|---|---|
| $15.00 and under | $5.95 |
| $15.01–$75.00 | $7.95 |
| $75.01–$150.00 | $9.95 |
| $150.01–$250.00 | $11.95 |
| $250.01 or more | $13.95 |

| | |
|---|---|
| Subtotal | |
| Shipping & Handling | |
| 5% Tax *(Maryland residents only)* | |
| **TOTAL** | |

3. **Payment Options** (please check one).

❑ A. By **Credit Card** (VISA, MasterCard/EuroCard, American Express, Diners Club), clearly indicating account number and expiration date and billing address. **Proceed to Item 4 below.**

❑ B. By **Bankers' Draft/Check** forwarded together with the order form PAYABLE IN US DOLLARS ONLY to:

PDA, Inc., P.O. Box 79465, Baltimore MD 21279-0465

❑ C. **Wire Transfer Payments**/By bank-to-bank transfer to: (required if paying in foreign currency; Contact Janny Chua at +1 (301) 656-5900 ext. 133 or chua@pda.org for quotes in various currencies.)

**UBS AG Basel** Swift Code: **UBSWCHZH40M**

Account number (please specify correct account number for currency being remitted):

❑ CHF: Account No. 292-568-280-03Z
❑ EUR: Account No. 292-568-280-68L
❑ GBP: Account No. 292-568-280-69R
❑ USD: Account No. 292-568-280-70P
❑ YEN: Account No. 292-568-280-71K

**Bank Address:**
UBS AG Basel
Postfach
Aeschenplatz 6
4002 Basel, Switzerland

Wire Transfer Confirmation: _____

(insert your confirmation of receipt by UBS Bank here.)

4. **Please check the appropriate box:** Charge: ❑ MasterCard/EuroCard ❑ VISA ❑ AmEx ❑ Diners Club

Account Number: _____ Exp. Date: _____

Name *(exactly as on card)*: _____

Signature: _____ Date: _____

Billing Address: _____

**Federal Tax I.D. #52-1906152**

5. **Return completed form with check or bank draft made to:** PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA **Fax Credit Card Payments to:** +1 (301) 986-1093 (credit cards only)

PDA USE:
Date: _____ Check: _____ Amount: _____ Account: _____

# Meet your new headhunter.


## The PDA Career Center
## *www.pda.org/careers*

Looking to make a career change or take your career to the next level? Look no further, The PDA Career Center is here! Top employers are posting new positions to find qualified candidates across all segments and levels of the pharmaceutical and biopharmaceutical communities. Log on today to enjoy these features:

- Create, edit, and store your résumé and cover letter for employers to see.
- Confidentiality – You have the power to control what information is viewable to prospective employers.
- Search and apply to a variety of careers, ranging from entry level to executive level positions.
- Receive e-mail notifications when new jobs are available *(Available to PDA Members only)*.
- Schedule in-person interviews at PDA Career Fairs.

PDA
An International Association For Pharmaceutical Science And Technology

**PDA Global Headquarters**
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Phone: +1 (301) 656-5900
Fax: +1 (301) 986-0296
Web: *www.pda.org*

*Williams, from page 20*

**Dr. Williams:** To me that is not the issue. A lot of things are hard to do. It is hard to make generics now for some products. That to me is a business risk—whether a company wants to take on the challenge of creating a data set that documents therapeutically equivalent product.

The more important issue in my mind is to establish the concept of equivalence and the kind of studies needed to show consistency, comparability, and equivalence. When you think about it, there are only so many studies you can do. You have marketplace surveillance studies, clinical comparative studies, pharmacokinetic and pharmacodynamic studies, non-clinical studies, biologic potency tests, and then, of course physical/chemical tests. For any given ingredient/dosage form there may be hundreds of tests that could be used in a given setting to show equivalence. Is the agency going to ask for a hundred tests in every case? I hope not. That would be counterproductive. But once you establish the concept then a "toolkit" can be developed to establish equivalence, in which a case-by-case judgment can be made as to what is needed for a peptide, a protein, or a monoclonal antibody, etc. The goal for industry and for the public is to keep the tests to a reasonable minimum in a given setting (consistency, com-parability, equivalence). Asking for a repeat of clinical safety and efficacy studies for trivial changes simply adds to the cost of the products and delays market access.

**Editor:** One of the barriers is the perception that for biological products, the process is the product.

**Dr. Williams:** I don't buy that. You can always endeavor to determine equivalency of products even when products are made by completely different processes. You might perform all those studies and find that the products are not equivalent. That is okay. That is what science is all about: You may fail in your showing of equivalence. However, you may find that under various manufacturing conditions you can make two equivalent products.

**Editor:** Since biologics is a new side of the pharmacopeia, how successful has USP been in getting the biopharmaceutical industry involved in the process?

**Dr. Williams:** Many stakeholders will work with us on general chapters. It is much more difficult to get them to give us monographs for recombinant proteins or vaccines. USP is working on ways to resolve that. Every pharmacopeia in the world usually works on the basis that submission of information is voluntary, and the information is considered by a volunteer standard setting body, which at USP is the Council of Experts.

What we are doing now is developing ways to work with manufacturers, or create on our own monographs, to make *USP-NF* complete. I think if we didn't do that, we would be deficient in our public health responsibility. Every now and then somebody asks me, "Why do you want a public monograph?" And that question is like going into General Motors and saying, "Do you want automobiles?" The purpose of a pharmacopeia is to create monographs. If we only develop general chapters, those would end up just being a text book technical discussion of how to execute certain technical procedures.

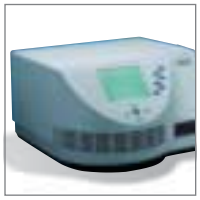
**Editor:** What would happen to USP if in ten or so years we see the industry dominated by complex and protein-based therapies with manufacturers no longer submitting monographs?

**Dr. Williams:** USP doesn't want to give up on the idea of public monographs. USP believes that public monographs are highly important to the industry, and we are publishing an article to that point. From a practitioner standpoint—and USP is ultimately a practitioner-based organization—practitioners want public standards for the products that they give to their patients. The need for public monographs at USP arises in part from its practitioner base. It was these practitioners after all who started the USP in 1820. In an era of parallel import, counterfeit drugs and substandard drugs, the need for public monographs seems to be increasing.

Key issues will always remain for a pharmacopeia: How do you get to an understanding of what the public standard should be for a therapeutic product? And even more importantly, how do you get the public material that can be used to test to the public standard? The United States does not have public standards (monographs) or reference standards for many ingredients and products. What does that mean to a regulatory agency when they want to take an enforcement action and they cannot even obtain independently developed test materials for their own regulatory analysis? What is the relationship between private reference standard material and official USP Reference Standards? These are key questions for the public, USP and manufacturers.

The perception of the public standards model—manufacturers provide the standard, we sell it back to them—is too simplistic. The donation of the material is only the start of a laborious process to create a public standard. USP has to re-characterize material, determine its content through collaborative testing, and assure its continued suitability for use. These are non-trivial tests that require considerable expenditure of resources. At heart it is a science-based activity that falls under the general heading of 'metrology' and USP has done it well for many years, working collaboratively with industry and the FDA. It is testimony to the success of the independent, non-governmental pharmacopeia. ■

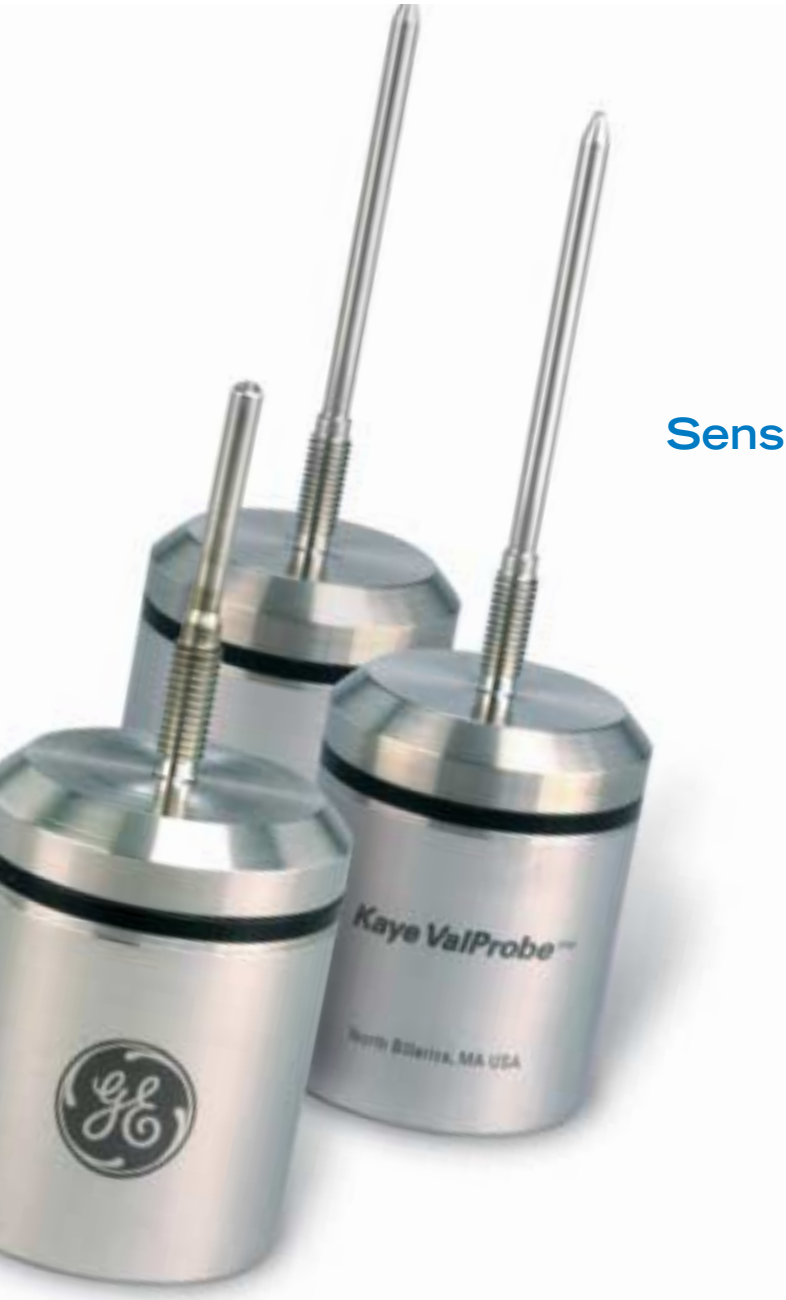
**This interview will conclude in the July *PDA Letter*.** Next month, PDA asks Dr. Williams to explain how manufac-turers can make sense of the overlap that sometimes exists between guidances provided by health authorities and scientific associations like PDA and USP's general chapters and general information chapters. Also, PDA and Dr. Williams discuss USP's work in the sterile product and aseptic processing areas. The interview concludes with Dr. Williams reflecting on his distinguished career with the U.S. FDA.



For over forty years the **Kaye** name has been recognized for uncompromising accuracy and reliability in thermal process measurement. We've always been very good at what we do, and we're about to get even better.

With GE's technical expertise, global reach and financial strength we now have the horsepower to take on even greater challenges. In the months and years ahead look for new and exciting solutions from the people you've trusted for decades, but look for us under a new name.

**GE Infrastructure - Sensing**




## Sensing change for the better.

imagination at work

**Formerly GE Kaye**
For now, you can still find us at gekaye.com

Be sure to see us at:
PDA SciTech Summit, Booth 501, and
INTERPHEX, Booth 1421

**Turn to pages 28, 35 and 36 for PDA's new event calendars.**

21st Century Initiative

# How will FDA's new guidances affect you and your company?

*Get the answers you need for successful implementation!*

PDA
An International Association For Pharmaceutical Science And Technology

FDA

# *2004* PDA/FDA *Joint Regulatory Conference*

## The New Guidances

Washington, D.C.

| | |
|---|---|
| Conference: | September 20-22, 2004 |
| Tabletop Exhibits: | September 20-21, 2004 |
| Training Courses | September 23-24, 2004 |

Face to Face with FDA

Shift to Implementation

*Your first opportunity to hear from FDA leaders who are driving the Initiative!*

**Pharma, biopharma and combination products associates, managers, directors and senior executives:**
Directly interact with FDA and key industry leaders to get the take-aways you need to begin implementing the new guidances right away!

- cGMPs/Quality Systems
- Aseptic Processing
- Risk Management
- Process Analytical Technologies
- Comparability Protocols
- Dispute Resolution/Pharmaceutical Inspectorate
- SUPAC

**PDA Training and Research Institute Courses**
Job-focused interactive training courses designed to help you improve your processes, performance and bottom line!

- Compliance Auditing of Cleanrooms and Controlled Environments
- Change Control and Documentation
- Qualification and Validation of API Manufacturing
- Auditing Pharmaceutical Microbiology Laboratories
- Basic Concepts in Cleaning & Cleaning Validation
- Auditing Techniques for cGMP Compliance

To register, get more information or to reserve exhibit space, visit
***www.pda.org/PDAFDA2004***
Tel: +1 (301) 656-5900 • E-mail: *info@pda.org*