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PDA Letter

January 2004

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

Make the Most of Your PDA Membership, page 25

PDA Programs and Meetings Off and Running in 2004!

International Perspectives on Science, Technology & Regulations in Basel—International Congress

The 2004 PDA International Congress—the year's premier international event for new science, technology and regulations in the global pharmaceutical and biopharmaceutical industries—has something for everyone, whether you are new to the industry or a seasoned veteran. The Congress and Exhibition begins **February 16**, Training Courses start **February 19**, and the skiing, sightseeing and fun in beautiful, historic Basel, Switzerland will last all week long!

Organized by a diverse group of senior industry experts and regulators from Europe and the U.S., the 2004 PDA International Congress will be an exciting and unique forum to examine global perspectives on key pharmaceutical developments and manufacturing issues.

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Something New in Orlando—SciTech Summit™

The leader in education, training and scientific and technological guidance for the pharmaceutical manufacturing industry, PDA, presents an innovative conference for information, benchmarking, and networking—the 2004 SciTech Summit™, **March 8–12**.

SciTech Summit is PDA's "new" annual meeting—a combination of the best of both the traditional PDA Annual Meeting and Spring Conference.

Global industry and regulatory **experts** from Abbott Laboratories, Amgen, AstraZeneca, Aventis-Behring, Baxter, Chiron, Eli Lilly, EMEA, GlaxoSmithKline, Johnson & Johnson, Pfizer, FDA and more will focus on the use and application of new science and new technologies to meet regulatory demands.

Participants can focus on one of several tracks or choose to attend a variety of sessions. Featured tracks

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PQRI's First Project to Save Industry Hundreds of Millions

• Economic Impact Study of PQRI's Science-Based BU Proposal Completed

The pharmaceutical industry will reap "big savings" as a result of FDA's decision to adopt the science-based policy recommendation made by the Product Quality Research Institute (PQRI) on blend uniformity (BU) testing alternatives. In November, FDA released a draft guidance on stratified dosage unit testing that incorporates the peer-reviewed and publicly-vetted recommendation.

The PQRI recommendation was developed by the Institute's first working group, the Blend Uniformity Working Group (BUWG), which was formed in 1999. The working group's final recommendation on stratified sampling was published in the *PDA Journal of Pharmaceutical Science and Technology* (March/April 2003, p. 64).

The savings stemming from the proposal and the science underpinning it were the topics of discussion at a Dec. 4–5 workshop on the draft guidance and the BUWG recommendation. As a founding association and active member of PQRI, PDA hosted the workshop at the Hyatt Regency in Bethesda, Maryland. The successful conference drew nearly 150 participants, mostly from industry. PQRI representatives were greatly appreciative of the high level service provided by PDA staff in assuring all meeting delegates' needs were properly addressed so that the focus remained on this important and challenging scientific and regulatory topic.

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- Must-see keynote presentations from **Dr. Carlo Pini**, Chief Executive of QA, Instituto Superiore di Sanita and **Dr. Frank Hallinan**, Chief Executive, Wyeth Medica

For more information, to register or inquire about exhibit opportunities, visit **www.pda.org**.

Exhibit spaces are still available
Call today to reserve your space!

PDA
An International Association For Pharmaceutical Science And Technology

www.pda.org

PDA Global Headquarters
Bethesda, Maryland USA
Tel: +1 (301) 656-5900

PDA European Headquarters
Basel, Switzerland
Tel: +41 61 321 83 49

PDA Training and Research Institute
Baltimore, Maryland USA
Tel: +1 (410) 455-5800

Important Dates...

- **Jan. 31, 2004**–deadline for public comment on EMEA Note for Guidance on Assessing the Risk for Virus Transmission, page 19
- **Feb. 16–20, 2004**–International Congress, cover
- **March 8–12, 2004**–SciTech Summit™, cover

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Walter Morris
Senior Editor

Neal G. Koller
President

Janet Raysick
Production Manager

Matthew Clark
Director of Marketing Services

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IN THIS ISSUE...

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
Gautam Maitra
Director, Europe
R-1059.747
Postfach
CH-4002 Basel
Switzerland
Tel: +41 61 321 56 30 (Fixnet)
Mobile: +41 79 439 59 56
Fax: +41 61 321 83 48
E-mail: *maitra@pda.org*

PDA Training & 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*

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Neal G. Koller
PDA President

Helping Chapters Pursue and Achieve Strategic Plan Objectives

PDA will be introducing a number of new and exciting initiatives and programs in 2004 as part of our ongoing effort to pursue the six Strategies of the **PDA Strategic Plan**. The **Strategic Plan** is intended to create a stronger vehicle for industry, government and academia to advance pharmaceutical and biopharmaceutical science and technology, to enhance the impact and reputation of the organization worldwide, and to increase the value of PDA to its members.

One of these programs is the *PDA Chapter Points Program*. This new and innovative program will support Chapters as they pursue the six Strategies of our **Strategic Plan**.

We would like to thank **Grace Chin** (SNC-LAVALIN), President of the PDA Canada Chapter, for getting the idea of a Points Program rolling. We would further like to thank each of the Chapters, whose invaluable input over the past six months shaped the Program, bringing it to life.

In 2004, Chapters can earn *"Points"* for pursuing the PDA Strategic Plan. At the end of the year, all PDA Chapters achieving the minimum number of *Points* will receive a "PDA bank account" with $1,000 (U.S.). Additional levels of awards will be given to the top three point earners. Award money can be used to advance Chapter activities, such as paying for speaker travel expenses or buying audio/video equipment for meetings. The *PDA Chapter Points Progam* will provide guidelines for how Chapters can spend the money.

The Activities of the *PDA Chapter Points Program* correlate directly with Strategic Plan:

For example, **Strategy 1—**

> **"Increase the accessibility of services, education and training offerings both internationally and domestically"—**

is one that Chapters can play a critical role in advancing, by holding education seminars, workshops and meetings. The *PDA Chapter Points Program* will award points both to encourage Chapters to sponsor events and activities and to reward those Chapters which have excelled in this area. *Points* also will be awarded to Chapters for notifying PDA Chapter Coordinator KiKi Coffman of events so that PDA can help in the effort to promote them. Additionally, points can be earned by Chapters when their members attend PDA events and training courses, all furthering PDA's Strategic Plan of expanding the accessibility of its education and training offerings.

The *PDA Chapter Points Program* supports **Strategy 2**, an invaluable one for our members:

> **"Building a stronger liaison with regulatory bodies."**

Chapters play an important role in this activity. To award excellence in this area, points will be awarded to Chapters for submitting to the PDA Regulatory Affairs Department science-based comments on regulatory guidances and policies for incorporation into approved PDA documents.

PDA Task Forces, Interest Groups, and publications like the *PDA Journal of Pharmaceutical Science and Technology* play are central to the fulfillment of **Strategy 3**:

> **"Continually improve the relevance and quality of scientific information and programs offered by PDA to reach appropriate audiences."**

Under the *PDA Chapter Points Program*, Chapters will be rewarded for encouraging their members to get involved with PDA Task Forces/Interest Groups, submitting manuscripts to the journal and contributing to Chapter newsletters, the *PDA Letter* and the *PDA Chapter News*.

The *PDA Chapter Points Program* also will support **Strategy 4**:

> **"Assure the financial resources are in place to support PDA's mission to be an international influence."**

To encourage Chapters to do their part, points will be awarded to those who submit their financial statements to headquarters.

Furthermore, the *PDA Chapter Points Program* will reward *Points* to Chapters whenever new industry professionals from their region join PDA, in support of **Strategy 5**:

> **"Continue to expand and market PDA."**

Chapters also will be encouraged to reach out to universities and colleges in their regions to generate student membership and help form student Chapters. Such activities will support the **Strategy 6**:

> **"Improve PDA's operating structure domestically and internationally."**

The *PDA Chapter Points Program* is an exciting initiative that will advance the PDA Strategic Plan and ensure that Chapters are supported and rewarded. More information on the *PDA Chapter Points Program* will be available very shortly. I look forward to announcing other enhancements to PDA members in future months. ■

From the Editor

I cannot express how proud and excited I am to be the new editor of the *PDA Letter.* Coming from *"The Gold Sheet,"* I know that PDA is an important and well-respected association in the global pharmaceutical and biopharmaceutical community. PDA's members are an incredible group of academic, industry and health authority professionals who donate a lot of time and energy to the association. Among other things, PDA members: actively serve on a variety of committees, interest groups, task forces, and the Board; contribute to PDA publications and technical documents; and author books—all on top of their professional duties. Through their hard work, PDA members regularly make positive contributions to their professions and the regulatory environment in which they work by advancing sound science and technology.

The *PDA Letter* is an important cog in the machinery that makes PDA successful.

The *PDA Letter* is an important cog in the machinery that makes PDA successful. As *the* document of record for PDA, it helps our members perform their association-related activities and their professional duties, communicates all the programs, courses, and events important to the membership, and provides valuable information on new science, technology and regulatory initiatives.

Now that I've worked on the newsletter for a few months and attended several PDA events from the "inside," I would like to discuss some of the enhancements members can anticipate in 2004. There will be expanded coverage of member contributions via the interest groups, task forces, etc. Readers will see more detailed summaries of PDA events. As an international association, regulatory briefs will be presented in a single, global section, rather than region-specific sections. There will be an increased focus on the activities of chapters, and consistent and timely information on how to maximize the value of membership. Additionally, readers should expect to see more features like "Meet the Scientist," "Meet the Member," and "Meet the Regulator," as well as other types of useful and interesting content, such as interviews with key industry and regulatory officials.

Other, more subtle changes will be made regarding format and design—all to ensure that the *PDA Letter*, the Web site, and other PDA publications have a coherent and consistent look and are easy to use and read.

Most importantly, this is *your* newsletter. Your feedback is critical to the continual enhancement of PDA offerings and to the ongoing effort to increase the value of membership. Questions, comments and concerns, as well as queries about making announcements or submitting articles, can be directed to me at +1 (301) 656-5900, ext. 148 or morris@pda.org. Please don't hesitate to contact me anytime.

The next 12 months promise to be as exciting as they will be challenging. I look forward to a great year serving PDA and its members. ■

—Walter Morris

Volunteer Needed For Audit Committee

PDA's Board of Directors is forming an Audit Committee to ensure that PDA maintains the highest level of integrity in its financial governance. Though associations are not subject to the requirements of the Sarbanes-Oxley Act, PDA has chosen to proactively conform with good audit oversight practices in anticipation of future regulation affecting not-for-profit organizations.

As part of this effort, the Audit Committee needs a PDA member with extensive accounting or related financial management experience. Ideally, the volunteer will have a certificate in accounting, i.e., a CPA or CFA . Preference will be given to those candidates with executive-level experience and profit and loss responsibilities, such as CEO, CFO or senior officer of a corporation or operating division.

For additional information or to express your interest in this volunteer opportunity, please contact Lance K. Hoboy, VP, Finance & Strategic Planning, at +1 (301) 656-5900 (ext. 114) or hoboy@pda.org. ■

PQRI's Science-based BU Proposal, from cover

As part of an effort to convince industry that the new approach is desirable not just from a regulatory point of view, FDA contracted the Eastern Research Group (www.erg.com) to conduct an economic impact study of the proposal.

Helen Winkle, Office of Pharmaceutical Science Director, FDA Center for Drug Evaluation and Research (CDER), discussed the ERG study at the workshop. The agency felt the study was "an important thing to do," explained Winkle. She noted that the Agency had received "a lot of questions" regarding the financial implications of the proposal. The results of the study provide a "better feel for the economic impact of making the changes to the requirement" and "help PQRI in determining the value of their research with respect to helping reduce the regulatory burden." The precedent for conducting economic impact studies already existed at CDER, which had the scale-up and post-approval changes (SUPAC) initiative examined during the 1990's. ERG is one of the groups the Agency has contracted in the past to perform such studies.

ERG determined that the generic drug industry as a whole could save anywhere from $146 mil. to $150 mil. by following PQRI's recommendation.

ERG determined that the generic drug industry as a whole could save anywhere from $146 mil. to $150 mil. by following PQRI's recommendation. These savings will stem from the stratified testing approach developed by the PQRI working group which reduces the amount of blend testing a firm needs to perform. The estimate is based on the assumption that generics companies manufacturing tablets and/or capsules routinely performed in-process blend uniformity testing on commercial batches to fulfill the CGMP requirement to control the mixing "to assure uniformity and homogeneity."

FDA may ask ERG to further explore the potential economic impact to innovator firms. The study found that research-based companies may actually incur costs ranging from $2–4 mil. as a result of the approach. This finding was based on the assumption that most innovator companies currently do not perform routine blend testing during manufacturing, and, as such, would incur costs to implement the stratified system. FDA, however, believes that some innovator firms already conduct in-process blend testing "outside normal channels," and actually will save money, stated Winkle. "We talked about going back and looking again at the innovator companies," she explained, "with the assumption that they do some testing." Under that assumption, FDA believes that ERG can "sort of amend the survey to more adequately address this part of the savings."

The November draft guidance, entitled, "Powder Blends and Finished Dosage Units—Stratified In-Process Dosage Unit Sampling and Assessment," replaces a withdrawn 1999 guidance on blend uniformity analysis for abbreviated new drug applications (ANDAs). That document faced criticism from the generics industry because it endorsed blend uniformity testing—a scientifically challenging and imprecise exercise—as a routine, quality control for in-process powder mixing, per 21 CFR 211.110(a)(3). Backlash to the ANDA guidance came not only from generic companies, but also from innovators. Researched-based pharmaceutical companies believed that the guidance, if finalized, would lead to an extension of the blend uniformity testing policy to them.

At the same time, PQRI was just starting to come together, and its founders, including PDA, were searching for a project that would impact a large number of firms in the pharmaceutical industry, address a serious regulatory challenge and solve a scientific question. The blend testing issue was a perfect fit.

Several of the members of the original BUWG spoke at the December workshop, elaborating on the science that underpins the final recommendation. For example, Jerome Planchard, Ph.D., Statistical Leader, Patheon, statistically demonstrated how stratified sampling can identify blend sampling errors. If the variance of the blend within a location is significantly larger than that for the dosage form or if the blend mean is significantly different than the dosage form mean, blend sampling error is indicated.

Thomas Garcia, Ph.D., Assistant Director, Regulatory CMC, Pfizer, compared the U.S. Pharmacopeia (USP) content uniformity test with the dosage form stratified testing developed by PQRI and provided in the FDA draft guidance. The USP content uniformity test is to be performed on finished tablets and results are not to be adjusted for weight. The FDA recommendation, on the other hand, includes weight adjustment of the results and is to be performed on in-process (non-coated/packaged) product.

Garcia presented data on a tested batch that demonstrated the equivalency of the two methods. He concluded that "in-process stratified samples for this batch were as sensitive to the lack of uniformity as the random sample of film-coated tablets used to perform the USP test" (see Table 1 for statistical comparison presented by Garcia). The only caveat noted by Garcia was that the in-process sampling "had a slightly broader range of values and a similar RSD value compared to the USP test results." The correlation "must hold for the remaining validation batches," said Garcia, "to justify using the in-process stratified samples as an alternative to the USP test."

The draft defines stratified sampling as: "The process of sampling dosage units at predefined intervals and collecting representative samples from specifically targeted locations in the

Table 1.

Stratified Samples

Use non-weight corrected data from validation batches

Mean: 99.3%
Range: 90–107%
RSD: 3.9%

USP C.U. Test

Random sample of coated tablets tested according to USP test

Mean: 99.2%
Range: 93–104%
RSD:3.8%

compression/filling operation that have the greatest potential to yield extreme highs and lows in test results." If used for in-process monitoring of areas of the process "most responsible for causing finished product variability," writes FDA, the results can help a company develop "a single control procedure to ensure adequate powder mix and uniform content in finished products." The stratified sampling technique for dosage units is discussed in the context of process development (section six of the guidance) and routine testing (section seven).

FDA states that the draft guidance "reflects CDER's effort to incorporate" PQRI's recommendation into regulatory policy. Overall, the draft guidance is intended to help firms:

- Conduct powder blend sampling and analyses.
- Establish initial criteria for stratified sampling of in-process dosage units (before coating/packaging) and evaluate test results.
- Analyze the stratified samples and evaluate data.
- Correlate the stratified sample data with the powder blend data.
- Assess powder mix uniformity.
- Correlate the stratified sample data with the finished dosage unit data and assess uniformity of content.
- Test exhibit and validation batches for adequacy of powder mix.
- Test and evaluate routine manufacturing batches.
- Report the use of stratified sampling in the application.

The CGMP draft guidance is available at: www.fda.gov/cder/guidance/index. The public comment period closes March 8 (docket no. 2003D-0493).

During the PDA-managed workshop, industry participants broke into three small discussion groups to comment on the document. Session moderators compiled numerous scientifically-oriented questions and concerns raised by meeting participants and presented them on the last day of the workshop. A sampling of the issues raised are provided below. The session moderators intend to submit them formally to the FDA docket for the draft guidance. ■

The following is a sampling of the science-based concerns about FDA's draft guidance on stratified sampling raised by industry representatives at the Dec. 4–5 workshop. Session moderators organized the concerns into four categories: process development, validation, routine manufacture, and miscellaneous. All of the concerns raised will be formally submitted to the docket for FDA consideration.

Process Development

- Can you waste portions of a batch that are related to problems (such as material that has segregated at beginning or end of a batch?
- Must you perform an investigation if trends are noted, but stay within acceptance limits?
- At what time do you apply the document during development? At the start of Phase 3? During validation? At 1/10th scale?
- How do you demonstrate sampling bias exists?
- How do you justify increasing the blend sample size beyond 1-3X? Do you have to justify using 1-3X sample sizes?

Validation

- If you know sampling bias is going to be a problem, can you skip blend sampling and automatically default to Stage 2 dosage unit testing?
- The revised flow chart needs to be corrected to reflect the text, to allow the progression to filling/compression as part of the investigation into failed stage 1 blend testing. This investigation could involve the collective analysis of both the blend and dosage unit data.
- Some large blenders are too dangerous or big to sample. Is blend sampling allowed in either mixers, discharge streams, and/or drums or IBCs following discharge? Sampling from drums may disguise hot spots in the mixer.
- Why is there a need to have a correlation between blend and in-process dosage units?
- What does "correlation between blend and dosage unit data" mean? Did we mean compare or correlate?
- In the definition of stratified sampling plans, what qualifies as a significant event?

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Interest Group Session Reports from the 2003 PDA Annual Meeting

At the 2003 PDA Annual Meeting in Atlanta, Georgia, various PDA Interest Groups, Task Forces and Discussion Groups met to review current issues and/or report on their progress. The following groups have submitted reviews of their meetings:

Contract Manufacturing Interest Group

Leader: **Thomas Handel, VP Homeland Security – Pharmaceuticals, Meridian Medical Technology**
E-mail: **tom.handel@meridianmt.com**

The following, pre-selected questions/topics were addressed:

1) "Acquisition of your contractor—what to do, how to prepare for?"

- **Pre-acquisition:** Contracts should be designed for what happens when things go wrong. Determine, in advance, if the contractor should be able to assign the contract, and if so, under what conditions. Carefully define change of control and what is acceptable. Execute a quality agreement and fully detail roles and responsibilities.
- **Post-acquisition**: Read the contract and know your rights. Arrange a meeting with contractor, and if necessary, with the new management. Communicate concerns. Establish a clear transition plan, if necessary.

2) "What to do when things go wrong at a contractor (e.g., warning letter)?"

- **Options: Ignore, stay and wait, or support** (personnel, financial, etc.) the contractor. Most sponsors will want to provide assistance. The time involved with moving sites is too costly, opens regulatory filings and would be expected to be longer than time to implement corrective action at contract site.
- **Contractor will have to manage the offers for assistance** and will have to work with sponsors on product specific resolution.
- Contracts should already be in place which **define roles, rights and responsibilities** of each party.
- **Contract amendments may be necessary** to accommodate specific issues.
- **The key to success is communication** and openness on behalf of contractor and sponsor. Both parties have common goal: resolution and maintaining product flow.

3) "How to manage customers' request to use their own procedures" (Varies by contractor and sponsor.)

- Some contractors use **SOP's** for general facility and process information**. Batch records** are used for product or client-specific information.
- **Contractor needs to document** why client-specific changes were made and justify the unique application of the procedures. Expect that FDA will inspect procedures which are implemented at sponsor request and are not implemented facility-wide.
- **Contractors seem to be open** to reasonable product-specific protocols, but both parties need to be open to the cost implications (development and commercial) which come along with unique procedures.

4) "Point of contacts at contractor and sponsor."

- Most contractors and sponsors have a **single point of contact** who manages the relationship. Discipline-specific communication is still encouraged, but the point of contact is copied on all communication and is responsible for task follow-up.
- Some contractors have developed **internal project management databases** which contain all project-specific information, including resource contact information, milestones, schedule, costs, etc.
- **Clients are copied on all meeting minutes** and are instrumental in project management.
- **Clients typically do not have direct access** to internal project management databases. Printouts are provided by fax/ e-mail.

5) "Quality Agreements—resolution of templates ... client vs. contractor templates."

- Depends on the **elements/details** of each template.
- Depending on the thoroughness of the contractor's template, it is logical to **allow them to use their template** with minor modifications. Consistency in Quality Agreements should equate to a higher level of compliance.
- **"Legal" should be involved** in late stage, after key stakeholders agree on major content.

6) "Early stage products (IND, tox studies, etc.)"

- **Industry capacity** available? Yes. Key challenge is that many of the early stage companies do not appreciate the expense involved with parenteral development and manufacturing.

- Sponsor must decide whether **GMP vs. GLP** is necessary.
- Some contractors are **allocating space** within commercial facilities.
- **Accounting process** should be accommodating and allow different overhead structure for development products as opposed to commercial products.

7) "Project Bioshield"

- **No apparent impact** on capacity at this time.
- For **risk management** reasons, the federal government seems to be awarding redundant contracts for development of some products, possibly using up to three distinct contract sites.
- **RFQ's and grant money** is flowing.
- **Timelines** are very aggressive.

8) "Bio-Generics"

- Starting to see development of **bio-generics outside the U.S.**
- **FDA** does not yet have the systems or policies to handle bio-generics. How to determine equivalency? Contractors may be vary wary … how to bring on bio-generics and not damage relationships with legacy clients.
- Contractors may find themselves in **litigation over proprietary**, highly-patented processes.
- Potentially **volatile issue** for the outsourcing industry.

Computer Validation Modernization Discussion Group

Leader: **George Grigonis, Sr. Consultant, QA Edge**
E-mail: **grigonis@comcast.net**

Greater than 99% of all executable code operating in businesses today is store-bought. Our computing solutions were acquired and assembled from marketplace components. Little if any was actually the result of an "act of creation" by our systems development organizations. The reality is that we largely implement computing solutions through actions that can be categorized as an "act of composition." The IT horizon today is even more exotic in that many companies are beginning to outsource their business computing needs (application service providers and utility computing) to various services that are even more creative in assembling business solutions. As we adopt these new technologies and concepts, we face their attendant validation issues at a pace that renders applying "classic validation" a nearly impossible chore. The bottom line is: Computer validation concepts are now stressed to the breaking point. Solving this problem requires a way of thinking not predicated on traditional 'waterfall' approaches.

This Interest Group session introduced a PDA initiative to modernize computer validation (CV) thinking. The initiative is to evolve CV from a "document-centric" activity to a "process-centric" activity, harmonizing compliance expectations with business computing needs and utilizing and endorsing state-of-the art IT concepts and tools that define current "good system practice" (cGSP).

The facilitated discussion that followed was very supportive of the new ideas in this regard. Representatives from both suppliers and regulated establishments confirmed the difficulties in applying classical CV thinking to emerging IT concepts and new advancements in computing technologies. Applying cGSP's prescriptively for CV—as opposed to descriptive, document-centric CV—can potentially facilitate agility in corporate behaviors regarding computing technologies. This would enable the adoption of new technological advancements rather than disabling adoption.

The general consensus was to proceed with establishing academic relations with Carnegie Mellon University's Software Engineering Institute (SEI) for: 1) training and education in modern methods, beginning with COTS based systems; and 2) a study of any original GSP work by PDA, similar to what was done for TR-32.

Next steps should be: 1) broader sampling of PDA membership on cGSP initiative, 2) second meeting with SEI and the PDA Training and Research Institute on cGSP courseware, and (3) investigation of a Task Force to establish cGSP curriculum as a PDA Training and Research Institute offering.

Part 11 Compliance Alternative Discussion Group

Leader: **George Grigonis, Sr. Consultant, QA Edge**
E-mail: **grigonis@comcast.net**

In September, the U.S. FDA issued a final industry guidance on 21 CFR Part 11. The guidance has somewhat helped industry better understand language in the initial draft document, released for comment early in 2003. In other respects, initial draft language has not changed significantly enough to promote a clear understanding of the Agency's new interpretation of Part 11. On some issues, open

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Recent Sci-Tech Discussions

"G-Radiation" & "Increased Usage Time of Eye Drops After Opening"

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.

This month's posting...

Question 1

What is the main reason that g-radiation is not (widely?) used for pharmaceutical products (injectable)?

In my company we have tested g-radiation for three batches of an injectable product which we already produce using final sterilization and the results for the sterility & LAL tests were OK. The chemical stability of those batches (same methods as with the finally sterilized product already licensed) seems to be proper so far. So, I tend to believe that if we can also demonstrate a 10^-6 SAL we should be able to propose the change of the sterilization method and feel pretty confident about the product. However, I have not ever seen an injectable product sterilized with this method and this gives me the feeling that I'm missing something major about g-radiation that everybody else knows except for me :-) ...am I ?

What is your professional opinion?

Response 1

The sterilizing effect of g-radiation is based on ionization of molecules. G-radiation for solids and for inorganic solutions may be O.K. Organic solutions change the purity, depending on the concentration and type of the compound.

Response 2

G-radiation is not heard off being used in pharmaceutical products. But if all the required studies are flawless why not use it? Best way out is to get in touch with your local drug controlling authority, produce your findings and see what they have to say/offer. This should be your best way out.

Response 3

It is my understanding that from a product perspective g-radiation will perform the task required. However, from a safety perspective g-radiation is not ideal. This is due to the fact that g-radiation is the most penetrating of the radiation types (alpha<beta<gamma) and exposure can have severe health impacts, the least of which is carcinogenic. As well large masses are required to stop or reduce gamma radiation, this creates certain design challenges.

Response 4

The issue is not so much can a drug be sterilized but what the old drug has become in the process. After irradiation, the old drug is a new drug and you are back to square one. I cannot cite a CFR reference but I once worked on an NDA for an irradiated drug. It took five years to clear the agency and it was only a topical. They had a million questions (approximately).

Response 5

Gamma is less used than would appear obvious because:

a) in liquid solutions, it generates a free radical which accelerates product decomposition
b) it causes clear glass bottles to turn amber
c) it costs more than other methods of sterilization
d) for water for injection, it causes release of the free radical, causing the WFI not to meet WFOI pharmacopoeal monograph specifications

Response 6

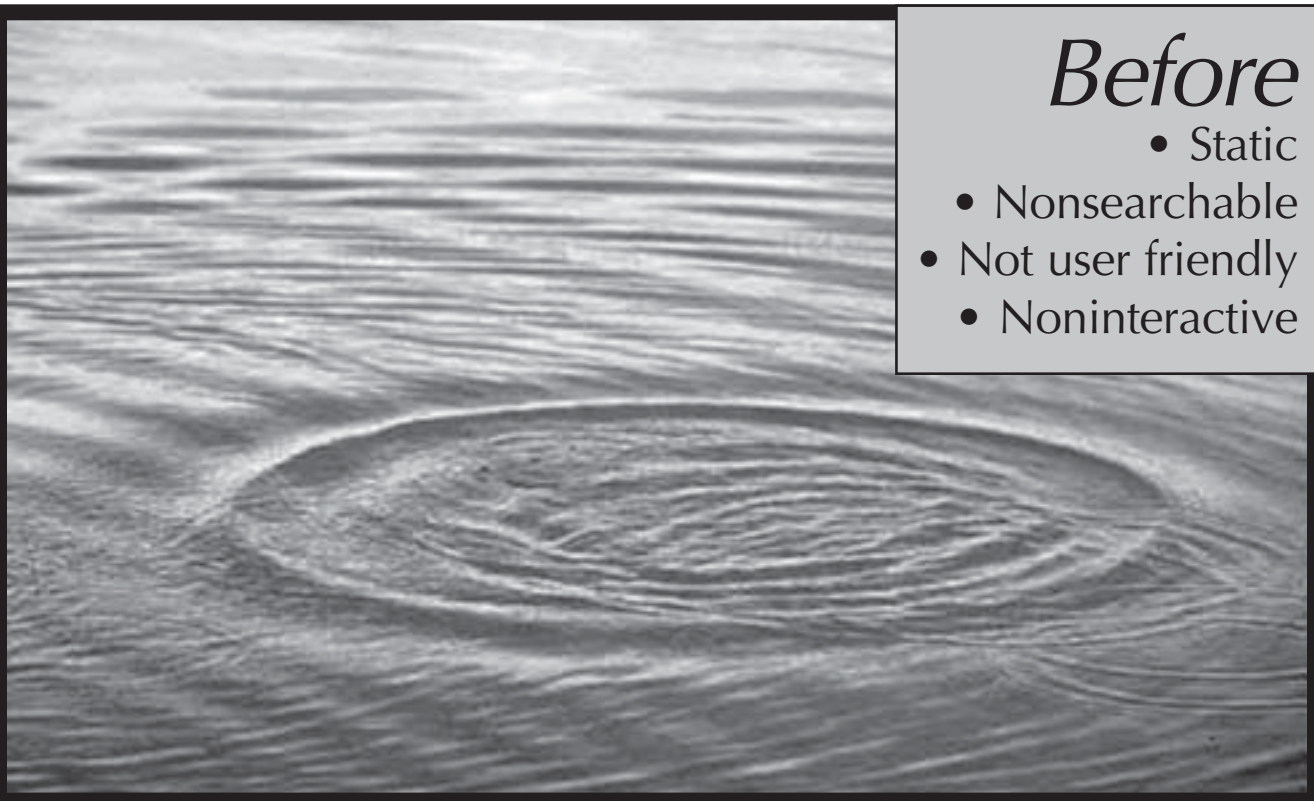
Steam sterilization is considered the most effective and efficient sterilization procedure for injectable products where as gamma radiation is used mainly for the sterilization of heat sensitive materials or products (using temperatures of generally less that 60 degree centigrade) and is permissible only when the absence of deleterious effects on the product has been confirmed experimentally.

Liquid pharmaceuticals are more difficult to sterilize by gamma radiation because of the potential effect of the radiation on the vehicle system (free radical formation) as well as the drug.

Response 7

The impurity method for our licensed (terminal sterilization) injectable product consists of an HPLC test where only one known impurity is present. Assuming that I need to test for impurities the "new" (sterilized with g-radiation) product,

continues on page 14



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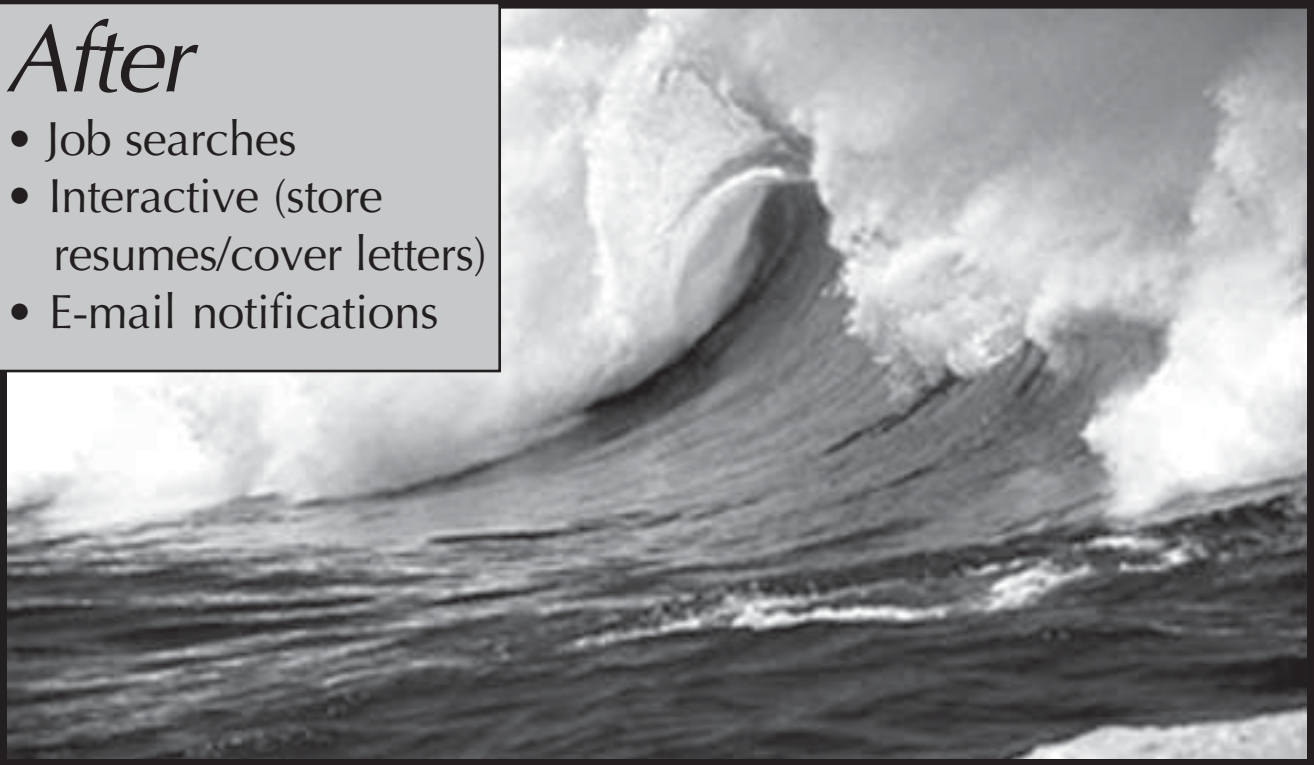

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Recent Sci-Tech Discussions, from page 12

does this method of chemical stability cover us? I understand that the "old" and "new" HPLC profiles should be compared on a statistical basis but how can I be sure that the same HPLC method would be able to detect some potential new impurity? I mean, what if HPLC is not able to even identify (let alone to calculate the percentage) of this unknown impurity? Is there any procedure described for such cases (like a CFR statement or any guideline)?

Response 8

There are two approaches coming to my mind:

1. Risk-assessment: Radiation makes smaller molecules out of the larger molecules; re-configures structures and may cause dimerization of organic molecules. All these changes should change the HPLC-retention time of the product. Under extreme conditions will the impurity elute in the injection peak or outside the chromatographic range. This is possible but not likely. There is limited control by comparing the potency of the radiated and the non radiated materials of the same batch.
2. Apply a 10 fold or 100 fold radiation doses and extrapolate back to the actual radiation dose (forced degradation). It can be concluded, that the changes are less than 1% if potency and purity remain the same after 100 fold radiation. As an example: less than 0.001% impurity was formed, if the potency remains 98.2% after a 100 fold radiation dose.

Question 2

We want to increase usage time of eye drops after opening. What should be the parameters that should be included in the study? I think preservative efficacy should be included. How should we plan the study?

Response 1

The data package should, as a very minimum, include preservative efficacy testing using product near the end of its shelf life and in addition suitable in-use stability testing regimes. Microbiological and chemical stability should be followed. You might find it interesting to read TGA News back issues for advice from the Australian authorities on how to design a repeated challenge preservative challenge test. There is also a relevant article in the latest issue of the European Journal of Parenteral Science and Technology (October 2003).

Response 2

In general, it is good to avoid extending usage time. But if you must:

Probably the most critical evaluation wills a simulated in-use test. This is done as follows:

a) Open and take product from the bottle as per label directions.
b) This should be done as often as indicated in label use directions.
c) Keep doing this until the end of the proposed new and extended usage period.
d) Test the product at the end of your current usage period and the new, extended usage product.
e) Minimum test: drug content, preservative content, bacterial count
f) (bioburden) and preservative effectiveness.

You need to have enough preservative so that there is sufficient antibacterial activity at the lowest concentration in the product at the end of shelf life.

You need to do the in-use test on initial product, and a sample near end of shelf life. You may also want to do an intermediate time point.

Alternately, study the initial product sample and make a commitment to continue sampling periodically until end of shelf life. I highly recommend that you write a protocol that is approved through your company review system. Also, if you can, review it with appropriate regulatory agency personnel. ■

Interest Group Session Reports, from page 11

questions remain unanswered. Certainly, answers to these questions may only be achieved through experiences and enforcement discretion. While industry and FDA continue to work on a common understanding of the issues, the PDA-ISPE *Good Electronic Records Management* (GERM) documents (Parts 1 and 2) and the pending "Models" document (Part 3 of GERM) can serve as a universal road map toward the compliant paperless operations.

Attendees were introduced to an alternative compliance approach through visualizing the record lifecycle in contrast to technology approaches that focus on computing tools. Principles from GERM Part 1 ("Electronic Information Assurance for the Regulated Industry—Guide to Current Good Practice for Electronic Records and Signatures") were applied to understanding and mitigating information assurance risk during record life. A framework for information assurance that partitions record life cycle segments and activity sets was presented as a primer for a defined process in managing records and technology tools.

Finally the pending "Models" document was introduced. The document will show how modern methods for implementing and sustaining computing environments can enable information assurance objectives.

Examples provided by attendees of this Interest Group forum demonstrated how GERM principles, the "Models" document, and the information assurance framework presented can provide a simple and managed approach to Part 11. This approach is not technology-centric but practical in establishing a good faith effort to comply with regulations, a 2 for 1.

Next step: Investigate a PDA Task Group to further define the organizational activity sets that put the GERM documents to work—the basis for a real electronic records management process that is measurable and capable. ■

PDA Interest Group Leaders

Biotechnology
Frank Matarrese
Chiron Corporation
4560 Horton Street
Emeryville, CA 94608
Tel: +1 (510) 923-3128
Fax: +1 (510) 923-3375
E-mail: frank_matarrese@chiron.com

Computer Systems
Barbara L. Meserve
The Hollis Group Inc.
Station Square Two #109
Paoli, PA 19301
Tel: +1 (610) 889-7350
Fax: +1 (610) 296-2339
E-mail: bmeserve@acculogics-usa.com

Contract Manufacturing
Thomas Handel
Meridian Medical Technology
10240 Old Columbia Road
Columbia, MD 21046
Tel: +1 (443) 259-7870
Fax: +1 (443) 259-7871
E-mail: Tom.Handel@meridianmt.com

Drug–Device Delivery Systems
Raymond A. Pritchard
Alkermes, Inc.
88 Sidney Street
Cambridge, MA 02139
Tel: +1 (617) 250-1621
Fax: +1 (617) 494-5504
E-mail: ray.pritchard@alkermes.com

Filtration
Jack Cole
Jack Cole Associates
115 Turtle Cove Lane
Huntington, NY 11743
Tel: +1 (631) 424-3658
Fax: +1 (631) 424-3658
E-mail: jvcole@aol.com

GMP Purchasing
Nancy M. Kochevar
Amgen, Inc.
MS 9-1-E
One Amgen Center
Thousand Oaks, CA 91320-1799
Tel: +1 (805) 447-4813
Fax: +1 (805) 447-1904
E-mail: nancyk@amgen.com

Inspection Trends/ Regulatory Affairs
Robert L. Dana
Elkhorn Associates Inc.
4828 Patrick Place
Liverpool, NY 13088
Tel: +1 (315) 457-3242
Fax: +1 (315) 451-7363
E-mail: elkhornassoc1@aol.com

Isolation Technology
Dimitri P. Wirchansky
Jacobs Engineering Group, Inc.
Three Tower Bridge
Two Ash Street, Ste. 3000
Conshohocken, PA 19428
Tel: +1 (610) 567-4452
Fax: +1 (610) 238-1100
E-mail: dimitri.wirchansky@jacobs.com

Lyophilization
Edward H. Trappler
Lyophilization Techology
30 Indian Drive
Ivyland, PA 18974
Tel: +1 (215) 396-8373
Fax: +1 (215) 396-8375
E-mail: frzdry@lyo-t.com

Microbiology/ Environmental Monitoring
Jeanne E. Moldenhauer, Ph.D.
Vectech Pharmaceutical Consulting, Inc.
16100 W. Port Clinton Rd.
Lincolnshire, IL 60069
Tel: +1 (847) 478-1439
Fax: +1 (847) 478-1745
E-mail: jeannemoldenhauer@yahoo.com

Ophthalmics
Chris Danford
Alcon Laboratories Inc.
Mail Code Q-108
6201 South Freeway
Ft. Worth, TX 76134
Tel: +1 (817) 551-4014
Fax: +1 (817) 568-7004
E-mail: chris.danford@alconlabs.com

Packaging Science
Edward J. Smith, Ph.D.
Wyeth Pharmaceuticals
2100 Renaissance Blvd.
King of Prussia, PA 19406
Tel: +1 (610) 313-4338
Fax: +1 (610) 313-4644
E-mail: smithej@wyeth.com

Pharmaceutical Water
Theodore H. Meltzer, Ph.D.
Capitola Consulting Co.
8103 Hampden Lane
Bethesda, MD 20814-1124
Tel: +1 (301) 986-8640
Fax: +1 (301) 986-9085
E-mail: theodorehmeltzer@hotmail.com

Production and Engineering
Frank Bing
Abbott Laboratories
D-968/AP4B
100 Abbott Park Road
Abbott Park, IL 60064-6076
Tel: +1 (847) 937-8191
Fax: +1 (847) 938-6569
E-mail: frank.bing@abbott.com

Quality Assurance/ Quality Control
Don E. Elinski
Johnson & Johnson Merck
1734 Valette Drive
Lancaster, PA 17602
Tel: +1 (717) 207-3858
Fax: +1 (717) 207-3556
E-mail: elinski@aol.com

Solid Dosage Forms
Pedro J. Jimenez, Ph.D.
Eli Lilly & Company
Eli Lilly Corporate Center
Indianapolis, IN 46285
Tel: +1 (317) 277-3618
Fax: +1 (317) 276-3618
E-mail: jimenez_pedro_j@lilly.com

Stability
Rafik H. Bishara, Ph.D
Eli Lilly & Company
DC 2623 Eli Lilly Corporate Center
Indianapolis, IN 46285
Tel: +1 (317) 276-4116
Fax: +1 (317) 276-1838
E-mail: rhb@lilly.com

Training
Thomas W. Wilkin, Ed.D.
Schering-Plough Corp.
M/S R-40
2000 Galloping Hill Road
Kenilworth, NJ 07083-1328
Tel: +1 (908) 298-5213
Fax: +1 (908) 298-5120
E-mail: thomas.wilkin@spcorp.com

Vaccines
Frank S. Kohn, Ph.D.
FSK Associate
1899 North Twins Lake Rd.
Manson, IA 50563
Tel: +1 (712) 297-8074
Fax: +1 (712) 297-8074
E-mail: fsk@lowatelecom.net

Validation
Bohdan M. Ferenc
Qualification Services
116 Route 10
Succasunna, NJ 07876
Tel: +1 (973) 927-9823
Fax: +1 (973) 927-9823
E-mail: biferenc@aol.com

Visual Inspection of Parenterals
John G. Shabushnig, Ph.D.
Pfizer Inc.
7171 Portage Road
MS 2043-41-104
Kalamazoo, MI 49001-0199
Tel: +1 (269) 833-8906
Fax: +1 (616) 833-9987
E-mail: john.g.shabushnig@pfizer.com

FDA Draft CP Guidance: "Excellent Beginning"

December 4, 2003

US Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref.: [DOCID: 03D-0385, CBER200338]
Guidance for Industry—Comparability Protocols—Protein Drug Products and Biological Products—Chemistry, Manufacturing and Controls Information; Draft Guidance—September 2003

Dear Sir/Madam:

PDA is pleased to provide these comments on the Draft Guidance for Industry on Comparability Protocols- Protein Drug Products and Biological Products - Chemistry, Manufacturing, and Controls Information. PDA is an international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical manufacturing and quality.

The comparability protocol represents a potentially useful mechanism to reduce the regulatory burden in keeping with the principles of the Food and Drug Administration Modernization Act (FDAMA) of 1997 and the Prescription Drug User Fee Act (PDUFA) of 1997 and its 2002 renewal. Though useful, the proposed Comparability Protocol guidance, as written, does not fully realize the objective of the FDAMA to ease the regulatory burden of post-approval changes. PDA believes that the clarifications, modifications, and scope redefinition proposed below could make the comparability protocol a more useful tool for the industry and the FDA.

Our comments were prepared by a committee of experts in this field. The committee believes that the guidance is an excellent beginning in the development of meaningful guidance on comparability protocols. Detailed comments are provided in the enclosed table. Comments are identified by section and line number corresponding to the PDF version of the Draft Guidance available on the FDA website. The following is a brief list of some of the major conclusions reached by the PDA review team:

1. The current draft guidance could be greatly enhanced by a companion guidance document and/or an interactive website that provides specific examples of when comparability protocols can be applied, along with detailed test documentation requirements. PDA suggests that FDA develop other mechanism(s) for sharing of FDA/industry experiences with the execution of successful comparability protocols. This information could include a listing of examples of changes to which comparability protocols could be applied, as well as details regarding the necessary content of such protocols. PDA has enclosed with this letter, 3 examples of changes, each with a listing of the type of content that should be considered for the relevant comparability protocol. PDA feels that the exchange of this type of information, as a separate listing or even as an interactive web site, would greatly facilitate the sponsor compilation and FDA review of comparability protocols.

2. The ability to "bundle" the same or related changes for one or multiple products should be explicitly provided. We acknowledge the Agencies reluctance to allow for the provision of general protocols for multiple, unrelated changes to a single product; however we encourage the Agency to re-consider this concept as it may apply to the use of a general protocol that specifies procedures and testing that are common to more than one change in a unit operation. The protocol could be reviewed and approved prior to implementation of the first intended change covered and then subsequent changes could also be covered under such a protocol if the procedures and testing are applicable and no other changes have been introduced in the interim.

3. The inclusion of information related to Drug Master Filings (DMF) is of concern to us. Previously, such information was submitted by the DMF Holder and reviewed, but not subject to approval. It is currently not clear to PDA what mechanism(s), if any, are available to signal to the DMF Holder and to each of the specific Authorized Users of the information, that a Comparability Protocol has been received, reviewed, and approved by the Agency. However, PDA believes that this could be a useful tool for both the DMF holder and the Authorized Users of the information if

continues on page 18

PDA Comments on FDA Draft CP Guidance, from page 17

specific Guidance is made available to the industry; either as a part of this Guidance or that for Master Files.

4. Inspection timing should be considered in the chronology of events between the submission of the original Comparability Protocol and the eventual supplement that provides the resultant data. The Guidance should be more clear and should provide that the Prior Approval Supplement which contains the Comparability Protocol may be the trigger for scheduling any necessary Pre-Approval inspections. In this case, the sponsor's Comparability Protocol should be accompanied by a projected manufacturing schedule that illustrates when production of supportive batches may occur and when resultant data will be available so that the Agency reviewers, inspectors and sponsor can agree on the optimal timing for the PAI. PAI's should be scheduled by the Agency so as to ensure timely implementation of the change commensurate with the eventual reporting category for the supplement that contains the resultant data. Furthermore, the Guidance should more clearly state whether FDA would permit a supplement in a non-prior-approval reporting category for a change to a new site that has not been inspected or does not have a satisfactory CGMP inspection, because an inspection is usually prompted by, or requested via, the PA supplement process.

5. Use of Comparability Protocols for Combination Products. When feasible, guidance regarding the mechanism(s) and data expectations for making changes to combination products should be made available to the industry. Information regarding the use of Comparability Protocols for changes to be made to combination products could be captured in such a guidance. Alternatively, the use of Comparability Protocols in this regard could also be captured in a companion Guidance or as an update to the two Guidances on Comparability Protocols.

More specific comments are in the attachment. If you have any questions regarding our comments, or how we may assist with further development of the Guidance, please contact me.

Sincerely,

William Stoedter, RAC
PDA Director of Regulatory Affairs
301-656-5900 ext. 121
Stoedter@pda.org
www.pda.org

Enclosures: Comment Grid on Comparability Protocols, Protein Drug Products and Biological Products, Chemistry, Manufacturing and Controls Information; Draft Guidance.
Examples of Data Set Requirements for Common Changes.

Go to www.pda.org to see the full comment grid.

Regulatory Briefs

Key Regulatory Dates

Jan. 31–Deadline for public comment on **EMEA** Note for Guidance on Assessing the Risk for Virus Transmission—New Chapter 6 of the Note for Guidance on Plasma-Derived Medicinal Products (CPMP/BWP/269/95)

March 8–Deadline for public comment on **FDA** CDER Draft Guidance on Powder Blends and Finished Dosage Units—Stratified In-Process Dosage Unit Sampling and Assessment.

June 8–**FDA** E-Labeling Rule becomes effective.

U.S. FDA

FDA and ASTM International have developed a new ASTM committee for the use of process analytical technologies (PAT) in the pharmaceutical industry. Ajaz Hussain, Ph.D., Deputy Director of the Office of Pharmaceutical Science, FDA Center for Drug Evaluation and Research (CDER) announced the new committee at the PDA-managed workshop on the PQRI BUWG proposal and FDA draft guidance, Dec. 5. Noting that he had been at ASTM headquarters in Philadelphia earlier in the week to finalize plans, Hussain explained that the new committee will provides a venue for the development of scientific and engineering standards that can be used by the pharmaceutical/biopharmaceutical industry worldwide. By using ASTM as a vehicle to devise these standards, asserted Hussain, industry and regulators can circumvent an International Conference on Harmonization-type process in the future. Through ASTM, the pharmaceutical industry sectors can "actually build consensus standards which are international standards." He advised industry to "pay attention" because the formation of the committee is a "major milestone" and a "dramatic shift" that will positively impact the industry for years to come.

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PQRI's Science-based BU Proposal, from page 9

Routine Manufacture

- If you can't get a correlation between cores and coated tablets, and generate a significant body of data, at some point could you reduce in-process testing?
- Regarding the implementation of switching rules, the data from a previous batch may not be available prior to the manufacture of the next batch in the campaign. This could impact the number of tablets that you have to assay, if you have to switch from standard to marginal testing.
- How do we apply the recommendation to approved products that we no longer do blend testing during routine manufacture? Do we automatically default to MCM?
- Is it OK to use existing data to determine readily vs. marginally passes for products in late stage development or already approved?

Miscellaneous

- Provide clarity in the definition of exhibit batches, and clarify what is and isn't included.
- How early into development are batches considered to be exhibit batches? Should they be limited to full-scale batches? Only batches where the final commercial formulation and process are defined?
- Implementation of the switching rules could be difficult due to existing SOPs and computer systems.
- How/when are office and field inspectors going to be trained?
- How does the rest of the world feel about the guidance document? What (if any) venues are available for them to comment on the document?
- Are we expected to apply the recommendation to clinical batches? If so, at what stage?
- For multi-layer products, you can't determine the weight of each layer (for weight correction).
- What is the impact of batch size on the use of the approach?
- For common blends, how do you handle situations where one strength complies with the criteria, but another strength does not?
- If distribution is not normal (skewed), the criteria become harder to pass.
- If content uniformity of a product can be demonstrated through weight variation, do we have to apply this approach to it?
- Do we have to use this approach if we are using PAT to monitor processes?
- For NDA/ANDA, when can you stop blend testing and start stratified sampling? Compliance versus reviewers.
- Where does the blend have to be uniform? In the blender? Bins/drums? Hoppers? Feed frame? When tablets exit the press?
- Cores adequate weight corrected; finished product adequate not weight corrected?
- Timing of implementation for old products? How do you implement this?
- New ribbon blenders are more efficient. Do you still have to sample from 20 locations?

Regulatory Briefs, from page 19

FDA Publishes New Requirements for E-Labeling of Drug and Biologics Applications—FDA announced on Dec. 9 a final rule requiring the electronic submission of labeling for review with new and abbreviated new drug applications and biologics applications (NDAs/ANDAs/BLAs). FDA asserts that the new rule is another step in its efforts to use modern information technology to help inform the public and improve patient safety.

Specifically, sponsors are now required to submit to FDA in electronic format the content of the package insert or professional labeling, including all text, tables, and figures. Sponsor should use the electronic format described in the Agency's guidance on electronic submissions. This standard format will allow FDA to process, review, archive, and distribute the information publicly. In turn, electronic labeling information will improve the drug labeling review process and accelerate the approval and public dissemination of labeling changes—getting important, up-to-date information on medications to doctors and patients more quickly.

"Changes such as this one can make it easier and quicker to ensure that drugs and other products have appropriate labeling information for doctors and patients alike," declares Tommy Thompson, Secretary, U.S. Department of Health and Human Services. "Across the department, we are committed to putting modern information technologies to work to improve the way we do business and to promote higher-quality care for patients." The new e-labeling requirement represents an important addition to Secretary Thompson's "e-health" initiative.

"Using modern information technology to improve public health is no longer optional at FDA," explains FDA Commissioner Mark B. McClellan, M.D., Ph.D. "With mandatory electronic labeling, FDA will be better able to ensure that information provided by product's sponsor is accurate, and to communicate information that doctors and patients need in order to use a product. And FDA will be able to get updated information on risks and benefits to the public more quickly as well."

Until now, industry could choose not to make electronic submissions. This new regulation, however, makes e-submissions mandatory. FDA maintains that the requirement represents an important step in FDA's larger initiatives involving electronic medical records and electronic health information systems. FDA is currently collaborating with other federal agencies such as the National Library of Medicine, the pharmaceutical industry, and health care information providers on the "DailyMed" project, intended to promote patient safety through user-friendly, electronically accessible medication information.

This final rule is intended to supplement existing requirements which stipulate that copies of the label and labeling and specimens of enclosures be submitted. For example, copies of the package insert must still be submitted to FDA in an NDA, and copies submitted to the agency must be identical to the label and labeling and specimens of enclosures that appear in the package insert, on the immediate container, or in any other form distributed. As was the case before this new rule, these copies may be submitted electronically or on paper. FDA's ability to quickly identify changes in the different versions of labeling, and then make the necessary corrections, would minimize public exposure to any inappropriate labeling.

The rule goes into effect June 4.

FDA Releases New and Revised ICH Guidances on Stability Testing of New Drug Substances and Products—FDA recently published the second revision of the International Conference on Harmonization (ICH) guidance, Q1A—"Stability Testing of New Drug Substances and Products," first published in September 1994 and revised in August 2001. The purpose of this revision is to harmonize the intermediate storage condition for zones I and II with the long-term condition for zones III and IV recommended in the ICH guidance Q1F—"Stability Data Package for Registration Applications in Climatic Zones III and IV," which FDA also published recently.

Q1A (R2) is intended to define what stability data package for a new drug substance or drug product is sufficient for a registration application within the three ICH regions, climatic zones I or II. It does not seek to address the testing for registration in or export to other areas of the world. The guidance exemplifies the core stability data package for new drug substances and products, but leaves sufficient flexibility to encompass the variety of different practical situations that may be encountered due to specific scientific considerations and characteristics of the materials being evaluated. Alternative approaches can be used when there are scientifically justifiable reasons. Q1A (R2) can be found at: www.fda.gov/cder/guidance/5635fnl.doc.

Q1F broadens the applicability of Q1A by outlining the stability data package for registering new drug substances or drug products in countries residing in climatic zones III and IV. Q1F can be found at: http://www.fda.gov/cder/guidance/5532fnl.doc. ■

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Veltek Associates, Inc.
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PDA Chapter Focus: Central European Chapter

The Central European Chapter unites pharmaceutical and biopharmaceutical industry professionals in many countries, both large and small, including Germany, Switzerland, and Austria. While all PDA chapters are faced with the never-ending task of figuring out how to serve their members, the Central European Chapter (CEC) faces particular challenges due to the diversity of cultures, languages and regulatory traditions brought to it by its cross-border membership.

The CEC is adeptly lead by a well-qualified group of professionals: **President Erich Sturzenegger**, Contract Manufacturing Head, Novartis Pharma; **VP Georg Roessling**, Ph.D., Drug Delivery Systems, Schering (Germany); **Secretary Roger Seiler**, Product Manager, Sartorius (Switzerland); **Treasurer Carlo Voellmy**, Production Launch Manager, Novartis (Switzerland); and **interest group liaison Alexandra Schlicker**, Ph.D., lab lead—sterile dosage forms, Hoffmann-La Roche.

It is appropriate that the PDA Central European Chapter is headquartered in Basel, since the city serves as the hub of Switzerland's pharmaceutical industry, one of Europe's oldest and most innovative. It grew out of the chemical industry, which had settled in Basel by the sixteenth century. By the mid-1990's companies like Geigy, Ciba, Roche and Sandoz—all operating in Basel—were poised for rapid development and expansion. The ensuing period of growth resulted in the opening of plants by these firms in plants around the world. The pharmaceutical industry continues to be an important employer in Switzerland, with almost 28,000 employees concentrated mostly in the Basel region where 50 firms currently operate. Today, the Swiss pharmaceutical industry is dominated by multinational giants Novartis, Roche and Serono International.

Bernard Kronenberg, Executive Director, Bakrona Basel, following conversations with Clarence Kemper, Ph.D., industry consultant, formerly with KMI, assembled a group of professionals in the region to form the CEC. Joining Kronenberg and current officers Voellmy and Roessling in 1996 at the chapter's inaugural meeting were Hiltrud Horn, consultant, Horn Pharmaceutical Consulting (Germany), Finlay Skinner, consultant, Finlay Pharma-Assist (Switzerland), and Klaus Haberer, Compliance Advisor, Geschaeftsfuehrer (Germany).

The need for a PDA chapter in Switzerland became evident when the U.S. FDA began its foreign inspection program in the early 1990's. The Swiss drug industry experienced a GMP shockwave when the FDA field investigators made their first round. Investigator concerns with documentation and record keeping—a focus of the U.S. CGMPs—forced the industry in Switzerland and its neighboring companies to seek expertise regarding FDA expectations. Basel became a center of this activity.

PDA was a natural and reliable source for the companies in this region. In 1992, PDA held its first meeting in Europe—the PDA International Congress, Courses and Tabletop Exhibition—in Basel in 1992. The International Congress was so successful, it became an annual event, with its location alternating each year between Basel and other important cities in the region. The 2004 is scheduled for Basel in February (*see cover*). (Sturzenegger also co-chairs the Basel Congress.)

Firmly established by 1998, the Central European Chapter was looking for support from PDA for it ongoing efforts to serve the chapter membership and spread the presence of PDA to the European community at large. CEC's request for help prompted former PDA president Edmund Fry (currently, VP-Compliance, IVAX) to create the PDA European Headquarters to oversee all of PDA's activities and programs in Europe. James Lyda, former PDA VP (now Managing Director of European Operations, KMI/Parexel) guided the European Headquarters during its critical, early years. Today, Gautam Maitra manages the office. One of his most important responsibilities is to work with the CEC and its leaders to plan new events and promote PDA's science, technology and regulatory activities.

Besides the PDA International Congress, CEC is involved with planning other activities for 2004. On **March 29**, the chapter is sponsoring a one-day forum "Steam Sterilization, Filtration, and the FDA Aseptic Processing Draft Guideline." The final program for this event can be found on the PDA Web site in January. The chapter also is planning an aseptic processing course for **September**. The Chapter is in the exploratory stage of planning a potential forum on visual inspection for parenteral products to be held sometime at the end of 2004, possibly in Berlin, Germany. ■

—KiKi Coffman, Gautam Maitra and Walter Morris

For more information about the Central European Chapter, please visit its Web site at **www.pda.org/chapters/CenEurope/contact.html**.

More information on this and other PDA chapters is available in the *PDA Chapter News* (the association's monthly, electronic communication for members specifically targeted towards those active in our chapters), at: **www.pda.org/chapters/index.html**.

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.

Europe & Middle East

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

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

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

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

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 (847) 564-8181 x263
E-mail: PDAMidwest@northviewlabs.com

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

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

Pacific Rim

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

Japan Chapter
Contact: Hiroshi Harada
Tel: +81-3-3815-1681
Fax: +81-3-3815-1691
E-mail: van@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
Wyeth Pharmaceuticals
Tel: +65-6415-2000
Fax: +65-6415-2008
E-mail: Prasadk@labs.wyeth.com

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

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Make the Most of Your PDA Membership

Volunteer with a Chapter!

Chapters help members enhance leadership skills, expand networking opportunities, and offer the potential to influence outcomes and industry standards.

Volunteer activities within one of PDA's 20 regional chapters can take on many forms. From service on a chapter board to simply attending a chapter event and networking with new or student members, we know that members will find volunteer positions to fit individual needs and time constraints. While chapters usually have a central area, PDA members anywhere in the chapter's overall region are encouraged to become involved.

By volunteering as a PDA Chapter leader, PDA members can hone their leadership and management skills. These skills are transferable to members' own organizations or other volunteer activities. Involvement in a PDA chapter also can expand networking opportunities, exposing involved members to peers and industry leaders in a more meaningful way.

Chapters have different types of activities, categorized as high, medium, and low, depending on the level of responsibility involved. The following are brief examples of some of these tasks:

High-level Tasks

- Serve as publisher for an issue of the chapter newsletter
- Help plan future meetings and events with the chapter
- Spearhead a Student Day or Career Fair, where students are able to talk to companies and associations within the industry
- Represent the chapter at PDA events

Medium-level Tasks

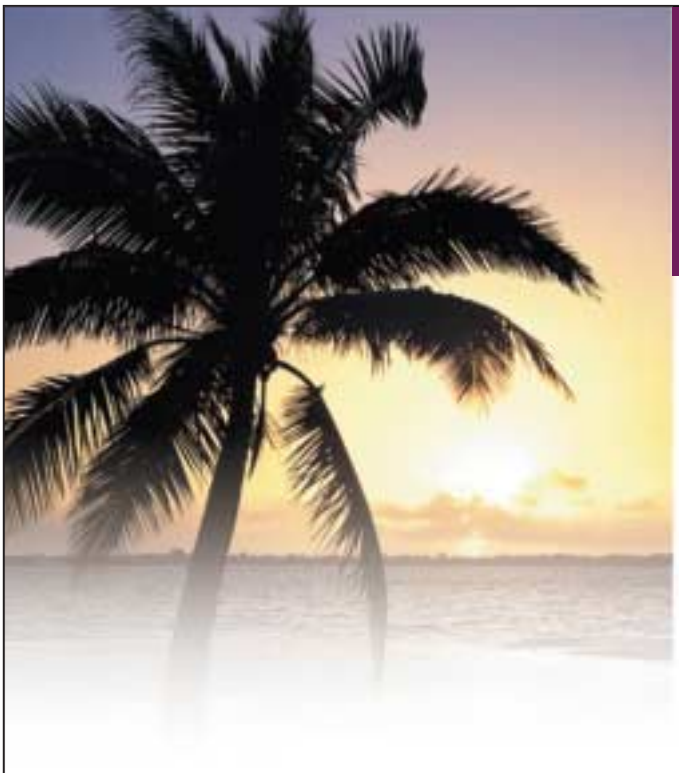
- Write one article about an upcoming chapter event.
- Give a presentation to university and collegiate programs to gain new student members.
- Call 20 prospective members and invite them to a program.
- Solicit sponsor to pay for chapter social event or dinner meeting.

Low-level Tasks

- Take photos at one chapter event.
- Welcome and orient a new or first-time attendee at a monthly program.
- Work registration for an event.
- Recruit three attendees for an upcoming PDA event.

To become involved in your regional chapter or to start one yourself, contact KiKi Coffman, Chapter Coordinator, at coffman@pda.org. PDA members are encouraged to contact their regional chapter directly for more specific information (see p. 23 for contact information). ■

—KiKi Coffman



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This March, PDA and CleanRooms Group are teaming to bring the pharmaceutical manufacturing and contamination control communities the science, technology and regulatory event of the year.

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See the latest state-of-the-art tools and technologies for pharmaceutical manufacturing and contamination control. Exchange ideas and success stories with a high-level group of professionals and management executives all interested in pharmaceutical, biopharmaceutical and contamination control issues.

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M

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Professional Interest (check all that apply)

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- ❑ Biotechnology
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- ❑ Liquids
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- ❑ Microbiology
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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.

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SciTech Summit™, from cover

will examine new sterile filling technologies, case studies in cold chain management, combination products issues, MEMs and nanotechnologies, the science of media fills, and risk assessment of microbiological contamination.

Don't miss the session on current applications for **process analytical technologies**, including a presentation on **rapid microbial methods**.

Expanded opportunities for discovery, discussion and networking include PDA's Interest and Discussion Group sessions. SciTech Summit will provide key information on the most critical issues facing you today. The week-long series of scientific sessions and training courses will provide pharmaceutical and biopharmaceutical professionals with a "one-stop-shop" for training and educational needs. More than 100 presenters will offer expert advice for addressing challenges in the workplace.

Featured Sessions:

- Advances in Fluid Processing Technology
- Documentation Prior to Sterility Testing
- Process Analytical Technologies
- Rapid Microbial Methods
- Visual Inspections
- Biopharmaceutical Cold Chain Management
- Counterfeit Issues
- Combination Products
- Microneedle Technology
- GMPs in Development

Plus, take advantage of these **great social and networking activities**:

- PDA Golf Tournament and Awards Banquet—Sunday, March 7
- PDA Members Only Networking Reception—Monday, March 8
- Reception at Universal Studios—Wednesday, March 10
- Expanded Exhibit Hall: Chance to take home an exciting Grand Prize Giveaway
- Interest Group and Task Force Discussions

This event will be co-located with CleanRooms East 2004. This coming year, the CleanRooms East 2004 conference will offer the perfect complement to the PDA SciTech Summit. CleanRooms East 2004 will offer three days of sessions geared toward facility design and construction, cleanroom ISO standards, HVAC and air filtration engineering issues, proper gowning techniques as well as panel discussions aimed to help end users find proper retrofit and construction solutions.

Exhibitors: Take advantage of this exciting event in Orlando, Florida, and increase your brand recognition along with unbeatable visibility for your products and services. What better way to promote your products and services than as a sponsor—your logo on a golf ball will go the distance in keeping your company at the top! Contact Nahid Kiani at +1 (301) 656-5900 ext. 128 for more information.

Delegates: Take advantage of all that Orlando has to offer—including a fun filled reception at Universal Studios—part of your full conference registration. Special discounts will apply to three or more individuals registering from the same corporate site. Chances to win a free conference registration are being offered to each chapter.

SciTech Summit includes a comprehensive line-up of PDA Training and Research Institute Courses. For more information see Calendar, back cover.

Join the pharmaceutical and biopharmaceutical manufacturing community in warm and sunny Orlando, Florida, in March 2004. This is one conference you won't want to miss! ■

Can't-Miss Session:
Tuesday, March 9, 2004

How to Make FDA-Mandated Compliance Work for You

An Executive Overview presented by
Harvey Greenawalt, President, The Audit Repository Center

Inconsistency, high costs, and redundancy of audits cause significant challenges to validation and compliance to FDA-regulated industries. Mr. Greenawalt will discuss how using the standardized process provided by **PDA Technical Report No. 32** and the secure **Audit Repository Center** is bringing a unique solution to these concerns by sharing audits.

The Pharmaceutical Blow Fill Seal International Operators Association to hold Annual General Meeting—March 6–8, 2004 in Orlando

BFS International has announced that it will host its Annual General Meeting in conjunction with the PDA SciTech Summit™ in Orlando, Florida. In addition to the general business of the association, comprehensive scientific presentations highlighting new "extruder challenge testing" and new data on the BFS aseptic survey results will be presented as part of PDA's SciTech Summit™. PDA members will receive a discounted registration fee to attend the BFS meeting, and BFS members will be eligible for a discount to the SciTech Summit™.

Additional information is available at www.pda.org or on the BFS web site: www.bfsinternational.com.

International Congress, from cover

Featured speakers at the Congress include: senior leaders from top global pharmaceutical and biopharmaceutical companies, including **AstraZeneca, Eli Lilly, Genentech, GlaxoSmithKline, Novartis** and **MedImmune**; veteran regulators from the **EU EMEA** and the **U.S. FDA** centers for drugs and biologics; and leading academics from universities worldwide, including the **University of Connecticut**, the **University of Calabria**, and the **Tehran University of Medical Science**.

Dr. Carlo Pini, Chief Executive of QA, Instituto Superiore di Sanita (Rome, Italy) and **Dr. Frank Hallinan**, Director of Quality, Wyeth Biopharma Campus (Dublin, Ireland), will kick off the proceedings with instructive discussions of prominent regulatory inspection issues.

Delegates will then have the opportunity to participate in interactive sessions on a number of critical science, technology and regulatory topics, including: **Annex 13 and Clinical Trial Directive; Biotechnology, Development, Information Technology, Manufacturing, Innovation and Regulation, Filtration, Cold Chain Management, Aseptic Processing and Quality**.

For the first time at a PDA meeting, presentations will be given on the European perspective of cold chain management, with the following **newly confirmed** presentations/speakers:

- An overview and status (C3) report of the European Cold Chain Committee activities by David Patrick, Customer Service Manager, Cilag International;
- a C3 Cold Chain Benchmarking Survey by Detlef Dichte, General Manager—European DC, Eli Lilly; and
- Supply Chain Integrity—a practical experience by Hugo W. Wegewi, Director Logistics, Centocor B.V.

Following this session, PDA's Cold Chain Management Discussion Group, led by Rafik Bishara, Ph.D. (Eli Lilly), will meet to further work on its draft guidance (see the October 2003 *PDA Letter*).

Another first-time talk will be given on nanotechnology by D.F. Chowdhury, Project Manager, Aphton Corporation. Mr. Chowdhury will lead the PDA European Nanotechnology Interest Group, which will hold its initial meeting at the 2004 PDA International Congress.

Critical information on the revised **EU Annex 13** and the new clinical trial directive will be discussed by three expert speakers: Alan Newbery, Senior Consultant European Operations, KMI/PAREXEL International; Anne-Marie Möritz, Ph.D., QA Staff Specialist, Novartis; and Trevor Deeks, Manager of Validation, Fluor. These authoritative and insightful talks will prepare industry for the types of deficiencies the various health authorities in Europe will be looking for under the directive. Participants will leave with a better understanding of the new rule and relevant guidances, and will be able to identify the challenges the new directive will place on quality professionals involved with an outsourced clinical supply.

Cutting-edge drug delivery systems will be the topic during the drug development session. Delegates will hear Dr. Rassoul Dinarvarnd, Associate Professor of Pharmaceutics, Tehran University of Medical Science, address development issues related to PLA microspheres of estradiol valerate and the preparation of gelatin microspheres containing losartan potassium. Dr. Diane Burgess, Professor of Pharmaceutics, University of Connecticut – Storrs, will discuss her work with novel anionic liposomal systems for the delivery of gene therapies.

Two biotechnology sessions will be held to accommodate six expert speakers who will discuss a variety of important issues, including: tech transfer; the advantages of using bacteriophages over mammalian viruses for size-exclusion-based virus removal technologies; contract manufacturing; and biotech comparability.

These and other informative presentations will make the 2004 PDA International Congress in Basel a conference professionals in the global pharmaceutical industry won't want to miss.

The industry-leading and well-trusted **PDA Training and Research Institute** will conduct five full training programs following the Congress: • Clinical Trials Directive & GMPs for Investigational Medicinal Products • Risk Estimation in Aseptic Processing • CGMPs for Bioprocesses • Ventilation & Airborne Contamination in Cleanrooms, and • Pragmatic Cleaning Validation.

When not in sessions or courses, delegates will have ample opportunity to network and relax in beautiful and historic Basel. Scheduled optional events include a gala banquet at Safran Guildhall, a walking tour of Basel, or skiing at the three local slopes. Special pricing for these events is available to delegates. Check the meeting brochure and registration form for more information on these optional events and the 2004 PDA International Congress, Courses and Exhibition: www.pda.org/PDF/Meetings/04Basel-Bro.pdf. ■

For the first time at a PDA meeting, presentations will be given on the European perspective of cold chain management...

Congress delegates shouldn't miss opportunities to visit the exhibit hall to learn about new products and evaluate vendors of a variety of products and services. Over 40 companies of interest will be located in the Exhibition Hall, which is conveniently located outside the conference rooms, near the conference registration desk. Space is still available. For more information, contact Nahid Kiani at +1 301 656 5900, ext. 128 or go to the PDA Web site: www.pda.org/exhibits/index.html.

2004 PDA Pharmaceutical and Biopharmaceutical Manufacturing Science and Technology Congress, Training Courses and Exhibition

The Ritz-Carlton Millenia Singapore

May 17–19, 2004 Courses: May 19–21, 2004

Join experts from international health authorities and the pharmaceutical manufacturing industry for the latest PDA Congress in the Pacific Rim. This two-and-a-half day conference will include sessions on biotechnology, outsourcing, aseptic processing, regulatory, pharmacopeial and ICH harmonization issues. Industry experts, along with representatives from international regulatory agencies, the U.S. Pharmacopeia, Japanese Pharmaceopeia and European Pharmacopeia, will be presenting. **Dr. Chor Hiang Tan, CEO, Health Sciences Authority of Singapore**, will deliver the regulatory keynote address and **Kenneth A. Bradley, Managing Director, Pfizer Asia Pacific**, is slated to present the industry keynote.

Q7A Workshop

As an optional track at the conference, attendees can attend one or all sessions of the ICH Q7A Workshop, conducted by members of the Expert Working Group that developed the Guidance. The ICH Q7A document, the first GMP guidance jointly developed between regulators and industry, is intended for use worldwide. It impacts any manufacturer who manufactures in, or intends to export to, the ICH regions (U.S., Europe and Japan). The ICH Q7A workshop has sold out in eight locations in North America and Europe; this is the first time it has been offered in Asia.

Educational Courses

The PDA Training and Research Institute will be offering a variety of courses in conjunction with the 2004 PDA International Congress in Singapore. Course topics include:

- A Practical Approach to Aseptic Processing and Contamination Control
- Basic Concepts in Cleaning and Cleaning Validation
- Qualification and Validation of API Manufacturing Operations
- Requirements and Preparation of Pharmaceutical Grade Waters
- Computer Products Supplier Auditing Process Model: Auditor Training

Exhibits

The exhibition will include information on the latest advances in pharmaceutical science and technology. A limited number of tabletop exhibits are being offered. Please contact Nahid Kiani at +1 (301) 656-5900 or via email at Kiani@pda.org for more details. ■

Mark your calendars and register now for the 5th biennial PDA Training Conference:

No Trainer is an Island—Developing and Leveraging Your Training Network for Success

May 16–19, 2004 at the Westin Rio Mar, Puerto Rico

This conference is intended for cGMP and technical trainers in the pharmaceutical, biotech, medical device, and related industries, and this year promises to be the best yet. For the first time, the conference is being held in the spring to better meet PDA members' budgetary needs.

Participants at this conference will have the opportunity to hear first hand from our distinguished panel of U.S. FDA speakers on: FDA's new risk-based cGMP initiative, including inspectional trends; updates on the new pharmaceutical inspectorate training at CBER and CDER; and innovative programs and activities happening at the FDA district offices.

Featured speakers include Harold Stolovich, Ph.D., author of the award-winning bestseller *Telling Ain't Training*. Dr. Stolovich is a leader in the field of Human Performance Technology and will present two sessions, one based on his book, *Telling Ain't Training*, and the other on the book, *Order Taker to Performance Consultant*. Also, back by popular demand, Dave Arch from the Bob Pike Group will conduct a full-day session entitled "Beat the Blah's: The Blended Learning Solution." Dave has written such training resources as *Tricks for Trainers*, Volumes 1 & 2, *First Impressions/ Lasting Impressions*, *Showmanship for Presenters*, and *Red Hot Handouts*.

Conference attendees will have **over 20 concurrent sessions** to choose from covering topics relevant to both new trainers and seasoned professionals. These sessions will cover such topics as curriculum design, innovative classroom techniques, developing e-learning, building training communities, and establishing trainer qualifications. **Optional PDA Training and Research Institute courses targeted for trainers follow the conference**.

A new feature this year: Everyone who pre-registers will be able to view available speaker handouts in advance on the PDA Web site. While individual participants will be able to attend only four concurrent sessions, all registrants will be able to "participate" in every session when they receive the slide presentations for the entire conference on a computer CD, shipped following the conference.

True to our conference theme, *No Trainer is an Island*, we will provide a valuable and informative **vendor expo** and other opportunities for registrants to interact and network with peers and vendors of training materials and services. A limited amount of space is still available. For more information, contact Nahid Kiani at +1 (301) 659-5900, ext. 128 or go to the PDA Web site: www.pda.org/exhibits/index.html.

We will also feature all of our finalists for the 2004 Trainer's Choice Award and provide ample opportunity to "hobnob", benchmark, and be inspired by these very creative individuals. The Westin Rio Mar is perfectly suited to integrate the meeting with the exhibits and the networking opportunities.

The last biennial PDA Training Conference, held in Tampa, attracted over 200 trainers worldwide. Based upon evaluations, our 2002 conference was a huge success, and we expect attendance to increase. Register early and we'll see you in Puerto Rico! ■

—compiled by the Training Conference Committee Chair, William O'Connor, Technical Training Manager, Bristol-Myers Squibb Medical Imaging

2004 PDA/R3 Nordic Conference—Scientific, Industrial and Regulatory Aspects of Clean Products and Devices

June 7–8, 2004, Stockholm, Sweden

This important two-day conference is being offered by PDA in cooperation with R3 Nordic, the Nordic Association for Contamination Control and Clean Rooms. The focus of the conference will be the scientific, industrial and regulatory aspects of sterile product manufacturing.

Confirmed FDA speakers presenting at the conference are: Anthony Mire-Sluis, Ph.D., CDER; Dan Schultz, CDRH; and Ajaz Hussain, Ph.D., CDER. Emer Cooke of EMEA will be delivering the keynote presentation on European Regulatory Perspectives on Pharmaceutical Manufacturing & Medical Devices. Speakers have also been invited from MCA, MPA and industry.

Those who will benefit include: manufacturing personnel, laboratory technicians, QA/QC officials, regulatory affairs and validation personnel, and cleanroom design technicians.

Stockholm is a modern city rich in history and culture. The city spans 14 islands, so visitors are never far from the water. The architecture includes an interesting mix of well-preserved medieval structures and modern buildings. Stockholm is a beautiful city to visit anytime of the year, but June is a particularly pleasant month of long days, with moderate temperatures.

Check www.pda.org for more details and registration information. ■

PDA Web Seminars

Check www.pda.org for new PDA Web Seminars regularly. We have selected some of our most popular presentations from recent conferences and made them available to you on-demand. View the slides and listen to the synchronized audio presentation at your convenience and from your desk- or laptop.

The following Web Seminars are currently available for purchase:

- How to Build an Effective CAPA Program
- Designing a Cleaning and Disinfection Program in GMP Controlled Environments
- Rapid Microbiology Methods: A Regulatory Viewpoint
- Opportunities to Employ Rapid Microbiological Methods in the Pharmaceutical Industry: Examples from Compendial Applications
- GMP Training Overview and Job Skills Training Requirements in an Aseptic Environment: or What Does the FDA Have to Say About That?
- Navigating Legal Waters & Compliance Currents & Riding the Changing Compliance Tides: Global Industry Perspective
- Biopharmaceutical Process Validation Issues
- PDA/FDA Joint Regulatory Conference Closing Plenary Session ■

Registration Fee per Web Seminar

…$150 for PDA Members
…$300 Nonmembers
…$60 for Government Member (must be an employee of an official government agency).

2003 PDA Annual Meeting Delegates Tour Saint-Gobain Desjonqueres' Facility

In conjunction with the 2003 PDA Annual Meeting in Atlanta, Georgia, Saint-Gobain Desjonqueres organized a tour of its molded glass facility in Covington, GA. Immediately after the conference concluded, 50 delegates and exhibitors traveled to the manufacturing facility to witness the Saint-Gobain's manufacturing process and to learn about the company's capabilities and the importance of back up manufacturing contingencies for Type I glass. PDA delegates also heard an introductory overview from the glass tubing manufacturer OMPI and a presentation from industry expert, Mr. Michael Eakins, Principal Consultant of Eakins & Associates, on the trends in container packaging.

Richard Johnson (Abbott) discusses PDA Glass Defects Task Force.

During a lunch provided by Saint-Gobain, PDA delegates were greeted by Howard Drake, Vice President of the Pharmaceutical Division of Saint-Gobain. The attendees then had the opportunity to hear from the leader of PDA's Glass Defects Task Force, Richard Johnson, information & policy director, Quality Center of Excellence for Drugs, Abbott Laboratories, who spoke about the scope of the Task Force, its goals and recent accomplishments. The scope of the Glass Defects Task Force is to address glass quality issues related to incoming and outgoing inspections. Its goals are to standardize the terminology of the attributes within the industry, bringing Pharma companies and glass manufacturers to an agreement regarding the criticality of these attributes, as well as to identify ways to improve the handling and usage of glass containers.

PDA wishes to thank Saint-Gobain for inviting our members to tour their facility. The event placed an exclamation point on the end of a very successful 2003 PDA Annual Meeting. ■

—Andrea Agalloco

PDA Training and Research Institute Director's Message


Bob Mello, Ph.D.

Happy NEW Year!

It's January 2004 and another year has rolled past. Instead of looking back at what we accomplished last year, I would rather look forward and tell you about some of our plans for 2004. Since it is a NEW year, the emphasis (if you haven't already guessed) in our planning is what is NEW—hands-on laboratory courses that are NEW; lecture courses that are NEW; locations, worldwide, that are NEW. Not every course is NEW, however. Updated, yes, but not necessarily NEW. I recognize that with each NEW year, there are NEW individuals entering our industry or other colleagues advancing into NEW areas of responsibility in their careers. They need to learn; they need training. Therefore, basic courses on topics covering manufacturing, quality, regulatory, information and engineering sciences will continue to be offered. After all, it's NEW information to them.

So what's NEW? At our training and research laboratory we will be offering at least four NEW hands-on laboratory courses. (I say 'at least' because several other courses have yet to be confirmed.) For example, the control systems on the lab's clean-in-place (CIP) unit will be the centerpiece for a NEW course on remediation of computer legacy systems. Also, to complement our current Environmental Mycology course, there will be a NEW course in "Advanced Mycology" which will include more automated identification methods as well as traditional visual techniques.

With so much yeast and mold being prepared for these courses, we thought it would be prudent to offer another NEW course in Disinfection and Sanitization of Controlled Environments. Then, to complete this 'microbial circle' we will be offering a NEW course in steam sterilization. Should any microbe dare to survive this, we will hunt them down and identify them with our NEW hands-on lecture/lab course on 'Rapid Microbial Methods'.

In Europe, we are planning another demonstration workshop on blow-fill-seal technology in conjunction with the BFS-International Operators Association. Current planning has this event scheduled for Fall, 2004, in Stuttgart, Germany.

The University in Basel, Switzerland, will be the site for a NEW European lecture/demonstration course on the fundamentals of aseptic processing. Lecture elements of PDA's popular 2 week Aseptic Processing Lab course will be augmented with a demonstration of an ampoule filling process.

Lecture course series have not been overlooked in this plan. We will be offering approximately 100 courses in 2004. The lecture year kicks off with a return to beautiful Lake Tahoe, Nevada, on February 4–6 where we will provide established courses for those NEW to our industry as well as to those seeking to broaden their current knowledge into other functional areas. There is still time to register for these courses. Also in February, following the International Conference in Basel, Switzerland, three of the five course offerings will not only be NEW, but will be taught by instructors from Europe. To my European colleagues, you asked me for courses in Europe taught by Europeans. I have just started to deliver on my promise to you. Now it is up to you to show me your support with your attendance and feedback.

NEW lecture courses will also be offered at the training conference in Puerto Rico, the Orlando, Florida SciTech Summit, and at various other locations across the U.S. and Canada.

On a more personal note, and as another NEW item—I will be teaching a course on Contamination Control in Aseptic Processing during the Singapore course series. After all, I did spend more than 16 years in that area of our industry, and I look forward to sharing my lessons learned with my students!

In conjunction with our European office we hope to provide even more courses throughout Europe as the year progresses. To find out more details on all upcoming course events, go to the PDA website at www.pda.org on a regular basis.

So there it is—a glimpse at what's NEW for 2004. A NEW year, a NEW plan, same focus—to provide the best educational service to our membership and our industry.

Happy NEW Year ■

—Bob Mello

2004 Aseptic Processing Training

The 2004 dates for the PDA Training and Research Institute laboratory course on Aseptic Processing have been established. Due to the intensive hands-on nature of this course, class registration must be limited to 20 students per session. In response to the overwhelming registration requests for the four session dates in 2003, PDA Training and Research Institute has added a fifth session for 2004. This extremely popular two-week course sells out rapidly, so we urge you to register early. The registration information is now available on our Web site, www.pda.org/PDF/TRI-Courses/TRI-04-Aseptic-RegForm.pdf.

The 2004 dates are as follows:

Session I
Week 1 January 26–30
Week 2 February 23–27

Session II
Week 1 March 22–26
Week 2 April 26–30

Session III
Week 1 May 24–28
Week 2 June 14–18

Session IV
Week 1 August 16–20
Week 2 September 13–17

Session V
Week 1 October 4–8
Week 2 November 1–5

$7,800 members/$9,300 nonmembers; *Faculty:* John Lindsay and David Matsuhiro ■

PDA Training and Research Institute Thanks the Following...

Sponsors

Atlantic Technical Systems
Becton Dickinson Microbiology Systems
Berkshire Corporation
bioMerieux Vitek, Inc.
Biotest Diagnostics Corporation
Bonfiglioli Pharma Machinery
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Raven Biologicals, Inc.
Sartorius AG
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Upcoming PDA Training and Research Institute Education Courses

Course No.	Title/Topic	Dates
230	**Environmental Mycology Identification Workshop**	February 12–13, 2004 May 13–14, 2004 December 2–3, 2004
322	**Validating a Steam Sterilizer**	March 16–17, 2004
NEW 319	**What you to know to select adequate thermal validation equipment**	April 1–2, 2004 November 22–23, 2004
NEW	**Developing and Validating Cleaning and Disinfection Programs**	April 15–16, 2004 November 18–19, 2004
400	**Cleaning Validation**	April 19–21, 2004 November 15–17, 2004
142	**Designing, Operating and Controlling High-Purity Water Systems for Regulatory Compliance**	May 5–7, 2004 October 25–27, 2004
NEW	**Remediation of Existing Computer Systems**	May 10–11, 2004
NEW	**Developing a Moist Heat Sterilization Program Within FDA Requirements**	August 9–11, 2004
NEW	**Advanced Environmental Mycology Workshop**	September 1–3, 2004
301	**Fundamentals of D, F and z Value Analysis**	October 14–15, 2004
NEW	**Rapid Microbiological Methods**	October 18–22, 2004

These courses will be held at the PDA Training and Research Institute (PDA-TRI) in Baltimore, Maryland, unless otherwise noted. **For course content information,** call PDA-TRI directly at +1 (410) 455-5800. For registration information, call PDA's world headquarters in Bethesda, Maryland at +1 (301) 656-5900.

PDA Training and Research Institute Location/Lodging Information

Unless otherwise noted, PDA Training and Research Institute courses are held at the UMBC Technology Center, 1450 South Rolling Road, Baltimore, MD 21227.

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

Baltimore Hilton & Towers Inner Harbor
+1 (410) 539-8400
+1 (410) 625-1060 – fax

Baltimore Marriott Inner Harbor
+1 (410) 962-0202
+1 (410) 625-7892 – fax

Courtyard Baltimore Downtown/Inner Harbor
+1 (443) 923-4000
+1 (443) 923-9970 – fax

Courtyard by Marriott—BWI
+1 (410) 859-8855
+1 (410) 859-5068 – fax

Embassy Suites BWI
+1 (410) 850-0747
+1 (410) 850-0816 – fax

Holiday Inn—BWI *
+1 (410) 859-8400
+1 (410) 684-6778 – fax

Holiday Inn Inner Harbor **
+1 (410) 685-3500
+1 (410) 727-6169 – fax

Homewood Suites BWI***
+1 (410) 684-6100
+1 (410) 684-6810 – fax

Hyatt Regency Baltimore Inner Harbor
+1 (410) 528-1234
+1 (410) 605-2870 – fax

Marriott Residence Inn BWI
+1 (410) 691-0255
+1 (410) 691-0254 – fax
1 (800) 331-3131

Sheraton International Hotel BWI
+1 (410) 859-3300
+1 (410) 859-0565 – fax

* A discounted room rate is also available from the Holiday Inn—BWI. You must call the number above and mention the PDA Corporate Rate (3-PDA) when making your reservations.
** A discounted rate is available for Holiday Inn Inner Harbor of $99. To receive this rate call the number above and mention the PDA-TRI Corporate Rate (ID #100196574) when making your reservations. Rooms are based on availability.
*** no on-site restaurant

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

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

Registration Form

PDA Training and Research Institute Courses

R

LTR 01/04

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.)

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.

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

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

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

❑ B. By **Bankers' Draft** 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] ❑

❑ 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

[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.

4. **Please check the appropriate box:** ❑ Check Enclosed ❑ Wire Transfer Charge: ❑ MastercardCard/EuroCard ❑ VISA ❑ AmEx

Account Number: _____ Exp. Date: _____

Name *(exactly as on card):* _____

Signature: _____ Date: _____

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

Federal Tax I.D. #52-1906152

5. **Return completed form with payment made to:** PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA **FAX:** +1 (301) 986-1093 (credit cards only)

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.**

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

Waters® Successfully Completes Pharmaceutical Industry PDA Audit and Joins Audit Repository Center

In October, Waters Corporation announced that it had successfully completed the PDA Pharmaceutical Industry Software Supplier Quality Audit. Conducted by independent, PDA-approved auditors, this evaluation allows Waters customers to meet the federal government requirements for companies that supply software solutions to the pharmaceutical industry. Following the PDA audit process, the auditors reviewed documented evidence of structural validation and assessed Waters compliance to the established software development life cycle.

Waters is a leader in three complementary analytical technologies: high performance liquid chromatography, mass spectrometry, and thermal analysis. The company's technologies—instruments, software, chemistries—and its related support services, enable scientists to derive key information about the composition of chemical mixtures and the thermal and mechanical properties of materials. Currently, Waters' largest market is the life sciences industry, comprised of companies and institutions engaged in researching and manufacturing small molecule pharmaceuticals and bio-molecules for disease therapy.

The results of Waters' audit are available through the Audit Repository Center (ARC), a global information sharing venue licensed by PDA, which created a six-step process for audit execution, outlined in *Technical Report No. 32: Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations*. This technical report was written by the PDA Supplier Auditing and Qualification Task Group—comprised of pharmaceutical companies, suppliers, auditors and FDA members—in response to an FDA challenge to create a standard method to assess the structural integrity of acquired software.

Pharmaceutical companies must demonstrate compliance with industry regulations, such as FDA's 21 CFR Part 211.86 and 21 CFR Part 11. It is both costly and time consuming to show compliance with the audit requirements. By making the results of Waters software audit available through ARC, Waters' customers do not need to conduct their own on-site audits, saving significant time and money.

"Waters is pleased to offer a solution to enable our customers in the pharmaceutical industry to be more efficient in their evaluation and deployment process," said Noor Malki, Regularly Affairs Manager at Waters. "The ARC audit process significantly reduces the audit burden on our customers."

Waters' audit report contains more than 110 pages of information detailing the objective evidence that was examined during the audit. The complete report is placed on a CD-Rom that can be mailed out to Waters customers, upon request and only through the ARC, within days. Highlighting Waters successful audit completion are the words of an audit veteran. "Waters received the highest marks of any company that I have audited in 20 years," commented Phil Lofty, lead auditor of Watson Pharmaceutical and PDA-certified auditor.

For additional information on the official report or to obtain a copy of the report from the ARC, please contact Noor Malki at noor_malki@waters.com or +1 (508) 482-3665.

About ARC

Since the Audit Repository Center began operating in June 2000, **58 major companies** in the pharmaceutical, biopharmaceutical and medical device industries have become members and **15 suppliers** of computer products and services to the industry have **voluntarily placed** their audit data in the repository for distribution to their pharmaceutical industry clients.

Overall, there **98 "PDA-qualified" auditors**, representing over 16 countries worldwide. Training on TR-32 is available through the PDA Training and Research Institute. Information on applications for qualification and course registration is available on the PDA Web site: www.pda.org.

Availability of Audits

Currently **54 audits** are either under consideration, in process or available for distribution and 30 audits are **available for immediate distribution**. See next page for a list of the 30 audits currently available for distribution from ARC.

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

—compiled by Brian J. Murphy (Waters Corporation) and Harvey F. Greenawalt (ARC)

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, Alacris products are designed to simplify identity management and maximize trust associated with Public Key Infrastructure (PKI) implementation and security technologies.
Applied Biosystems, Inc.	SQL*LIMS™ Software - Laboratory Information Management System
Automation Tooling Systems, Inc.	Custom programming services for Process Control Software
Decision Management International, Inc. (DMI)	Regulus™ Document Authoring (DA) a member of the Regulus™ off-the-shelf solution set.
Docent	Docent Learning Management Server Docent Content Delivery Server
Documentum, Inc.	Content Authentication Services (CAS); Documentum eContent Server; Document Control Manager (DCM); GXPharma
Documentum, Inc.	Document WebDAV Server; Document Media Services; Documentum Digital Asset Manager; Document Desktop for Macintosh
Documentum, Inc.	Documentum DocApp Installer; Documentum Administrator; Documentum Application Builder; Documentum DeskTop; Documentum Website Manager; Documentum WebTop; Web Development Kit; Documentum 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
Foss NIRSystems, Inc.	SLE Near-infrared analysis of chemical and physical properties
GE Kaye Instruments, Inc.	Thermal validation systems, monitoring systems, thermocouple references and turbine temperature monitoring equipment—LabWatch™, ValProbe™ and the Validator®2000 systems.
Inktomi Corporation	Enterprise Search. Providing performance, scalability, and ease-of-use, Inktomi Enterprise Search is a comprehensive information retrieval platform that delivers access to content a cross the enterprise, regardless of location, language, or file format.
Innovatum, Inc.	DataThread™—Data audit, workflow, 21 CFR Part 11 and E-signature solution for AS/400 applications, without programming changes.
Interwoven, Inc.	Web Publication Management
Lexign Corporation	Lexign Flow™ EPR Software
LoftWare, Inc.	Loftware Print Server (LPS) Lable Printing System
MARC Global Systems	Warehouse Execution Systems
Merant	PVCS Dimensions & PVCS Replicator Software Configuration Management Tool
Mercury Interactive	Test Management Tools: QuickTest Professional; Astra QuickTest; Astra LoadTest; Astra FastTrack; LoadRunner; LoadRunner TestCenter; TestDirector; WinRunner
Propack Data GmbH	Enterprise Production Management System, PMX 3.2 with Solutions MES and CTM.
Rational Software Corporation	Rational Suite® Enterprise Rational ClearQuest (for team-based change request and defect management) Rational ClearCase (configuration management for smaller development teams)
Serena Software, Inc.	Serena ChangeMan Automating the Software Lifecycle
Sparta Systems, Inc.	TrackWise®. 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

Company, Colleague & Product Announcements

Eli Lilly and Company entered into a Research Collaboration Agreement in December with Branford, Connecticut-based Cellular Genomics, Inc., (CGI), a chemical genetics-based biopharmaceutical company. Under the agreement, CGI will apply its chemical genetics Analog Sensitive Kinase Allele (ASKA) technology to the study of kinase drug targets selected by Lilly.

"We are extremely pleased that Lilly has chosen to collaborate with CGI to further enhance their kinase drug discovery programs," said Dr. Louis Matis, President and Chief Executive Officer, CGI.

CGI states that it develops cutting-edge chemical genetics approaches based on Analog Sensitive Kinase Alleles (ASKAs). ASKAs are genetically modified kinases that retain all the functions of normal kinases, but can be potently inhibited with exquisite selectivity and specificity by a specially designed proprietary small molecule analog inhibitor. This enables drug discovery scientists to quickly understand the pharmacological consequences of specific kinase inhibition and, therefore, the likely therapeutic benefit of inhibiting the normal kinase target with a small molecule drug.

Under the terms of the agreement with Eli Lilly, CGI will use its ASKA technology to generate modified kinases for Lilly. CGI's P-inhibitor technology will be utilized to design and validate unique cell-based assays specific for the kinases of interest to Lilly. These assays have the potential to accelerate

Lilly's lead identification efforts against the kinase targets.

Glaxosmithkline Biologicals And Institut Pasteur enter collaboration to find SARS vaccine. The Collaborative Research Agreement for the development of a candidate vaccine to prevent Severe Acute Respiratory Syndrome (SARS) was announced by the companies Dec. 17, 2003. This collaboration is based on the complementary competencies of several groups from Institut Pasteur, particularly in virology, with the ability of GSK Bio to develop novel vaccines.

The companies noted that, while the SARS outbreak is now under control, concern remains for a possible re-emergence of the disease. The development of an effective vaccine against SARS is a necessary step to efficiently control the spread of the virus. The aim of the GSK Bio and Institut Pasteur collaboration is to develop a sub-unit vaccine (a vaccine derived from viral proteins). Such a vaccine avoids the manipulation of large quantities of the virus and protects individuals from risk of infection, as the viral proteins themselves are not infectious.

The first objective of this research agreement is to develop immunological tools such as monoclonal and polyclonal antibodies specific to the SARS virus useful to test the potential of an effective SARS vaccine and to characterize among the viral proteins that induce the highest immune response. The second objective will be to introduce genes that encode for different viral proteins in the expression vectors developed at Institut Pasteur to produce the relevant antigens. The immunogenicity of these antigens, which reflects potential vaccine potency, will be assessed in preclinical models using novel, proprietary GSK Bio adjuvants in an effort to further enhance immune responses.

Jean Stéphenne, President and General Manager of GlaxoSmithKline Biologicals said "With our world-class know-how in vaccine development and production we are proud and pleased to be able to contribute to the development of a potential vaccine against the SARS virus. We are conscious however, that this may take quite some time and effort and will require much consultation and teamwork between scientists, vaccine companies and health authorities worldwide."

Philippe Kourilsky, President of Institut Pasteur said, "The SARS outbreak has reminded us that emerging infectious diseases remain one of the major hazards in public health. It also provides evidence of the urgent necessity for close worldwide cooperation between public and private research."

GSK also has been commended for its commitment to combat tropical diseases. On Dec. 4, Glaxo's CEO J. P. Garnier received an award from the American Society of Tropical Medicines (ASTMH) in recognition of GSK's leadership in alleviating tropical infectious disease worldwide for the improvement of global health. The award was presented by Dr. William Petri, Jr., President of ASTMH. The Society cited GSK's vital contribution to healthcare in developing countries through action in three areas: investing in research and development that target infectious disease particularly affecting the developing world; preferential pricing of antiretrovirals, antimalarials and vaccines; and for community investment activities and partnerships that foster effective health care.

In addition to accepting the Society's award, Dr. Garnier delivered the keynote address to the group, speaking on GSK's success in creating public-private partnerships as a model for combating tropical disease. In his remarks, Garnier stated that, while the world is responding to the immense challenges of developing world diseases such as HIV/AIDS, TB and malaria, "lasting change can only be secured through partnership and collaboration." GSK's chief also discussed the work that GSK is doing along with the World Health Organization in the Global Programme to Eliminate Lymphatic Filariasis (LF).

Earlier, GSK launched HepatitisBHelp.com. The company notes that the new Web site will serve as an important resource for US-based healthcare professionals and patients living with chronic hepatitis B. The site will also provide information about treatment using GSK's chronic hepatitis B drug, EPIVIR-HBVâ (lamivudine).

Bayer Business Services (BBS) and Agilent Technologies to integrate Agilent networked data systems with BBS COVIN instruments logistics solution. The companies announced the collaboration Dec. 16. The firms will jointly develop and market the integration of BBS's COVIN Instruments logistics solution and Agilent's

networked data systems, including Agilent Cerity NDS for Pharmaceutical Quality Assurance/Quality Control (QA/QC) and Agilent ChemStation.

The companies state that the integration will optimize the pharmaceutical manufacturing and QA/QC workflow by providing an online link between the SAP R/3 quality management systems, chromatographic data systems and analytical devices. Users will be able transfer information between the different systems directly instead of manually re-entering data. This agreement is expected to benefit analytical laboratories in a wide range of industries, specifically those that must comply with GxP, FDA 21 CFR Part 11 and related regulations.

The integration of the two companies' solutions is facilitated by the open-systems architecture of Agilent's networked data systems, which can seamlessly integrate with enterprise IT infrastructures.

BBS's COVIN Instruments bridges the gap between the mySAP Product Lifecycle Management Quality Management (PLM QM) solution and the laboratory instrumentation level. COVIN Instruments eliminates the need for a separate laboratory information and management system (LIMS) by enabling mySAP PLM QM to provide full LIMS functionality.

Bayer Business Services (BBS) is the Bayer Group's competence center for business, administration and IT services. Information about Bayer Business Services is available on the Web at www.bayerbbs.com. Agilent Technologies Inc., is a global technology leader in communications, electronics, life sciences and chemical analysis. Information about Agilent is available on the Web at www.agilent.com.

AstraZeneca Prilosec® patents upheld by U.S. Federal Appeals Court. On Dec. 11, a three judge panel of the U.S. Court of Appeals for the Federal Circuit upheld the October 2001 decision by U.S. District Court Judge Barbara S. Jones, finding that Andrx, Genpharm and Cheminor infringed AstraZeneca's patents for Prilosec (omeprazole), and that the two formulation patents are not invalid. The Court also upheld the judgment that Kudco's formulation did not infringe.

Novartis' Femara® for breast cancer boosted by recent study. Extended adjuvant treatment with Femara (letrozole tablets) in a group of postmenopausal women with early breast cancer who had completed five years of therapy with tamoxifen cut the risk of recurrence of early breast cancer nearly in half (43%), and newly analyzed data showed the quality of life for patients on Femara was generally comparable to that of patients taking placebo, according to data presented today at the San Antonio Breast Cancer Symposium, Dec. 5. This independent, international study was coordinated by the National Cancer Institute of Canada Clinical Trials Group, Kingston, Ontario.

"Femara is the first therapy shown to reduce the risk of recurrence in postmenopausal breast cancer patients after five years of tamoxifen," said Diane Young, MD, vice president, global head, clinical development, Novartis Oncology. "These new data are encouraging because they suggest that in addition to the potential benefit of reduced risk of recurrence, Femara was seen to be well-tolerated and the safety profile was consistent with previous clinical trials without unduly compromising patient's quality of life."

The international breast cancer trial of nearly 5,200 women, called MA-17, is the first study designed to examine the effectiveness of an aromatase inhibitor, Femara, in the extended adjuvant setting, which is the period following five years of post-surgery tamoxifen treatment. During this period, women do not typically receive drug therapy despite the ongoing risk of breast cancer recurrence.

At a median follow-up of 2.4 years, the data in the Femara group showed a 43% reduction in risk of overall recurrence compared with placebo (P=0.00008) as well as a significant reduction (46%) in contralateral disease (cancer occurring in the other breast). The estimated absolute improvement in disease free survival at four years was 6% for postmenopausal patients taking Femara compared with placebo (93% Femara vs. 87% placebo). These numbers are nearly twice those the investigators anticipated when they designed the trial. The study was originally designed to show a 2.5% improvement in four-year disease free survival, from a baseline of 88% in the placebo arm. Disease free survival is defined as the time from randomization to the time of first recurrence of the primary disease in the breast (including contralateral breast), chest wall, nodal or metastatic sites.

According to data from the Early Breast Cancer Trialists' Group, Oxford, UK, more than 50% of breast cancer recurrence happens in women later than five years after diagnosis. Tamoxifen, which reduces the risk of breast cancer recurrence during the first five years of post-surgical therapy, has been shown not to be beneficial beyond five years of treatment. Approximately one million postmenopausal women worldwide currently receive tamoxifen therapy for reduction of breast cancer recurrence.

A second Phase III adjuvant study with Femara is being conducted by the Breast International Group (BIG 1-98) in collaboration with Novartis. This study has four treatment arms comparing five years of Femara, five years of tamoxifen, two years of Femara followed by three of tamoxifen, and two years of tamoxifen followed by three years of Femara. Recruitment in the BIG 1-98 trial was recently closed, with more than 8,000 women enrolled.

For more information on the results of this clinical trial, please visit the National Cancer Institute at www.cancer.gov or call 1 (800) 4CANCER, or visit the Canadian Cancer Society at its website at www.cancer.ca, or information service toll-free number 1 (888) 939-3333.

Patients and physicians interested in more information regarding Femara or Novartis Oncology can contact the Novartis toll-free number 1 (866) 4Femara, or the websites www.novartis.com, www.us.femara.com, or www.novartisoncology.com. ■

—information taken from company releases

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The Japanese GMP Regulations 2003—combined English–Japanese Edition

This useful English-Japanese edition of the Japan Ministry of Health, Labour and Welfare's GMP regulations for pharmaceutical products is now available. Replacing a 1998 edition, this book explains recently made revisions regarding the review and license system for drug products and introduces the regulations for biological products. The book applies to API's, finished products, clinical supplies, traditional drugs, biologicals, etc. 2003, paperback, 181 pages.

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This professional multimedia program is a fully documented competency training course that provides a comprehensive Introduction to Laboratory Skills. Presented in 4 parts, plus a part-by-part Review section, this complete course is designed both for training new personnel and re-training all laboratory staff who are subject to regulatory control. Running time is 16 minutes

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PDA-DHI Press Selected Books

Filtration Handbook: Integrity Testing, Maik W. Jornitz and Theodore H. Meltzer: This complete guide explains the proper performance of filter integrity testing by clarifying its relationship to bioburden concerns and assessing its role in filter validation. It offers practical approaches to appropriate use of integrity testing, wetting and temperature requirements, the Bubble Point test, diffusive airflow testing and much more. Numerous regulatory citations and references complete this invaluable book. 2003; 150 pp; $185 member/$229 nonmember **Item No. 17197**

The Essence of GMPs: A Concise Practitioner's Guide, U.G. Barad: This book is a compilation of more than 20 years of experience working with multinational pharmaceutical manufacturing companies and with various regulatory authorities. It incorporates and addresses the essence of GMPs prevailing around the world. It is organized in four sections. The principal section, entitled "Essentials", covers policies that are expected to prevail in any pharmaceutical industry. The second section covers requirements for the prevention of contamination for non-sterile pharmaceuticals. This section is followed by complete coverage of sterile products, and the book culminates with a complete glossary.

The purpose of the book is to enable novices, busy executives, and hard-pressed colleagues to quickly gain access to excellent global GMP practice and expectations. Beginners will find that it provides a solid prescription in preparation for the constantly expanding global GMPs. Experienced readers will find this book invaluable as a tool for assistance in the preparation and design of common practices worldwide by enabling them to speak on common quality language regardless of location. 280 pp; $185 members/$229 nonmembers; hardcover **Item No. 17203**

Change Control, Soren Schwartze: This manual is one of the documents in the series: Computer Systems Validation; A Life Cycle Approach, edited by Chris Reid. It provides a well-organized, practical process for the management of changes to the Information and Control Systems used in GXP related operations. Contents include process definitions for system changes to databases, operating systems, standard software, and application software, and recommendations for ways to handle changes in hardware, process and the environment. It provides a complete example change control process, details about planned and unplanned changes, sample report forms for errors/changes, change requests, log of change-related actions, log of maintenance actions, recommended actions in case of changes to the hardware, software, users, and much more. A very valuable reference. 2001; 25 pp; $75 member/$90 nonmember **Item No.17189**

JUST RELEASED

Laboratory Validation: A Practitioner's Guide, Edited by Jeanne Moldenhauer: In recent years, regulatory inspections have focused on laboratory testing performed to assess the quality attributes of a product. In many cases, the testing is so specialized or complex, that the entire responsibility for validation has been transferred to the laboratory personnel. This excellent, three-part guide provides an overview of validation from a laboratory perspective. Part 1 includes an overview of many of the laboratory support systems and equipment common to both microbiology and chemistry laboratories. Part 2 is dedicated to systems applicable specifically to the chemistry laboratory. Part 3 covers the systems applicable to microbiology laboratories. Where the laboratory predominantly performs—the test—for example, cleaning and disinfection, requirements are included within the text. The book offers validation details representative of the most common types of laboratory systems, yet the information in these 38 chapters will likely be of great assistance in providing resources for compilation of requirements for all other systems. 1,224 pp; hardcover; $250 member/$309 nonmember **Item No. 17201**

Microbiology in Pharmaceutical Manufacturing, Richard Prince, Editor: Providing valuable knowledge for the novice and the expert alike, many of the world's greatest pharmaceutical microbiologists and engineers, as well as other prestigious thought leaders, have invested their considerable talents in developing this comprehensive collection of timely information on this critically important subject. This book encapsulates current knowledge in a truly wide array of microbiological applications for the reader. This book is intended to demystify the field of microbiology by describing it plainly and systematically from various scientific, technical, and functional perspectives. 900 pp; $240 members/$299 nonmembers; hardcover **Item No. 17185**

Rapid Analytical Microbiology: The Chemistry and Physics of Microbial Identification, Wayne P. Olson, Editor: The old, dendritic methods of identifying microbes can be found in the most recent edition of *Bergey's Manual* (Holt 1993). The issues with this approach to microbial identification (ID) include the time required to make a critical ID and the accuracy and reliability of IDs. Hence, the introduction and success of automated, rapid methods. This book focuses on the numerous new, efficient, and effective methods currently available and serves as both guide and reference to readers interested in improving performance and accuracy in a timely manner. 2003; 354 pp; ISBN 1-930114-36-2; $195 members/$239 nonmembers; hardcover **Item No. 17184**

Steam Sterilization—A Practitioner's Guide, Jeanne Moldenhauer, Editor: Contains pragmatic details on how to accomplish the tasks necessary for a sterility assurance program for steam sterilization processes. Each chapter author is an expert and has a minimum of 10 years of hands-on experience in the topic discussed. The authors use this experience to identify practical ways to perform research, development, validation, and production activities associated with steam sterilization. Many of the chapters include sample standard procedures or protocols that may be used as templates to generate documents for your facility. Other chapters outline and explain the requirements. The book also provides guidance for those individuals who oversee these processes and those who wish to update their knowledge. While written primarily for the pharmaceutical industry, much of the content may be applicable to the food and cosmetic industries as well. While this book does not specifically address the bulk drug industry, certain information may be applicable to bulk drug manufacturers. Whether your organization is small or large, this book contains insights and techniques that will prove invaluable in your effort to develop and maintain a sterility assurance program for steam sterilization processes. 740 pp; $215 members/$269 nonmembers; hardcover **Item No. 17183**

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Selected PDA Technical Reports

Points to Consider for Aseptic Processing Volume 57 Number 2 Supplement This document represents over 18 months of dedicated work by the Task Force members. It presents the issues framed as problem statements with both a recommendation and a rationale for the recommendation provided. Some of the topics included in this 72-page report are: airflow velocity and patterns; critical area environments; differential pressures; HEPA filter testing and patching; setting environmental monitoring alert and action levels; the relationship of environmental monitoring results to batch release; investigation of environmental monitoring excursions; critical surfaces; process simulation acceptance criteria; incubation of normally excluded units; interventions; duration of process simulation tests; and number of media-filled units. 2003; 72 pp; $75 members/$550 nonmembers **Item No. 03004**

Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations—Technical Report No.32 Developed in response to an FDA challenge to develop a standard way to assess the structural integrity of acquired software, TR 32 was written by the PDA Supplier Auditing and Qualification Task Group (SA&Q), which included pharmaceutical companies, suppliers, auditors and FDA members who used their experiences with supplier audits and performed research to draft a common practice to satisfy industry needs. The scope of the project included audits of computer products and services and describes how the SA&Q Task Group, led by George J. Grigonis, Jr., Merck and Co., Inc., developed and tested a Process Model and Data Collection Tool. Use of these tools will provide consistent audit information that can be shared within the industry. 1999; 277 pp.
Item No. 01032 ..... $100 member/$575 nonmember (Paper version)
Item No. 01132 ..... $75 member/$550 nonmember (CD-ROM version)

Technical Report No. 13 (REVISED 2001) Fundamentals of a Microbiological Environmental Monitoring Program The purpose of this document is to identify microbiological and particulate control concepts and principles as they relate to the manufacture of sterile pharmaceutical products. It expands substantially upon the first edition of Technical Report No. 13, *Fundamentals of a Microbiological Environmental Monitoring Program*, published by PDA in 1990. While this publication cannot possibly supplant the wealth of information published on this subject, it provides summary information and appropriate references for the reader to consult, if necessary. The objective was to contemporize the first edition through the utilization of current definitions, recognition of improved environmental monitoring procedures, and equipment. This document serves as a source on cleanroom environmental test methods, and although some non-viable particulate and endotoxin testing data are included, its primary focus is microbiological control. The concepts for sterile product manufacturing are the most stringent application, but these concepts can also be applied to non-sterile product manufacture. The focus is environmental monitoring as it relates to facility control and compliance. This document was compiled to aid in setting up a program that is meaningful, manageable, and defendable. 2001; 37 pp; $75 members/$550 nonmembers **Item No. 01013**

Environmental Monitoring: A Compilation of papers from the PDA Journal of Pharmaceutical Science and Technology A Compilation of Papers from the *PDA Journal of Pharmaceutical Science and Technology*. In response to a need for finding historical papers, members of the PDA Microbiology Committee conducted a review of the PDA Journal of Pharmaceutical Science and Technology from 1985 to 1995, and selected these papers which should have value for those working in this field. 1996; 220 pp; $100 member/$575 nonmember **Item No.01151**

PDA Books

Cleaning and Cleaning Validation: A Biotechnology Perspective Roger Brunkow, David DeLucia, George Green, Shane Haft, John Hyde, John Lindsay, Jill Myers, Robert Murphy, John McEntire, Karen Nichols, Ray Prasad, Brenda Terranova, Jon Voss, Caroline Weil, Edward White; This book is intended to serve as a source of practical technical information for those persons in the biotechnology industry. Case studies and/or actual industry examples are used to support the text wherever possible. While much of the material contained within this text is equally applicable to non-biopharmaceutical processes, the emphasis has been focused directly upon biopharmaceutical manufacturing. Section I provides an in-depth analysis of the design concepts that lead to cleanable equipment. Also covered are cleaning mechanisms and cleaning systems. The first section is particularly useful to those persons faced with the task of designing systems that will be cleaned and also provides the biochemical background of the mechanisms associated with the removal of common biotechnology soils. Section II focuses on cleaning validation concepts. While the material is equally useful for single product cleaning, emphasis is placed upon multi-product cleaning validation. Included are general validation principles as they apply to cleaning validation, detailed analysis of cleaning process validation, sampling techniques, analytical methods and acceptance criteria. The material in Section II will be useful to anyone responsible for the development of a cleaning validation program. Section III provides an overview of multi-product biotechnology manufacturing procedures. Included an analysis of the risk to benefit scenarios associated with the various forms of product manufacturing, analysis of changeover programs, equipment considerations and material transport as they are affected by multi-product manufacturing strategies. 1995; 190 pp; $125 member/$320 nonmember **Item No.13002**

PDA Technical Archive on CD-ROM The PDA Archive will give you easy access to more than 50 years of research papers written by highly qualified research scientists in the pharmaceutical and biopharmaceutical industries. All *PDA Journal* articles, Technical Reports and Monographs, and selected Meeting Proceedings are available on this fully-searchable CD-ROM.

The Archive is updated each year, adding six issues of the *PDA Journal*, all PDA Technical Reports and Monographs, and selected PDA Meeting Proceedings. The archive is a 4-CD set. Archive (contains data through the year 2002); $395 member/$1,200 nonmember **Item No. 01101**

2002 Update (only for those who already have an earlier version of the PDA Archive); $95 member $725 nonmember **Item No. 01002**

Pocket Code of Federal Regulations GMP Guide—2003 Edition 21 CFR Part 210-CGMP in Manufacturing, Processing, Packing, or holding of drugs; general. 21 CFR Part 211—CGMP for Finished Pharmaceuticals. Reproduced in pocket size by PDA. April, 2003. 56 pp; $4 members/$10 nonmembers **Item No. 13004**

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May 5–7, 2004
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Designing, Operating, and Controlling High Purity Water Systems for Regulatory Compliance
PDA Training and Research Institute, Baltimore, MD

May 10–11, 2004
PDA Training and Research Institute Laboratory Course
Remediation of Existing Computer Systems
PDA Training and Research Institute, Baltimore, MD

May 13–14, 2004
PDA Training and Research Institute Laboratory Course
Environmental Mycology Identification Workshop
PDA Training and Research Institute, Baltimore, MD

May 17–21, 2004
2004 PDA Biennial Training Conference, Courses and Vendor Exhibit
The Westin Rio Mar Beach Resort & Golf Club, Puerto Rico

May 17–21, 2004
PDA 2004 Pharmaceutical & Biopharmaceutical Manufacturing Science & Technology Congress, Training Courses, and Exhibition
Congress: May 17–19
Courses: May 19–21
Tabletop Exhibits: May 17–19
The Ritz Carlton Millenia, Singapore

May 24, 2004
PDA Presents—*European Rotational Forums*
Location TBA, Amsterdam, The Netherlands

May 24–28, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 1
PDA Training and Research Institute, Baltimore, MD

June

June 7–8, 2004
PDA/R3 Nordic—*Scientific, Industrial, and Regulatory Aspects of Clean Products and Devices*
Stockholm, Sweden

June 14–18, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA Training and Research Institute, Baltimore, MD

June 15–17, 2004
PDA Training and Research Institute—*Toronto Course Series*
The Westin Harbour Castle, Toronto, Canada

June 28, 2004
PDA Presents—*Basel Pharmaceutical and Biopharmaceutical Forums*
UBS Ausbildungs-und Konferenzzentrum, Basel, Switzerland

August

August 9–11, 2004
PDA Training and Research Institute Laboratory Course
Developing a Moist Heat Sterilization Program Within FDA Requirements
PDA Training and Research Institute, Baltimore, MD

August 16–20, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 1
PDA Training and Research Institute, Baltimore, MD

August 30, 2004
PDA Presents—*European Rotational Forums*
Location TBA, Berlin, Germany

September

September 1–3, 2004
PDA Training and Research Institute Laboratory Course
Advanced Environmental Mycology Identification Workshop
PDA Training and Research Institute, Baltimore, MD

September 13–17, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA Training and Research Institute, Baltimore, MD

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2004

February

February 4–6, 2004
PDA Training and Research Institute—*Lake Tahoe Course Series*
Hyatt Regency Lake Tahoe, Incline Village, NV
PDA Training and Research Institute Lecture Courses:
February 4:
A Comprehensive Guide to OOS Regulations
Failures/Deviations and Change Control
Training for Performance
February 4–5:
Preparing for an FDA Pre-Approval Inspection
February 4–6:
Introduction to Competency-Based Training
February 5:
Documentation Systems & Practices
Z1.4 Attribute Inspection Sampling In a CGMP Environment
February 5–6:
Design and Implementations of a World-Class Quality System
February 6:
Achieving CGMP Compliance During Development of a Biotechnology Product
A Practical Guide to Change Control
Biopharmaceutical QA/QC Strategy For Senior Management

February 12–13, 2004
PDA Training and Research Institute Laboratory Course
Environmental Mycology Identification Workshop
PDA Training and Research Institute, Baltimore, MD

February 16–20, 2004
2004 PDA International Congress—Basel
Science, Technology and Regulations in the Global Pharmaceutical Industry
Congress: February 16–18
Courses: February 19–20
Tabletop Exhibits: February 16–18
Messe Basel Convention Center, Basel, Switzerland
PDA Training and Research Institute Lecture Courses:
February 19:
Clinical Trials Directive & GMP for Investigational Medicinal Products
Risk Estimation in Aseptic Processing
February 19–20:
CGMPs for Bioprocesses
Ventilation & Airborne Contamination in Cleanrooms
Pragmatic Cleaning Validation

February 23–27, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA Training and Research Institute, Baltimore, MD

March

March 1, 2004
PDA Presents—*European Rotational Forums*
Location TBA, Barcelona, Spain

March 8–12, 2004
PDA SciTech Summit™
Conference: March 8–12
Courses: March 10–12
Exhibition: March 9–11
Orlando County Convention Center, Orlando, FL
PDA Training and Research Institute Lecture Courses:
March 10:
Achieving CGMP Compliance During Development of a Biotechnology Product
Design and Validation of a Cleaning and Disinfection Program
Designing, Monitoring and Validation of HVAC Systems
Environmental Monitoring in Pharmaceutical Manufacturing
March 11–12:
A Practical Approach to Aseptic Processing & Contamination Control
Bioassay Development and Validation
Compliance Auditing of Cleanrooms and Controlled Environments
Computer and Network Infrastructure (CNI) Qualification Using C3Q™
Sterile Pharmaceutical Dosage Forms: Basic Principles

March 16–17, 2004
PDA Training and Research Institute Laboratory Course
Validating a Steam Sterilizer
PDA Training and Research Institute, Baltimore, MD

March 22–26, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 1
PDA Training and Research Institute, Baltimore, MD

March 29, 2004
PDA Presents—*Basel Pharmaceutical and Biopharmaceutical Forums*
UBS Ausbildungs-und Konferenzzentrum, Basel, Switzerland

April

April 1–2, 2004
PDA Training and Research Institute Laboratory Course
What You Need to Know to Select Adequate Thermal Validation Equipment
PDA Training and Research Institute, Baltimore, MD

April 15–16, 2004
PDA Training and Research Institute Laboratory Course
Developing and Validating Cleaning and Disinfection Programs
PDA Training and Research Institute, Baltimore, MD

April 19–21, 2004
PDA Training and Research Institute Laboratory Course
Cleaning Validation
PDA Training and Research Institute, Baltimore, MD

April 26, 2004
PDA Canada Chapter
Current Regulations and Compliance
Holiday Inn—Midtown, Montreal, Quebec

April 26–30, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA Training and Research Institute, Baltimore, MD

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