Volume XXXIX, No. 9

PDA Letter

September 2003

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

Electronic Records, Electronic Signatures Update, page 6

Revision to Annex 1 to Cause Change in Aseptic Practices

PDA held a one-day forum on July 30, 2003 in Bethesda, Maryland, to discuss the many compliance issues contained in the revised European Commission (EC) Good Manufacturing Practice (GMP) Guide to Annex 1, "Manufacture of Sterile Medicinal Products". The revision to Annex 1, which was issued on May 30, 2003, is effective September 1, 2003.

Following opening remarks by Russell Madsen, PDA's Senior Vice President of Science and Technology, James P. Agalloco, Agalloco & Associates, presented an overview of the changes to Annex 1. Stephen J. Bellis, Astra Zeneca, next summarized PDA's comments submitted to Karin Krauss, EC Enterprise DG, Pharmaceuticals, on January 9, 2003. Gordon J. Farquharson, Bovis Lend Lease Pharmaceutical, then provided an up-to-the-minute summary of a meeting held in London the day before, which included information on the European Agency for the Evaluation of Medicinal Products' (EMEA) plans with respect to the Guidance by Emer Cooke, Head of Sector, Inspections, EMEA, David Cockburn, Principal Scientific Administrator, EMEA, and Paul Hargreaves, Medicines & Healthcare products Regulatory Agency (MHRA).

Annex 1 now sets a limit of Not More Than (NMT) one, 5.0 µm airborne particles per cubic meter in the Grade A area at rest and in operation.

continues on page 15

Are you up to date on the latest scientific, technical and regulatory information? Keep up or get left behind!—Be Sure to Attend PDA's Largest Conference of the Year

2003 PDA Annual Meeting, Courses and Exhibition

Janet Woodcock, Director, FDA, CDER, to provide update on FDA GMP Initiative

Overview

Annual Meeting highlights include:

- 40+ scientific sessions from leading industry experts;
- 15 interactive Interest Group discussions;
- 10 roundtable exchange breakfast topics;
- Interactive Exhibit Hall and Poster Session;
- Pre-Conference: online access to speaker presentations that you can download in advance*;
- A networking reception, and
- Annual business meeting of PDA to address "The State of the Association";
- Post-Conference: complimentary CD-ROM of all conference presentations.

*Contingent upon receipt of presentations by the deadline from speakers.

Three distinct session tracks: Compliance Issues; Manufacturing; and Science and Development will feature case studies and presentations from industry experts, which will:

- Discuss the importance of quality assurance and GMP in drug development;
- Discuss the new FDA Part 11 Guidance;
- Identify issues and technologies in environmental monitoring;
- Identify approaches for improving quality systems;
- Discuss new technologies for manufacturing, and
- Discuss issues related to cold chain management.

Register today at www.pda.org/PDF/03AnnMtg-RegForm.pdf. ■

—Leslie Zeck

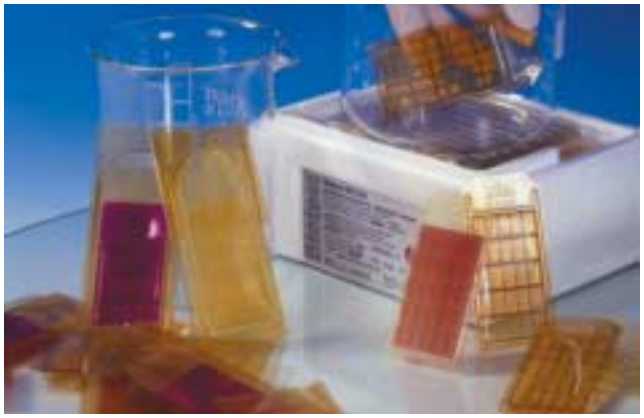
November 10–14, 2003

Atlanta Hilton Hotel on Courtland NE, Atlanta, GA

Building on Our Strengths: Quality, Science and Innovation

Conference: November 10–12
Exhibits: November 10–11
Courses: November 13–14

continues on page 31

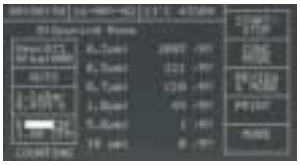


Complete Cleanroom Contamination Control.

Monitoring air quality is the first step to complete contamination control. Biotest designs and manufactures a distinctive line of environmental monitoring products including RCS microbial air samplers, APC airborne particle counters, and contact slides for surface monitoring.

NEW

Cleanroom Champion: The APC Portable.



Touchscreen keypad allows direct access to all settings. All relevant sample information is on screen at all times.

Now you can put another powerful Cleanroom Champion to work for you: The battery-powered, lightweight APC Portable Model P3610. With 0.3 µm sensitivity it measures six particle sizes simultaneously and features a backlit LCD touchscreen keypad for easy readout and programming.

Find more information and how to set up a trial evaluation at *www.APCportable.com*

Biotest Diagnostics Corporation
66 Ford Road, Suite 220
Denville, New Jersey 07834
Tel. 800.522.0090, Fax 973.625.9454
www.BiotestUSA.com

Biotest

Count on Biotest

Visit us at the 2003 PDA Annual Meeting—Booth #329

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

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

PDA European Headquarters
Gautam Maitra
Director, Europe
R-1045.P.18
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*

The ***PDA Letter*** is published monthly by PDA, exclusively for PDA members. Subscriptions are not available.

Neal G. Koller
President

Matthew Clark
Director of Marketing Services

Evelyn N. Heitman
Editor/Writer

Janet Raysick
Production Manager

Virginia Ventura
Membership Director

PDA Letter

Important Dates...

- October 10, 2003—deadline to sign up to host a breakfast roundtable discussion at the PDA Annual Meeting
- January 31, 2004—2004 Trainer's Choice Award Call for Papers deadline

IN THIS ISSUE...

Revision to Annex 1 to Cause Change in Aseptic Practices ..... cover

2003 PDA Annual Meeting, Courses and Exhibition ..... cover

Executive Message 4
PDA Meets with Israeli Health Authority and Industry Executives
PDA Seeks New Vice President of Science and Technology
Message from the Chair
Matthew A. Clark Joins PDA as Director of Marketing Services

Science & Technology 6
Electronic Records, Electronic Signatures Update
New Strategic Initiative for Computer Validation Based on Current Software Engineering Institute Research, Academic Peer Review, and Training
Risk and Science in Isolator Technology
Madsen Departs PDA
Recent Sci-Tech Discussions: Hard-to-Clean Areas
PDA Depth Filter Task Group Seeks Members
PDA Interest Group Leaders

Regulatory News 18
U.S. Regulatory Briefs
Assessing the Impact of PDA Comment Documents to Determine How to Effectively Comment on Regulatory Documents
Global Regulatory and GMP Briefs
Meet the Regulators: Thomas Lönngren, Executive Director, EMEA and Glenda Silvester, EMEA

Program and Meeting News 27
34th R3-Nordic Contamination Control Symposium
A3P—Association for Clean and Sterile Products: 16th International Congress in Biarritz, France
Basel Pharmaceutical and Biopharmaceutical Forum
PDA SciTech Summit™
PDA Web Seminars: An Affordable Training Tool
2004 PDA International Congress—Basel: Product Life Cycle Management for the 21st Century

PDA Training and Research Institute News 33
PDA Training and Research Institute (PDA-TRI) Director's Message: October Course Series to be Held in Boston
PDA Italian Inspectorate Training Program Update
Upcoming PDA Training and Research Institute Education Courses
PDA Training and Research Institute Location/Lodging Information
Sponsors & Contributors
2004 Aseptic Processing Course Dates

Membership and Chapter News 38
Chapter News Update
PDA Chapter Contacts

Industry News 40
Company, Colleague & Product Announcements

Technical & Regulatory Resources Available 41

PDA Membership Application 45

PDA Calendar of Events ..... back cover

Neal G. Koller
PDA President

PDA Meets with Israeli Health Authority and Industry Executives

Forging ahead on PDA's Strategic Plan initiatives, we continued our effort to highlight the strength, breadth, and value of PDA Science and Technology with health authorities and industry representatives around the world. We are building our partnerships.

As previously reported in this column, in April we met with FDA, and in May with the World Health Organization; Finland's National Agency for Medicines; Swissmedic; and executives from Novartis Pharma, Bakrona AG, Sartorius, and Skinner Pharm-Assist. In June, PDA met with Italy's Instituto Superiore di Sanita, and on July 2 we met with the Executive Director of EMEA, Thomas Lönngren, and members of his staff.

PDA continued these efforts July 7, meeting with the Israeli Ministry of Health, arranged and attended by our Israel Chapter leaders, Benny Klener—President; Karin Baer—Treasurer; and Karen Ginsbury—Chapter Liaison. Israel is well-known for its considerable pharmaceutical and biopharmaceutical science and technology work and is an important country for clinical trials. Gautam Maitra, Director, PDA Europe, guided our meeting with Miriam Kaplan, Ph.D., Head of the Division of the Quality of Pharmaceutical Drugs and Ofra Axelrod, Ph.D., Head of the Unit for the Quality of Biological Products.

We presented the details of PDA membership and chapter structures, focused on the mission and activities of SAB and RAQC and expanded on the value PDA science and technology can have for the Israeli Ministry of Health. PDA was very well received. It was productive for both sides. Drs. Kaplan and Axelrod expressed a need for knowledge about GMP and GLP. We discussed ways PDA could assist the Israeli Ministry of Health to enter PIC/S as an affiliate member, as well as involving them with the PDA/EMEA European Virus Safety Forum to be held September 29–October 1 in Germany. Drs. Kaplan and Axelrod voiced an interest in courses similar to the ones offered by PERF. One area that needs particular emphasis is the regulations on post-approval changes. Additionally, key individuals were identified who could assist PDA in drafting monographs for several important biotech issues where no guidelines exist yet.

After our meeting with the Israeli Ministry of Health, Mr. Maitra and I visited a mainstay of the Israeli pharmaceutical industry, TEVA Pharmaceutical Industries, Ltd., where we had the opportunity to meet with the Israel Chapter Committee members. TEVA provided us a tour of their production facility following a presentation by Benny Klener, QA Director for TEVA. Mr. Maitra met separately with InterPharm (a SERONO group company), where he was given a tour of their facility after a presentation by Mordechai Izhar, Ph.D., a PDA member and InterPharm Validation Manager. InterPharm's high level of scientific and technological knowledge was very impressive. Dr. Izhar expressed an interest in becoming actively involved with the PDA Biotech Interest Group.

I was very pleased that PDA had the opportunity to meet with these organizations. Such meetings are the foundation of PDA's Strategic Plan to build interactive, mutually beneficial partnerships with health authorities and industry executives around the world. Through these interchanges, PDA is working to strengthen the exchange of science and technology across the worldwide pharmaceutical and biopharmaceutical communities.

In next month's column, I will report to you on PDA's very strong science and technology activities in Asia-Pacific. ■

PDA Seeks New Vice President of Science and Technology

PDA is currently searching for an experienced senior level executive to serve as Vice President of Science and Technology. This individual will represent the organization globally on a broad range of science and technology issues, including their impact on and inclusion in regulations, and will focus on all aspects of planning and coordinating PDA's scientific and technology activities. The duties and responsibilities include:

- Manage and build PDA's Science and Technology program, executing the association's comprehensive global Strategic Plan
- Oversee the enhancements of the *PDA Journal of Science and Technology* and all other scientific documents, writing and editing papers and articles on Science and Technology activities
- Actively increase scientific collaboration and use of PDA science with health authorities around the world
- Actively increase scientific collaboration with industry around the world
- Identify and present emerging scientific and technical issues and opportunities to the membership and work with the PDA Planning Committee and other volunteer leaders to recommend new science and technology initiatives
- Serve as advisor/leader for program committees regarding science and technology content and develop new scientific program initiatives
- Act as liaison with outside organizations regarding Science and Technology projects of mutual interest
- Develop and implement staffing and annual plan to support task groups, organizational committees, subcommittees, and Interest Groups, and serve on these groups

The ideal candidate will have extensive experience working with multiple constituencies and committees and must possess exceptional written and oral communication skills, strong analytical skills, natural leadership abilities, the ability to organize and lead major initiatives, and public relations skills. Candidates must possess an understanding of the complex scientific issues pertaining to the development, manufacture, and quality control of pharmaceuticals, biopharmaceuticals and related products. This position reports directly to the President; salary is commensurate with experience. Applicants should submit a letter of interest, including salary requirements, résumé, references, and writing samples to Neal G. Koller, President, at koller@pda.org. Applicants will be notified in writing; no phone calls please. ■

Message from the Chair

—*Floyd Benjamin*
Chair of PDA

Dear Colleagues:
I have recently received several inquiries pertaining to staff changes at PDA headquarters and PDA's continued commitment to science and technology. I will use this communication to address some of the queries regarding recent events.

There have been several staff changes since the appointment of Neal Koller as PDA's President. These changes have strengthened our staff capabilities and will better serve the membership. The new staff members are good examples of the positive direction being taken and will enhance the association's ability to meet the expanding needs of the members.

The recent resignation of Russ Madsen has caused concern on the part of some PDA members. This is understandable because Russ has been a recognized contributor to PDA's scientific initiatives over many years. His resignation from PDA will certainly diminish the staff 's scientific and technical capability in the short-term, but we are committed to find a successor for Russ who will maintain PDA's goal of scientific leadership. We have initiated a search for a qualified replacement and we will be successful with the help of the membership in finding a high-caliber VP of Science and Technology.

We all wish Russ good luck in his new endeavors and are pleased that he will remain an active member of PDA.

I want to assure you that throughout the process leading up to Russ's resignation, the Executive Committee of the Board of Directors, reporting into the full Board of Directors provided oversight for the PDA staff organization. I also want to encourage our members to engage any or all Board members in discussion on this and any other situation PDA must address. We are open to hear and discuss any issues our members desire to bring to us.

Change is always difficult but it is inevitable, and in the end an opportunity for our organization. PDA was forced to face a management change when Ed Fry resigned as President to pursue other interests. His resignation put into motion a series of decisions regarding PDA's infrastructure as well as personnel that needed to be made by the Board of Directors and by individual staff members. The Board of Directors addressed this responsibility in a very thorough and professional manner and selected a highly qualified new President from outside PDA to lead the association. Neal is a very experienced biomedical industry executive who has served as CEO of several companies. His background and experience will serve PDA well during the coming years to lead the association and implement its strategic plan.

The Board of Directors, PDA management, and members together have the responsibility to maintain the association's focus on its mission to support the advancement of pharmaceutical technology by promoting scientifically sound and practical technical information and education for industry and regulatory agencies.

PDA's vision has not changed but remains the same as established for our strategic plan; (1) Be recognized worldwide as an authoritative, easily accessible source of global technical and regulatory information about pharmaceutical and biopharmaceutical technology; (2) Be the preeminent provider of practical, technical lecture and laboratory education and training in pharmaceutical and biopharmaceutical technology; (3) Be recognized for leadership as an influential contributor of scientifically sound information to the worldwide regulatory process.

The challenge we all face today is to dedicate our energies toward meeting the mission and vision established for PDA. We must not be distracted by inevitable changes that have and will take place in our association staff as we move forward, but we must seize this moment to move PDA forward by adapting to these changes in a constructive and positive manner. PDA is an association that is very dependent upon its members for direction and scientific/technical expertise to address our industry needs. No other association is as uniquely positioned to meet these industry needs as is PDA.

I hope this communication addresses your concerns and clarifies any misunderstanding pertaining to the direction of PDA and its continued focus on science and regulatory affairs. The Board of Directors and I welcome your continued support and commitment to PDA.

Matthew A. Clark Joins PDA as Director of Marketing Services

PDA welcomes Matthew A. Clark as the new Director of Marketing Services. Matt will be responsible for leading PDA's communications efforts, including the *PDA Letter,* media kits, publications, catalogues, the Membership Directory, and other special publications. He will oversee the production and distribution of brochures and electronic communications, and will direct the management of PDA's Web site.

"Matt is a talented marketing communications professional with a proven track record in the health science and high-tech markets. He brings vision and creativity to PDA's strong management team," said Neal G. Koller, PDA President.

As Director of the Marketing Services team, Matt's primary focus will be to develop and implement marketing strategies for meetings, education courses, publications, and other PDA events, products and services. He will manage PDA's marketing communications and public relations functions, and will identify new marketing opportunities for the association.

Matt brings many years of experience to PDA; most recently he was the Marketing and Public Relations Manager for the Association of Clinical Research Professionals (ACRP) in Alexandria, Virginia. There he managed the strategic marketing and public relations initiatives for the 18,000+ member international association. Prior to ACRP, he was the Marketing Content and Editorial Manager at Respond.com, and the Senior Marketing Communications Specialist at Net2000 Communications, Inc.

A Central New York native, Matt earned his Master's degree in Mass Communications, specializing in Media Management and Magazine Journalism, from the University of South Carolina, and his B.A. in Psychology from Syracuse University. ■

Electronic Records, Electronic Signatures Update

2003 Good Electronic Records Management Conference

The Good Electronic Records Management (GERM) Conference, held in Chicago, June 23–25, 2003, sponsored by PDA and produced by Cohasset Associates, Inc., continues to sustain its unique position in the pharmaceutical industry as the leading national conference on electronic record and electronic signature issues and the regulatory scope of Part 11. Attendees have unanimously rated the event as the premier educational forum that maintains a continuity and balance between good business practice, regulatory compliance, and legal defensibility of authentic electronic records and electronic signatures.

Joseph C. Famulare, Director, Drug Manufacturing and Product Quality, CDER, FDA, delivered the message that the "sands are shifting" regarding current thinking in the application and utility of Part 11 to the Agency's mission for the protection of public health.

The keynote speaker at this year's conference was Joseph C. Famulare, Director, Drug Manufacturing and Product Quality, CDER, FDA, delivering the message that the "sands are shifting" regarding current thinking in the application and utility of Part 11 to the Agency's mission for the protection of public health. The paradigm shift is largely directed by risk management philosophies in the pursuit of public health and safety relative to the use of regulated consumables and devices. The Part 11 concepts are not so much in question as the application of the concepts to practical and effective Agency regulatory activities.

According to Famulare, the scope of Part 11 has been, and continues to be, those records required by the predicate rules and any record attribute, feature or practice to manage and control records also specified in the baseline regulations, i.e., audit trails, signings, copies, retention, and availability. Enforcement and applicability have been complicated by computing tools that were never contemplated in the predicate rules. One factor in the Agency's equation for applicability and enforcement discretion is the balance corporations have to establish between how electronic information is used in normal operating modes and the paper-based way of operating.

Famulare indicated that the expectations for validation remain as usual and will largely be driven by a corporation's dependence on reliable computing tools in performing regulated operations and in the creation and management of electronic information used to support or defend these operations. The concept of "legacy" technology continues to contribute to the turbidity of the validation waters. A better definition of "legacy systems" will have to be decided on as computing bases are rarely frozen in time and continue to evolve with changing business needs. Is the real issue "legacy information" or "legacy system" (installed computing technologies, pre-August 1997)?

As the Agency and industry continue to refine the concept of predicate rule records for a paperless world, the risk management factor will add yet another dimension to the issues, because all records are not equal in terms of public health risk. Quality of information and its trustworthiness will also be considered when discretionary action is taken by the Agency, according to Famulare.

It was stated that comments received on the recent draft Guidance indicated to the Agency that there is still much more work ahead and many opportunities for Agency and industry forums to work together to achieve a win-win for all stakeholders in solving the complex problems presented by electronic signatures and electronic records. Famulare indicated that the volume of comments received by the Agency was substantial, but not overwhelming. The content however, was in large part significant, and will require additional Agency effort to finalize the Scope and Applicability Guidance.

Plenary sessions at the conference clearly raised some interesting issues on the horizon, as well as possible solutions:

- the sourcing of regulated services that produce predicate rule records; in whole or in part;
- new concepts in the field of long-term digital preservation of records that ensure their accessibility and utility;
- risk management application to the electronic record life cycle from cradle to grave;
- GERM as guidance in good business behavior in managing electronic records; one size fits all, and
- electronic records on trial; a good faith effort per GERM guidance may be a corporation's best defense.

The body of the conference unfolded as three parallel tracks: technical, strategic, and legal/regulatory, during the two-day period. Presentations in each of the tracks were rooted in case studies and experiences by the speakers, and were rich in information content that presented practical solutions tied to GERM principles. Many of the attendees commented on their dilemma in deciding which talks to attend, as all sessions were of value and timely in the context of current events and issues. The latent dilemma was solved early in conference planning by the producers as recorded sessions. Attendees will be receiving their complementary audio CDs and slides in 8–10 weeks. CDs will also be available through PDA for a nominal charge.

It was clear at the conclusion of the conference that a GERM beachhead was established along the front lines of electronic record and electronic signature issues as they unfold in the transition from a paper-based operating world to a paperless operating world. Holding ground and advancing along the front lines are the next challenges for PDA and Cohasset Associates in serving the FDA-regulated industry. ■

—Russell E. Madsen

New Strategic Initiative for Computer Validation Based on Current Software Engineering Institute Research, Academic Peer Review, and Training

Reshaping the Vision of Validation for Computer-Based Technologies

by George J. Grigonis, Jr., Sr. Consultant, QA Edge

Studies and surveys of businesses around the world and across industries send a clear message that computer technology *is* the bottom line for many businesses today. Companies, who never thought they were in the technology business, are by default in that business in order to maintain their competitive edge. This is due to the painful reality that their services and products are unavoidably dependent on; (1) the digital infrastructure that runs their enterprise, (2) the microprocessor-based tools they employ to develop, improve and service their marketplace commodities, and (3) the technology components that are integrated into many of their products. The pharmaceutical industry is not immune to the digital reality of life. It is an undeniable fact that pharmaceutical science, today, is inseparable from computer technology and, it is an undeniable fact that it is dependent on this technology for its advancement.

Computer validation has been a reality for the FDA-regulated industry since the early 1980s. Since that time this industry has witnessed many computing advances that have challenged our concept of validation. Concurrent with these advances is the continuing evolution of systems development from the widely disparate forms of hacking and DoD rigor to a true engineering discipline, as evident by the formation of research centers like the Software Engineering Institute (SEI) at Carnegie Mellon University, and worldwide standards organizations supporting systems engineering philosophies and research.

Computer validation concepts, in keeping step with these advances, have to shift to fulfill compliance expectations that keep step with modern principles of good systems practices. New technology advances will continue to challenge these principles and may, in fact, redefine them as the FDA-regulated industry; (1) continues to implement and use Web-based technologies, (2) increases computational capabilities through distributed computing, (3) continues its dependence on commercial off-the-shelf (COTS) technologies, (4) sources technology infrastructures and applications to e-source providers, and (5) realizes that computer hardware and software are the foundations for trustworthy electronic records and signatures.

Several PDA Task Groups have worked on some of these issues; e.g., the Task Group for Technical Report No. 32, "Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations" (TR-32) and the Task Group for Part 11, Electronic Records, Electronic Signatures, resulting in very successful outcomes and benefits for the industry. The ever-increasing dependence on COTS products and FDA expectations for computer validation has contributed to the success of the TR-32 Supplier Audit Program and the Audit Repository Center (ARC). In fact, the program has gained recognition outside the industry. The Software Engineering Institute (SEI) published a case study in May 2003, (CMU/SEI-2003-TR-011). In the report, SEI recognized the PDA/ARC Supplier Audit Program as worthy of consideration for COTS programs in both industry and government.

Peer review case studies, such as the one for TR-32, are essential reality checks against emerging good practices in the computer discipline arena and in establishing academic creditability for current good science relative to validation techniques invented or published by FDA-regulated industry parishioners. Working with academic institutions, like SEI, has opened new avenues of exposure for PDA-endorsed work relating to computer validation. It is hoped that this will continue to be used as a measure of merit for all computer validation products endorsed by PDA, including those for network infrastructure practices.

On a similar and related note, education in current good systems engineering practice is fundamental to evolving computer validation thinking. It is also essential in averting repackaging of current or outdated methods, techniques, and templates documented in related disciplines outside of the FDA-regulated industry. And it is essential in creating a common scientific basis for understanding and communication between regulators and industry practitioners, avoiding the invention of new language to describe concepts and increasing the fog factor. SEI-PDA collaborative work for computer validation is presently pursuing this educational path to bring SEI courseware on the topic of COTS practices and related topics for mature systems, computing architectures, and security practices, to the FDA-regulated industry through the PDA-TRI vehicle, thus aligning validation concepts with contemporary IT thinking and systems engineering predicated on current good science.

Computer validation, from a Part 11 perspective, is becoming even more important in the context that installed computing systems and many new systems are engineered for productivity, not information assurance. The key principles of the 21 CFR Part 11, Electronic Records, Electronic Signatures Guidance have been "modeled" by other proposed or approved regulations from other regulatory authorities, including the Environmental Protection Agency and the Security and Exchange Commission. Thus, what began as a regulation for the food and drug industry has now taken on a new life as the model for key Electronic Records Management (ERM) principles that a spectrum of other

continues on page 13

It is an undeniable fact that pharmaceutical science, today, is inseparable from computer technology and, it is an undeniable fact that it is dependent on this technology for its advancement.

Risk and Science in Isolator Technology

Are the increasing costs and complexity in isolator decontamination warranted by the actual contamination risks that exist?

James P. Agalloco, Agalloco & Associates and James E. Akers, Akers Kennedy & Associates

In 1984, the authors of this article were already a couple of years into what has become an enduring friendship and over two decades of collaboration. That same year at the PDA Annual Meeting at the Wyndam Franklin Square Hotel in Philadelphia, we witnessed what we were sure would be a revolution in aseptic processing: La Calhène demonstrated a device that we would come to call the isolator. This isolator was called an "absolute barrier" (ominously, as it turns out) in a sign on the display, and had a RTP flange, which was the feature that really grasped our imaginations. Prior to this demonstration at a PDA meeting we had seen only a few pictures of the isolator in trade publications, and frankly we failed to grasp what it offered; it looked like nothing more than a slightly more elaborate glove box in advertisements. It wasn't until we saw it up close that the simple logic of the device became obvious.

At that point in time it created a minor buzz, but most attendees seemed to think the device had a future only in sterility testing, or perhaps research. A few others thought it was a bad joke with no future at all. We thought it was the future of aseptic processing, and we still think so 19 years later.

Within a couple of years one of us had started to build a sterility laboratory around one, and the other couldn't wait to get his hands on one. With our backgrounds in engineering and microbiology and our experience with aseptic operations, we both knew that there was only one simple secret to safe and reliable aseptic processing, and that was the elimination of human-borne contamination. We saw two ways in which the control of human-borne contamination could be improved: isolation and automation. It was apparent to us that ultimately aseptic processing would be done in systems that married these two technologies.

We are happy that isolators have, in fact, been widely implemented over the last 20 years; they should be, because they are far superior to manned cleanrooms in controlling microbial contamination. What saddens us is that the implementation of isolators for production operations, particularly in the United States, has gone far slower than it should have. This represents a tragedy for our industry, the patients we serve, and those who regulate us. This brief article examines just one element of the poor judgment that has led to a halting implementation of isolators.

Sanitize, sterilize, disinfect, or decontaminate? Does it really matter?

When we first saw an isolator and read the literature that accompanied it, we found that it was possible to purchase a peracetic acid "sterilizer", and that one could verify the efficacy of the treatment using biological indicators. We had often joked that the ideal environment for aseptic filling would be the inside of an autoclave when sterilized and fully closed, and here we were staring at a "sterili-zable" enclosure. What we failed to grasp that day was that it was probably only going to be possible to sterilize a very simple isolator with nothing in it at all. Almost immediately we realized that once one put a sterility testing pump, a rack of equipment, or a simple bench top filler in the isolator, it would be devilishly difficult to truly prove sterility, particularly if we followed the industry habit of using the biological indicator "kill" to define sterility. We kept trying to pursue the holy grail of a sterile box far longer than we should have. In retrospect, we should have recognized immediately that a claim of sterility was not possible, and wouldn't be for a very, very long time. In fact it still isn't really possible today.

In 1991 and 1992 we saw a vaporous hydrogen peroxide (VPHP) generator and got to put one through its paces. Like curious scientists anywhere, we couldn't wait to test it thoroughly to see what was possible and what wasn't. We discovered quickly that the vapor did not penetrate materials readily at concentrations that were sporicidal, and that if a BI was placed under a gasket or under a bottle sitting on the base of the isolator, complete kill was impossible. In short, we confirmed our suspicion that a claim of sterility was not really possible; however, this didn't really dampen our enthusiasm for isolators for long, because after a little deliberation it became obvious that it really didn't matter if the objective was to improve aseptic processing. In fact, the more we thought about it, the more we realized that we could never truly prove that gloves, or even the air handling system in an isolator, were truly sterile. Further, we realized it didn't matter because we've never been able to prove that *any* surface in a cleanroom was really sterile. This is a simple reality of aseptic processing and it applies as much today as it did in 1984 or 1992.

Unfortunately, the isolator can never be a true replacement for terminal sterilization. However, there are instances when aseptic proces-sing is a better choice than terminal sterilization because

micro-biological risk at the manufacturing level isn't the only risk that needs to be addressed in product manufacturing. What is needed is a better way to aseptically process than conventional, manned cleanrooms.

Experience has shown that aseptic processing doesn't need to achieve a 10^{-6} probability of non-sterility to be safe and effective. In fact, the one-in-a-million standard that we've applied to sterilization broadly was originally intended to apply only to the final drug in a terminally sterilized container. It is also useful to recall that the one-in-a-million standard is a form of risk analysis and not an immutable law of sterilization. One should also recognize that there is nothing magical about 10^{-6}; it is now, and always has been, no more than a number borrowed from NASA.

We assert the following is true both in terms of science and risk. *Any isolator that provides an environment in which it is possible to achieve a bioburden level of close to zero as detected by conventional environmental monitoring is more than safe enough for aseptic processing, regardless of how many spores were killed and on what carrier in the decontamination process*. We challenge any reader who disagrees to provide a clear scientific rationale for his position. The time has come for participants in this debate to come forward with science and risk analysis to support their contention with facts. Isolators don't need to be sterilized and, in fact, it is not possible to prove that they are sterile. Why then do we spend (waste?) years and vast quantities of human and financial resources in a fruitless effort to prove something that cannot be proven?

A highly respected member of the regulatory community recently opined to us that a two-log kill of resistant spores in an isolator would be more than enough. He's right, because if that isn't enough, we should be shutting down every aseptic processing cleanroom in the world. We've never been able to achieve even that modest level of spore reduction reliably in any cleanroom, and even if we could, we'd then send gowned humans into the room, which would immediately result in a detectable bioburden.

How much additional safety is attained by requiring a six-log kill, which incidentally in the strictest sense does not mean the complete kill of a BI with a population of 10^6? We believe very little. When we served as co-chairmen of the task force that wrote PDA's Technical Report No. 34, "Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products" (TR-34), the group reached a consensus that a three-log spore log reduction was adequate to ensure a safe aseptic processing environment. PIC/S in their original isolator inspection guidance also set a three-log reduction target.

Recently, PQRI, in collaborating to revise the FDA's aseptic processing "Concept Paper," issued last fall suggested a four- to six-log reduction, which we take to mean a spore log reduction rather than a complete kill. This is a requirement that we could probably live with in most isolator installations, but we still hold that the three-log spore reduction recommended in the original version of TR-34 is ample and is more than safe enough to eliminate bioburden in a clean environment. After all, the isolator is a piece of equipment used to maintain an environment: we are not going to inject the isolator itself into the patient.

In a study one of us published several years ago, we found that wild-type environmental spores were many times less resistant than commercial VPHP BIs. This is hardly surprising. It also follows that the vegetative bacteria that predominate in the environment are far less resistant than any spore. The truth is that one could do media fills in isolators that had nothing in them decontaminated except the gloves and the stopper bowl, and one would probably never see a positive unit. We have no doubt that such an isolator would be much safer than any manned cleanroom. In fact, recent studies done by John Lindsay at the PDA Training and Research Institute call into question to what extent the stopper bowl is likely to contribute to microbial contamination both in media fills and final product.

We also assert that the manner in which isolator decontamination is validated has evolved into a prime example of poor risk analysis and a lack of scientific judgment in standard-setting, and in some cases regulation. Here are a few of the more unreasonable practices/requirements that have been recommended and in some cases utilized:

1. Drying of at least a million spores on a solid surface, often stainless steel, to validate decontamination. This has resulted in BIs that are unpredictable in behavior and which vary enormously from lot to lot. Dense populations of spores and the organic and inorganic material in the inoculation suspension can result in a protective matrix around the spores, and non-linear spore kill results. The ISO guidelines on biological indicators suggest that a survivor curve when plotted on semi-logarithmic graph paper should result in a linear regression R value of at least 0.8. Actually, in steam sterilization we typically see R values greater than 0.95. However, in published graphs of VPHP-treated BIs, we often see results that are clearly biphasic and do not reflect linearity. When survivor curves do not follow first order kinetics, clearly something other than a simple chemical reaction between hydrogen peroxide and

continues on page 10

Isolators, from page 9

the macromolecules is taking place. We have inoculated lower concentrations of *G. stearothermophilus* spores or the mold *C. globosum* onto carriers, and we have found that at concentrations in the range of 10^3, calculated D-values are lower and kill curves more linear than if the same studies are repeated at higher concentrations. Sterilization science tells us that when all microorganisms in a population are subjected to a lethal treatment, their rate of death should follow first order kinetics. We believe that unless a linear kill curve is observed, the study conditions must be flawed.

2. We question the need to challenge multiple materials in an isolator or the suggestion that we should consider some materials unsuitable for use in an isolator because they allegedly result in more difficult-to-kill spores. Isolators are designed using good hygienic principles. Their surfaces are smooth and relatively non-porous, wall junctions have appropriate radii, and window junctions are smooth and without crevices. In short, there should not be biofilm in an isolator cleaned and prepared for use. What then are we supposed to be learning by creating an extreme biofilm by inoculating a million spores onto an otherwise clean surface in a milieu of inorganic salts and organic residues, and then testing our ability to kill a concentrated population of greater than a million spores trapped in this artificial biofilm? The existence of biofilm in an isolator would reflect very poor practices on the part of the user and could not be considered acceptable under any circumstance. Based upon our experience, we would expect that the worst case bioburden on an isolator surface is less than 50 CFU/25cm^2. We also believe that this environment will, in almost every case, consist primarily of normal human flora, which means predominately Gram + cocci and diptheroids, which are far less resistant than biological indicator spores. In fact, in one study recently published on an isolator operated in an uncontrolled environment, the bioburden found around the isolator was typically in this range. Is it not obvious that a biofilm of a million spores concentrated in 10-50μL represents an unrealistic challenge? We have always been in favor of conducting validation studies under most challenging conditions, but that doesn't mean we favor testing under wholly unrealistic conditions. It is also worth pointing out that even if achieving a 10^{-6} probability of bioburden survival were the objective (and it should not be) this could be achieved at a much lower challenge level. We have previously pointed out that it is not necessary to kill a million resistant spores to demonstrate a 10^{-6} probability of non-sterility for the bioburden. We urge those who think this is necessary to consult a textbook on sterilization and to think about risk analysis a bit harder.
3. We have heard it argued that the production of biological materials in an isolator might result in spillage of product and formation of biofilm. We do not understand why this is so. This could only occur if the user was careless, had a poorly designed system, and also failed to clean it properly. Even if in the operation of an isolator a temporary biofilm were created, there is simply no way that it would present a challenge equivalent to 10^{-6} spores dried in 10-50μL. In fact, spores are generally a relatively minor component in facility bioburden, and as we know, it is not easy to grow a spore crop in conditions that favor a mixed population of mesophilic organisms. Further, we don't decontaminate cleanrooms in this manner, and we make biological products in cleanroom environments. Are we to infer from the expectation of a 10^{-6} kill in isolators that all cleanrooms filling biologicals are inherently unsafe? Of course not. Safe biological products are made in cleanroom environments every day of the year. Why should isolators be considered a greater risk, and therefore impose a processing requirement many orders of magnitude more rigorous than applied to manned cleanrooms? Why should an isolator's aseptic environment be expected to meet performance requirements that manned cleanrooms deemed safe enough to gain regulatory approval do not have to meet?
4. It has been asserted that fraction negative studies are inappropriate to validate a spore log reduction value in isolator decontamination. PDA suggested the use of fraction negative studies in isolator decontamination evaluation in TR-34. PDA was then and is still now correct in that position. There is absolutely no reason why a three-log spore log-reduction demonstrated using a fraction negative approach is not adequate. If the user desired a six-log spore reduction, there is no valid scientific reason why this level of kill could not be demonstrated by extrapolation from fraction negative studies. Fraction negative studies are how D-values are established in the first place. If we know the rate of kill of a spore population under reproducible test

conditions, there is absolutely no scientific reason why this approach can't be used to tabulate a suitable spore log reduction. We think the assertion that fraction negative studies shouldn't be used in isolators betrays a poor understanding of the methods used to analyze microbial death. If anyone has a valid objection to fraction negative studies, they should bring it forward with appropriate scientific data to support their position. We once again assert that a three-log kill of *G. stearothermophilus* is more than enough to result in an isolator that is free of bioburden and safe for aseptic processing. As previously stated, where this not so, every cleanroom currently in operation should be immediately shut down.

Some readers are probably already thinking that all this is well and good, and that it might even make some sense scientifically, but since other firms have already tried to meet expectations exposed from one podium or another, haven't they set the CGMP bar higher than it needs to be? This is only true if we, as concerned industry scientists and organizations like PDA, allow CGMP to be defined in the absence of the science- and risk-based analysis that regulators say they are using as a basis for current and future regulation. Choosing the most extreme approach isn't necessarily a good idea, and if risk assessment is to be meaningful, then extreme perspectives as are evidenced with isolation technology should no longer prevail. We seem to have evolved into an attitude toward CGMP that is based upon the idea that the more extreme the objective we set and the more intensive and expensive the means by which we attempt to comply, the more likely we are to have achieved CGMP compliance.

We believe this method for defining CGMP is wrong. Just because a firm has felt forced to take an extreme approach doesn't mean there was a good scientific or risk-based reason to do so. CGMP shouldn't be an effort to give an inspector what he or she wants—it should instead be based upon what is scientifically defensible. If an inspector, vendor, consultant, or firm doesn't have science or engineering right they have no business establishing a CGMP target. There may be perfectly good reasons for a firm choosing to take what appears to be an extreme approach, but that doesn't mean that an individual firm's decision or an inspector's opinion should be allowed to establish CGMP for everyone. We can't think of a better example of poor science and risk analysis leading to irrational expectations and inappropriate proposed standards than in isolator decontamination.

We don't need an entirely new set of aseptic processing requirements for isolators: what we do need is common sense. We also don't need to waste time and money in a fruitless quest to attain an unachievable absolute. Our industry, the scientists and engineers who serve the industry (including our regulatory community), and most importantly our patients deserve much better. ■

References

1. FDA "Concept Paper" on aseptic processing. 2002.
2. PDA Technical Report 34. 2001 *PDA Journal of Pharmaceutical Science and Technology*. Volume 55, No. 5.
3. Akers, J., and Agalloco, J. 2000. Isolators–Validation and sound scientific judgment. *PDA Journal of Pharmaceutical Science and Technology.* 54(2): 110–111.
4. Kokubo, M.; Inoue T.; and Akers, J. 1998. Resistance of common environmental spores of the genus *Bacillus* to vapor hydrogen peroxide. *PDA Journal of Pharmaceutical Science and Technology*. 52(5): 228–231.
5. Sigwarth, V., and Moirandat, C. 2000. Development and quantification of H_2O_2 decontamination cycles. *PDA Journal of Pharmaceutical Science and Technology*. 54(4):286 – 304.
6. FDA. "Pharmaceutical GMPs for the 21st Century: A Risk-Based Approach." 21 August 2002.
7. Akers, J, Kokubom, M. and Deguchi, M. 2003 Manuscript in preparation.

Madsen Departs PDA

PDA President Neal G. Koller announced with regret that Russ Madsen, Senior Vice President of Science and Technology, resigned from his position with the PDA on September 11, 2003. Russ worked for PDA for 10 years, and he was a vital member of the association. A search committee has been formed and the search is underway to find a new Vice President of Science and Technology.

Russ was responsible for many critical achievements of the organization. He represented PDA on the creation of the Good Electronic Records Management (GERM), Part 1 of the series on Good Practice and Compliance for Electronic Records and Signatures. He managed the formation of a strategic partnership that provides training and certification services for computer infrastructure assurance engineers and auditors working in the life sciences industries. Russ was also instrumental in developing guidelines on such important areas as: validating existing plasma fractionation processes, sterilizing the filtration of air and gases, the use and calibration of biological indicators, and the validation of aseptic manufacturing processes, as well as publishing numerous Technical Reports and Bulletins.

Russ will remain an active member of PDA, and we look forward to working with him on many more endeavors in the future. ■

Recent Sci-Tech Discussions

Hard-to-Clean Areas

The following remarks are taken from an exchange in the Pharmaceutical Sci-Tech Discussion Group, a PDA-sponsored Online Forum held 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 at www.pda.org and join.

This month's posting...

Question

Is there specific study or exercise required to determine the hard-to-clean area before execution of equipment cleaning validation? Suggest relevant guideline or literature.

Response 1

One way to determine the hardest-to-clean location is:

Spray the entire equipment surface, or process the equipment with a 0.2% resorcinol solution. Then undergo the cleaning methodology. If you then shine a UV lamp on the equipment, areas where the resorcinol has not been cleaned "the hardest-to-clean location" will fluoresce.

Response 2

I agree with this approach but recommend using 0.01 % wt./V fluorescein in 2-propanol for non-organic, solvent-based processes (aqueous) cleaning processes and 0.05 % wt. /wt. fluorescein sodium in water for organic-solvent-based cleaning processes.

In my experience, not only does this find the hardest-to-clean area or areas but, when properly coupled with the appropriate cleaning agents, can be used to quickly establish whether a vessel or other equipment is truly clean (down to the less than 1 ppb level) without requiring any sample work-up beyond rinsing the swabs & qs. to vol. when swabs are used.

As to the guideline or reference, I would recommend reading 21 CFR 211.160—especially the part that requires all that is done with respect to the control of the manufacturing of drug products to be, first of all, scientifically sound and, second, appropriate. In addition, firms are required to establish and/or justify (prove) the validity of their samplings and testing, or examinations.

Response 3

I would only partially agree with the other postings that recommend a resorcinol or fluorescein coverage type test to determine the hardest-to-clean areas for cleaning validation. There are other factors not considered in these procedures which are important for determining hardest-to-clean. These other factors include the type and nature (dried, for example) of the product (soil) to be cleaned, as well as the engineering of the manufacturing process and the cleaning process. For example, knowing that the product is an aqueous one, and if experience has shown there is a dried residue on the equipment surfaces the liquid/air interface, then one might conclude that such an interface is going to be a hard-to-clean area.

What I generally recommend to assess hardest-to-clean areas is to base hardest-to-clean on:

1. Good engineering (common) sense based on an understanding of the manufacturing and cleaning processes;
2. Past experience with what areas of the equipment are more difficult to clean, and
3. Any information from scale up experiments which result in failures. Those failures might suggest difficult to clean locations.

The problem with just using a coverage-type test (and I realize the two procedures described are different from the riboflavin coverage test) is that these procedures only tell you what areas are hardest to clean because coverage is poor. Do they really add anything to the information one gets from a riboflavin test? If they involve the full cleaning cycle, they may add more information. However, if a full cleaning cycle were used, and particularly if the cleaning agent were an alkaline cleaner (where fluorescein is more soluble), any fluorescence after a cycle would probably lead me to redesign my cleaning system, not to select those areas with fluorescence as the hardest-to-clean locations.

If one assumes that the purpose of picking the most difficult-to-clean areas is so that those areas can be swab sampled, and if the resorcinol or fluorescein tests described were used, I would expect 100% cleaning (no fluorescence), and therefore the test would be of no help in determining the most difficult-to-clean areas.

I am not a toxicity expert, but I would also question the use of resorcinol for such an evaluation.

Response 4

It depends on the cleaning method: if you're tal-king a CIP system with spray balls, then a riboflavin surface pattern test will be able to tell you "hardest-to-clean" areas. If you're talking other kinds of cleaning methodology, it is my understanding that a scientific rationale of what you think is "hardest-to-clean" based on spatial configuration, difficult access, etc. is O.K., but you need the rationale behind sample site selection.

continues on page 14

Join this lively online discussion group, where more than 2,000 of your colleagues from around the globe meet and find solutions to complex issues. Access is open to both PDA members and nonmembers, and discussions may be accessed via e-mail or the Web. Visit PDA's Web site at **www.pda.org** to sign up via the Web or send an e-mail to *requests@www2.pharmweb.net*.

New Strategic Initiative, from page 7

regulatory authorities (besides the FDA) believe they should include in their regulations. The PDA Task Group, enjoined to address this industry need, has received the attention of others external to the FDA-regulated industry. The work products that define Good Electronic Records Management (GERM) and models for technology compliance are being touted as comprehensive "de facto best practices" guides for managing all types of electronic records.

The key to compliance for 21 CFR Part 11 is turning out to be a complex equation with functional dependencies on regulatory and legal issues associated with information assurance, management of computing environments, technical features of computing tools, and legacy e-information as evident from the recent PDA GERM Conference in Chicago in June 2003.

21 CFR Part 11 has been the principal driver for FDA-regulated establishments to reassess the importance of how computers are used and validated in our companies with a refocus on electronic information requirements. It was noted in a recent publication by ISPE[1] that, in part, technical compliance to 21 CFR Part 11 is inherently solvable by applying a systems-engineering approach to computer validation. The implication here is that engineering or reengineering, as the case may be for installed computing bases, is predicated on getting the requirements to conform to the information assurance attributes. The bottom line is that mature systems engineering processes, predicated on total quality management (TQM) principles will ensure the features are constructed, tested, and delivered to the business. The Models Document for technology compliance authored by the Part 11 Task Group has advocated this same level of thinking, as does SEI for organizational maturity with regard to computing disciplines, and as do new Agency initiatives for Process Analytical Technology and Corrective and Preventative Actions relative to the drug commodity. It appears that the spheres of scientific disciplines are beginning to align along a common thread of TQM.

In the last five years the PDA members involved in computer-related Task Groups have been taking some major steps in establishing a foundation for PDA to offer an alternative to traditional computer validation thinking and to be the authoritative resource relative to the use of computers in support of the FDA-regulated businesses. Reshaping computer validation as a systems engineering activity is unavoidable; it is beginning to make sense from a number of perspectives, including an intrinsic alignment with Agency initiatives driven by a TQM way of thinking, and when complying with the diversity of regulations that are focused on information assurance. The common tool set is the human engineered assembly of processors and software used to execute the day-to-day operations and regulated activities of businesses. Corporations are dependent on their computing technologies to be correct, reliable, and suitable for their intended purpose. They cannot exist or effectively compete without a healthy digital nervous system. ■

[1] Computer Systems Validation: A Systems Engineering Approach", Uzzaman, Sameh, Pharmaceutical Engineering, Vol. 23, Number 3, May/June 2003, pp. 52–66.

Hard-to-Clean Areas, from page 12

Response 5

First of all, the points you make (concerns you raise) are valid ones.

In my limited experience with a variety of systems, most all of the cleaning systems used contained some cleaning aqueous solution whose pH is greater than 8 and involved the cleaning of stainless steel surfaces [usually type 316 (SS 316)].

In those instances, if one first treats the entire system, including all air/liquid or air solid interfa-ces with the appropriate fluorescein solution and allows it to dry on the surface, then, even though fluoresce-in is "soluble" in basic aqueous solutions, one finds that the fluorescein's affinity for SS 316 (and SS 304) and for "glass-lined" vessels, the flawed areas, if any, where the metal surfaces are accessible to the coating solution is sufficiently high that more than one clean-ing cycle is required to reduce the background level of fluorescein fluorescence to below the level detect-able by a modern high-sensitivity differential dual-monochromator spectrofluoremeter.

In my experience, if the cleaning system were properly selected, fluorescein fluorescence would be a more than adequate indicator of the failure to clean the surface completely.

This experience included the cleaning of systems where "resin" type coatings (shellacs) were used in coating beads containing the active where the first cleaning step was essentially a barely wetted silica-based sand and solid sodium-hydroxide slurry (pH > 13) to remove most of the resin.

Having "serendipitously" found that the affinity of fluorescein for "steel" surfaces was significant, I was able to assist the firm for which I was working at the time to develop a robust cleaning procedure that en-sured:

1. The cleaning procedure was effective;
2. The cleaning procedure left all surfaces contacted by the cleaning solutions and rinses used clean;
3. The least soluble component at the surfaces being cleaned, using the simple fluorescein-containing non-ionic surfactant/sodium silicate-based system used in the final cleaning cycle was the fluoresce-in [provided the water used for the solution was hot (>160° F) softened water and de-ionized or better water was used for the rinses], and
4. Residual differential fluorescence in the water rins-es could validly be used to track the cleaning of the vessel and the removal of the residual fluorescein from the surfaces of the vessel after the "process residues" and the other components in the final cleaning solution.

In cases where the drug itself strongly fluoresces at a different wavelength maximum than the fluorescein, the typical behavior observed was the removal of the drug to below its limit of detection (sub ppb), followed by the removal of the fluorescein to below detection level (sub ppb).

In most cases, the change in fluorescein level with rinsing showed a steady decline with each suc-cessive rinse until, at usually the second or third rinse, the level drops precipitously to below the sys-tem's limit of detection (0.1 ppb in the differential spectrofluoremeter system being used in these stud-ies). As you pointed out, unlike resorcinol, fluores-cein is relatively non-toxic, and like riboflavin, has a low limit (ppb) of detection and can be (and is) di-rectly incomparable in all surfactant-based or strongly basic aqueous cleaning solutions.

Hopefully, the preceding has adequately addressed your concerns and provided sufficient detail to allow you and others to check this approach out and see if it is suitable for use in a given system—after all, no ap-proach is universally applicable.

Response 6

What I have found in my experience is that "hard-to-clean" areas cannot be predicted. And in my opinion, they should not be. I have had a few "eye-openers" where surfaces that should have been "easy to clean" had higher residue levels than the selected "hard-to-clean" surfaces. It happens. Without data to back up your choice, you are guessing. More often than not, "hard-to-clean" selections are made by someone sit-ting behind a desk using "common sense".

I believe in "fingerprinting" the equipment surfaces to determine what the cleaning process is capable of. That is, take samples all across the equipment—what looks easy and what looks hard—all of it. Then you know what your cleaning process is capable of. This can be done during initial cleaning development studies. Then, maybe during the validation runs, or during any monitoring you may be doing, you can limit your sam-pling to surfaces that have been demonstrated to be "hard-to-clean," not just the ones you guessed at. How-ever, I would still take all sample sites. It's not a lot of extra sampling work, and the instrument you are using (HPLC, TOC, etc.) is already set up to run. It will just have a longer run time. ■

PDA Depth Filter Task Group Seeks Members

Depth filters play an increasingly important role in the manufacture of a wide range of pharmaceutical and biopharmaceutical products. Yet there are no readily available standards and practices that manufactur-ers strive to meet to be accepted in this market as there are for sterilizing filters. It is not the purpose of this group to develop standards but to recognize and characterize practices that are in use in terms of removal ratings, validation, materials of construction, physical formats, qualifica-tion testing, test parameters, flowrates/differential pressures, extract-ables, toxicity testing, particle and bacterial challenge and the ability to protect final filters.

The objective is to provide guidance to users that will allow them to make comparisons of all available depth filter products on a common basis. This is considered a necessity in a field where the information cited above, particularly regarding removal ratings, is often contentious and frequently not conducive to making valid comparisons.

All who wish to participate in this activity should contact Jack Cole (jvcole@aol.com), leader of PDA's Filtration Interest Group, by providing your name and e-mail address. ■

—Russell E. Madsen

Revision to Annex 1, from cover

Some of the key issues with Annex 1 are:

1. Annex 1 now sets a limit of Not More Than (NMT) one, 5.0 μm airborne particles per cubic meter in the Grade A area at rest and in operation. This is in contrast to the widely accepted EN/ISO 14644-1 that sets a limit of NMT 29 5.0 μm particles per m^3.
2. The mandated use of continuous particle monitoring in Grade A and B zones is confusing and is not clear. Is it acceptable to use a monitoring unit that stops monitoring for a short time while the unit calculates and prints the results? Problems like this are due to the terminology used in the document.
3. The document uses terms such as "laminar flow" (now widely referred to as unidirectional air flow). True laminar flow is difficult to achieve and measure.

In his comments regarding the need for revisions to Annex 1, Hargreaves said the International Organization for Standards (ISO) 14644-1 was the trigger for the review, not the trigger for adoption, and the scope of review was the particle concentration only. He said that after the approved draft was issued for comments, the magnitude of the response was an enormous shock to the drafting group. This created a problem since the administration system is not resourced to transparently record the consideration of comments on this scale. Further complicating the situation was the fact that many comments were outside the remit of the modified text subjects.

Based on the comments, the EMEA ad hoc Inspectors Group has formed a working party from four nations (UK, France, Germany, and Italy) to develop a view as to whether Annex 1 should be thoroughly reviewed. This working party will report their opinion to the ad hoc Inspectors Group in October. Hargreaves believes that a full review is appropriate. Meanwhile, MHRA has agreed in principle to support the effort required. Also, EMEA recognizes the process will be high profile and will want to find an effective way of working with industry through pan-European groups to improve the transparency of the drafting and review process.

The following summarizes Farquharson's report of the activities in Europe:

The European Regulatory System Responsibilities:

- The supervision of GMP is a national responsibility;
- The publication of guidelines on GMP is the responsibility of the EC;
- EMEA has responsibility for the coordination of centralized inspections;
- EMEA's ad hoc GMP Inspectors Group was originally set up to deal with process and procedures for inspections for centrally authorized products. (This has now extended into matters of GMP writing), and
- The EC set up a group in 1981 to deal with general GMP harmonization issues and the drafting of the EU GMP Guide.

What is the EMEA:

- One of 15 independent European Community agencies;
- Is composed of a secretariat (EMEA staff), management board, scientific committees, working parties and expert groups (members are nominated by European Union (EU)/European Economic Association (EEA) Member States);
- Mobilizes existing scientific and inspection resources of the EU/EEA for the:
  - evaluation of centralized medicinal products;
  - preparation of guidelines on safety/quality efficacy, and
  - the coordination of verification of compliance with the principles of GMP, Good Clinical Practices (GCP), and Good Laboratory Practices (GLP).

EMEA's ad hoc GMP Inspectors Group—Origins:

The 1981 European Commission established "Working Party on Control of Medicinal Product & Inspections" which:

- Drafted the first European GMP guide and subsequent revisions until 1998;

continues on page 17

Pictured L to R:
Jim Agalloco (Agalloco & Associates), Russell Madsen (PDA), Stephen Bellis (AstraZeneca), Gordon Farquharson (Bovis Lend Lease Pharmaceutical)

Biotechnology
Frank Matarrese
Chiron Corporation
4560 Horton Street
Emeryville, CA 94608
Tel: (510) 923-3128
Fax: (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: (610) 889-7350
Fax: (610) 296-2339
E-mail—
bmeserve@hollisgroup.com

Contract Manufacturing
Michael R. Porter
Eli Lilly & Company
DC 3852
Eli Lilly Corporate Center
Indianapolis, IN 46285
Tel: (317) 277-2595
Fax: (317) 276-8116
E-mail—
porter_michael_r@lilly.com

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

Filtration
Jack Cole
Jack Cole Associates
115 Turtle Cove Lane
Huntington, NY 11743
Tel: (631) 424-3658
Fax: (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: (805) 447-4813
Fax: (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: (315) 457-3242
Fax: (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: (610) 567-4452
Fax: (610) 238-1100
E-mail—
dimitri.wirchansky@jacobs.com

Lyophilization
Edward H. Trappler
Lyophilization Techology
30 Indian Drive
Ivyland, PA 18974
Tel: (215) 396-8373
Fax: (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: (847) 478-1439
Fax: (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: (817) 551-4014
Fax: (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: (610) 313-4338
Fax: (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: (301) 986-8640
Fax: (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: (847) 937-8191
Fax: (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: (717) 207-3858
Fax: (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: (317) 277-3618
Fax: (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: (317) 276-4116
Fax: (317) 276-1838
E-mail—
rhb@lilly.com

Sterilization/ Aseptic Processing
James P. Agalloco
Agalloco & Associates
2162 US Highway 206
Belle Mead, NJ 08502
Tel: (908) 874-7558
Fax: (908) 874-8161
E-mail—
jagalloco@aol.com

Training
Thomas W. Wilkin, Ed.D.
Schering-Plough Corp.
M/S R-40
2000 Galloping Hill Road
Kenilworth, NJ 07083-1328
Tel: (908) 298-5213
Fax: (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: (712) 297-8074
Fax: (712) 297-8074
E-mail—
fsk@lowatelecom.net

Validation
Bohdan M. Ferenc
Qualification Services
116 Route 10
Succasunna, NJ 07876
Tel: (973) 927-9823
Fax: (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: (269) 833-8906
Fax: (616) 833-9987
E-mail—
john.g.shabushnig@pfizer.com

Revision to Annex 1, from page 15

- Is responsible for the harmonization of inspections;
- Provides for the management of Mutual Recognition Agreements (MRA);
- Collaborates sessions with EMEA (as of 1995);
- Convened the first ad hoc meeting of Inspection Services in 1996;
- Provides for coordination of centralized inspections, and
- Provides procedures, policies, sampling and testing, training, and provides for the exchange of information.

EMEA's ad hoc GMP Inspectors Group:

- Meets four to five times per year;
- Is made up of representatives from Member States' inspectorates covering both human and veterinary products, and
- Works on:
  - GMP-related guidelines;
  - Agreement on GMP-related procedures;
  - The exchange of information;
  - The harmonization of GMP inspections in the EU/EEA;
  - The implementation of MRAs;
  - The practical implementation of GMP guidelines, and
  - The coordination of the sampling/monitoring of medicinal products.

What does this mean in practice?

- The Commission is responsible for the publication of the GMP;
- The Commission relies on technical input from EU GMP inspectors;
- EMEA coordinates this input through the ad hoc Inspectors Group;
- Initiatives for revisions may be prompted by:
  - Industry proposals;
  - Regulator proposals, and
  - International developments, e.g., ISO 14644-1&2.
- When a concept paper or problem statement is developed:
  - It is discussed in an ad hoc group;
  - A rapporteur volunteer is requested, and
  - A drafting group may be set up if there is a need for additional input to the normal meeting process.

PDA plans to host a meeting in Europe on Annex 1 as soon as the situation surrounding the further revision of Annex 1 is clear. ■

—Russell E. Madsen and William Stoedter

U.S. Regulatory Briefs

The U.S. Food and Drug Administration's Initiative Against Counterfeit Drugs
On July 16, 2003, the Food and Drug Administration (FDA) launched a major initiative to more aggressively protect American consumers from counterfeit drugs. Counterfeit prescription drugs are not only illegal but are also inherently unsafe. The initiative is designed to:

- better identify the risks and threats from counterfeit drugs;
- establish a public and private coalition to fight drug counterfeiting and distribution, and
- develop new tools to aid in identifying, deterring, and combating counterfeiting.

As part of the initiative, FDA will create an internal task force to explore the use of modern technologies and other measures, such as stronger enforcement, to make it more difficult to distribute counterfeit drugs. The task force will submit its initial findings and recommendations in 60 days and will issue a final report in six months, after public comment.

Protecting the Public Health: FDA Pursues an Aggressive Enforcement Strategy
FDA is committed to pursuing Federal Food, Drug, and Cosmetic Act violations. Enforcement activities include warning and untitled letters, injunctions, recalls, arrests, and convictions. Overall, these point to dramatically increased enforcement, particularly in areas related to the most serious threats to public health, such as arrests and convictions on criminal charges involving potentially dangerous activities and actions against manufacturers making misleading claims about product risks and benefits.

FDA's most decisive actions, those that remove products from the market and that bring criminal charges against people who would harm the public, have increased the most. Data from fiscal years 1998 to 2002 show:

- Injunctions rose from 11 to 15;
- Recalls increased from 3,532 to 5,025;
- Arrests went from 250 to 286, and
- Convictions went from 194 to 317.

FDA encourages those interested in learning more about the Agency's enforcement record to consult the FDA Web site at www.fda.gov.

Electronic Review-Electronic Common Technical Document FDA would like to work closely with people who plan to provide a submission using the eCTD specifications, and the Agency offers several steps to help smooth the process. (Posted 6/23/2003; corrected file posted 7/3/2003.)

The ICH eCTD specification calls for a regional Module 1 Document Type Definition file to allow regional information to be submitted along with information from ICH Modules 2 to 5. The Agency is using the FDA draft eCTD module 1 DTD version 2.01 (to download, right click on the link and choose "Save Target As") to gain experience on working with an electronic table of contents viewer. After downloading, the file can be viewed with any text software. (Updated 7/1/2003.)

The FDA draft eCTD module 1 DTD version 2.0 file is meant for informational purposes only and will likely change. The file should not be considered a component of any guidance, policy, or FDA regulation. Consult FDA regulations and guidance or send inquiries to esub@cder.fda.gov for information on submitting electronic applications to the Agency. To save this file, right-click on the link and choose "Save Target As". The file can be viewed with any text software. Please direct any comments on this file to Timothy Mahoney at mahoneyt@cder.fda.gov.

The FDA has been working on software for reviewers to navigate electronic submissions based on the ICH eCTD. The agency has listed some of the general understanding it has gained to date of the useful requirements review staff may have when viewing an electronic table of contents. FDA thinks this list will change as the Agency gains more experience viewing electronic submissions. See General Considerations for FDA Reviewers Viewing an Electronic Table of Contents (Posted 2/24/2003).

Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format-Postmarketing Periodic Adverse Drug Experience Reports FDA is announcing the availability of a draft Guidance for industry entitled "Providing Regulatory Submissions in Electronic Format-Postmarketing Periodic Adverse Drug Experience Reports". A postmarketing periodic adverse drug experience report includes individual case safety reports (ICSRs), attachments to ICSRs (ICSR attachments), if applicable, and descriptive information. The descriptive information includes the narrative summary and analysis of the information in the report, an analysis of the 15-day alert reports submitted during the reporting interval, and the history of actions taken since the last report because of adverse drug experiences (e.g., labeling changes, studies initiated). This draft Guidance discusses general issues related to the electronic submission of postmarketing periodic adverse drug experience reports. It provides guidance on the submission of periodic ICSRs, ICSR attachments, and descriptive information in electronic format. Applicants are referred to the draft Guidance for industry "Providing Regulatory Submissions in Electronic Format-Postmarketing Expedited Safety Reports" (May 2001) for details on submitting periodic IC-

SRs and ICSR attachments to FDA. Applicants are also referred to the Guidance for industry "Providing Regulatory Submissions in Electronic Format—General Considerations" (January 1999) for details on submitting the descriptive information to FDA on physical media.

For further information contact: Randy Levin, Center for Drug Evaluation and Research (HFD-001), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, (301) 594-5411, Levinr@cder.fda.gov; or Michael Fauntleroy, Center for Biologics Evaluation and Research (HFM-588), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, (301) 827-5132, Fauntleroy@cber.fda.gov. Persons with access to the Internet may obtain the document at either http://www.fda.gov/cder/guidance/index.htm or http://www.fda.gov/cber/guidelines.htm.

Draft Guidance for Reviewers and Industry on Good Review Management Principles (GRMPs) for Prescription Drug User Fee Act (PDUFA) Products The FDA has announced the availability of a draft Guidance for reviewers and industry entitled "Good Review Management Principles for PDUFA Products." This document is intended to provide guidance to industry and the review staff in CDER and CBER on GRMPs for the conduct of the first-cycle review of a new drug application (NDA), a biologics license application (BLA), or an efficacy supplement under PDUFA.

A key aspect of the GRMPs is their emphasis on effective communication between the Agency and applicants throughout the drug and biological product development and review process.

For further information contact: John Jenkins, Center for Drug Evaluation and Research (HFD-020), Food and Drug Administration, 1451 Rockville Pike, Rockville, MD 20852, (301) 594-3937; or Robert Yetter, Center for Biologics Evaluation and Research (HFM-25) Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, (301) 827-0307.

The draft Guidance may be obtained at either: www.fda.gov/cder/guidance/index.htp or www.fda.gov/ohrms/dockets/default.htm. ■

—William Stoedter

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

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

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

TW Texwipe®

Better solutions, together.

www.texwipe.com

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

Visit us at the 2003 PDA Annual Meeting—Booth #323

Assessing the Impact of PDA Comment Documents to Determine How to Effectively Comment on Regulatory Documents

by Jean-Paul R. Gleeson

PDA is a non-profit international association of members who are involved in the development, manufacture, quality control and regulation of pharmaceuticals and related products. Its mission is to "support the advancement of pharmaceutical technology by promoting scientifically sound and practical technical information and education for industry and regulatory agencies," (PDA, 1998a, p. 1). They provide technical information to regulatory agencies through commenting on proposed regulatory documents from the FDA and other regulatory bodies. To review and comment on documents, PDA typically assembles a panel of experts from its membership. They also make these comments available to the public through publishing them on their Web site at www.pda.org. This allows pharmaceutical companies and other organizations to see their comments and to determine what else they may want to add or reiterate from the PDA comments. Before a regulatory document (i.e., guidance document or federal regulation) from the FDA becomes a final draft, it is first published in the *Federal Register*, or made available through their Web site as a draft document. It is then available for review and comment by companies and organizations like PDA for a certain time period. Soon afterwards, the document is published in final form in the *Federal Register* and through the FDA Web site with the reviews and comments incorporated accordingly into the final document.

To review and comment on documents, PDA typically assembles a panel of experts from its membership.

Even though PDA has existed since 1946 and began commenting on regulatory documents very early after its establishment, they have yet to assess the impact of their comments on the final publication of such documents on which they have commented. This project was sponsored by PDA to explore the effectiveness of PDA's comments on the final wording of regulatory documents. This project was necessary to complete my Master's degree at San Diego State University's Regulatory Affairs program.

In comment documents published by PDA, there are often general comments and specific comments on sections of draft documents. To assess the impact of comments, the draft document was compared to the final publication where comments were made. If any change occurred in the final publication of the document in the sections commented on by PDA, this comment was considered to have an impact.

The impact of PDA's comments on draft FDA documents is assessed below.

1. PDA published comments on the Guidance Document "Changes to an Approved NDA and ANDA" while it was still in draft form. Out of 84 comments, 27 comments had an impact on the final Guidance Document. Therefore, 32% of the comments resulted in modification of the final Guidance Document.
2. PDA published comments on the proposed rule 21 CFR Part 11.1-300 that was published in 1992. Out of 25 comments, 21 comments had an impact on 21 CFR Part 11. Therefore 84% of the comments resulted in modification of the final Guidance Document.
3. PDA published comments on the draft Guidance Document entitled "BACPACI Intermediates in Drug Substance Synthesis." Out of 33 comments, 22 comments had an impact on the final Guidance Document. Therefore, 66.7% of the comments resulted in modification of the final Guidance Document.
4. PDA published comments on the draft Guidance Document entitled "Submission of Documentation in Drug Applications for Container Closure Systems Used for the Packaging of Human Drugs and Biologics." Out of 11 general comments, six had an impact on the final Guidance Document. Therefore, 54.5% of the general comments resulted in modification of the final Guidance Document. Out of 72 specific comments, 32 had an impact; therefore 44.4 % of the specific comments resulted in modification of the final guidance document.

This project also explored how to effectively comment on draft regulatory documents published by FDA. The comments above were further categorized into nine categories such that

continues on page 25

Global Regulatory and GMP Briefs

EMEA News

Updating the Notice to Applicants Volume 3B (C7A) The European Commission's (EC) Directorate General Enterprises has released an updated version of the guideline "Excipients in the Label and Package Leaflet of Medicinal Products for Human Use".

The EC Directorate General Enterprises has also released an updated version of Annex 13 of the "Guide to Good Manufacturing Practice (GMP) For Medicinal Products". Annex 13 of the EC Guide to Good Manufacturing Practice provides supplementary guidance on the application of the principles and guidelines of GMP to investigational medicinal products. The revision takes account of the requirements of Articles 13 and 14 of Directive 2001/20/EC, as well as the experience of industry and regulators with the existing annex.

Maximum Residue Limits of Veterinary Medicinal Products in Foodstuffs of Animal Origin A new consolidated version of the Annexes I to IV of Council Regulation n°2377/90, updated on 22.07.2003, is now available in all official EU languages.

New Guideline on the Dossier Requirements for Type 1A and Type 1B Notifications for Minor Variations to the Terms of Marketing Authorisations in the Mutual Recognition Procedure or the Centralised Procedure The new Guideline on the dossier requirements for Type 1A and Type 1B notifications for minor variations to the terms of marketing authorisations granted following the mutual recognition procedure or the centralised procedure. It contains in a convenient format both the conditions applicable to these types of variations in accordance with the new Commission Regulations (EC) No. 1084/2003 and (EC) No. 1085/2003 and the corresponding dossier requirements to be fulfilled. This Guideline replaces the previous guidance in Volume 2C and 6C of the Notice to Applicants for Medicinal Products for Human Use and Veterinary Medicinal Products.

For details on the above-mentioned updates, please visit the EMEA Web site at: http://pharmacos.eudra.org/F2/pharmacos/docs.htm#news.

Australian Regulatory and GMP Briefs

Therapeutic Goods Administration

The Australian health authority, the Therapeutic Goods Administration, has released the following news…

Statement by the Therapeutic Goods Administration (TGA) on Regulations for Sterilisation of Single Use Devices—21 July 2003 Single-use devices (SUDs) are those devices that are intended by the manufacturer to be used once and then discarded. However, a number of States and Territories have facilities that undertake the sterilisation of SUDs.

TGA, the national regulator for medical devices, does not permit the reuse of SUDs, unless the reprocessing of those devices is done to a standard that ensures the devices are safe and perform as originally intended. TGA's reach does not extend to public hospitals in the States and Territories where most reprocessing of SUDs occurs.

TGA has taken its concerns up directly with States and Territories through Australian health ministers, and an agreement has been reached on the implementation of a national regulatory framework for any remanufacture of SUDs.

TGA's policy is that if there is to be reuse, it can only be done on premises licensed by the TGA, and any remanufacturing that takes place must be in accordance with the standards that apply to the original manufacture of the device. In other words, the sterilised SUDs must be of the same quality, performance, and safety as if it were a new device.

Health ministers charged TGA with the role of developing the regulatory framework which ensures that if a healthcare facility remanufactures an SUD, that facility will be regulated as a medical device manufacturer and will need to be licensed by the TGA and comply with rigorous good manufacturing requirements.

TGA is now moving to implement the regulatory framework in consultation with the health departments of the States and Territories. It is proposed to phase in the new regulatory requirements over a two-year period to enable public hospitals to implement the new requirements. For more information, please contact Kay McNiece, Media Adviser, TGA, at +011 0412 132 585.

The Global Collaboration for Blood Safety—28 July 2003 Recognition of the need for a Global Collaboration for Blood Safety (GCBS) was first endorsed by 41 countries represented during the Paris AIDS Summit in 1994 and adopted by the 48th World Health Assembly as WHA resolution 48.27 (1995), by all 191 World Health Organization (WHO) Member States prioritising the need for global collaboration to improve blood safety.

Over 1999–2000, the TGA took on a leadership role in furthering collaboration and was pivotal in a series of meetings at WHO which assessed the need for senior health policy makers to set up collaboration in blood safety at various levels. This led to a meeting involving policy makers and scientists in Geneva in March 2000 where the state-of-the-art in blood safety was reviewed and key outcomes were discussed. This fed directly into the setting up of the GCBS in November 2000 with TGA as a founding member.

GCBS is a voluntary partnership of internationally recognised organisations, institutions, associations, agencies and experts from developing and developed countries sharing expertise, identifying problems, seeking solutions and working towards the common goal of global blood safety as equal, collaborative partners. WHO is a member of GCBS and also provides its secretariat.

TGA is honoured to be in the GCBS, and is a member of the senior leadership through Dr. Albert Farrugia's chair of the Policy Group of the Collaboration.

For details on TGA, please visit the Web site, www.health.gov.au/tga/new/new.htm. ■

—Gautam Maitra

Eliminate Filter Sterilizing

Disinfectants & Sporicides

SIMPLEMIX®

What Is SimpleMIX?

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

US and Foreign Patents Pending

Features of SimpleMIX:

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

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

vai
Veltek Associates, Inc.
1039 West Bridge Street
Phoenixville, PA 19460-4218 USA
(610) 983-4949 • Fax (610) 983-9494

INNOVATIVE CLEAN ROOM PRODUCTS

Visit us at the 2003 PDA Annual Meeting—Booth #521

Meet the Regulators

Thomas Lönngren, Executive Director, EMEA

Contact information:
EMEA
7 Westferry Circus,
Canary Wharf
London E14 4HB, UK
E-mail:

Thomas Lönngren was trained as a pharmacist from the University of Uppsala, Faculty of Pharmacy. He holds a M.Sc. in social and regulatory pharmacy. Mr. Lönngren did his post-graduate studies in management and health economics. He was a lecturer at the University of Uppsala from 1976 to 1978. From 1978 to 1990 he worked for the National Board of Health and Welfare, Sweden, during which time he was responsible for herbal medicines, cosmetics, medical devices, narcotics and contraceptives. From 1982 to 1994 Mr. Lönngren acted as senior pharmaceutical consultant for the Swedish Health Cooperation Programme in Vietnam. He joined the Swedish Medicinal Products Agency in 1990, serving as Director of Operations and later as Deputy Director-General. He has been the Executive Director of the EMEA since January 2001. ■

—Gautam Maitra

Glenda Silvester, EMEA

Contact information:
EMEA
7 Westferry Circus,
Canary Wharf,
London E14 4HB, UK
E-mail:
glenda.silvester@emea.eu.int

Glenda Silvester is a Specialised Group Leader within the Quality of Medicines Sector of the European Agency for the Evaluation of Medicinal Products (EMEA). This group specialises in biotechnology and biologicals and has a particular interest in blood products (both plasma-derived and recombinant alternatives), monoclonal antibodies, and gene therapy products. She is the Secretary of CPMP's Ad Hoc Working Group on Blood Products (BPWG), which addresses safety and efficacy aspects of blood products.

Glenda joined EMEA in 1997 after many years in the UK Medicines Control Agency (now known as the Medicines and Healthcare Products Regulatory Agency), with responsibilities including the evaluation of the quality of biological and biotechnology medicinal products; her particular interest was in plasma-derived medicinal products. Glenda has also worked in industry and in the regulatory fields. Currently, she is in the program committee of the PDA/EMEA European Virus Safety Forum, which will be held in Langen, Germany from 29 September to 1 October 2003. (Visit www.pda.org/PDF/PDA-EMEA-VirusSafety-Bro.pdf for more information.) ■

—Gautam Maitra

Assessing the Impact of PDA Comment Documents, from page 21

one comment could be considered in more than one category. A qualitative predictor was created for evaluating the total percent likelihood and the moving average for each comment type. This qualitative predictor generally predicts the likelihood for most comments for most documents. Most of the error occurred when there was only a small number of comments that belonged to one category.

Low and moderately effective comment types were further evaluated by looking at impact and non-impact comments of the same category. These comments were compared and contrasted to determine what techniques qualitatively gave more likelihood of impact. These results are summarized below for easy reference. In general, comments should:

1. Include a simple and valid justification for the proposed revisions;
2. Not attempt to limit the scope of the guidance or regulation;
3. Not ask the Agency to include what is already provided for in the guidance or regulation, and
4. Suggest an alternative mechanism by which the Agency can provide the amount of guidance or regulation they think is necessary.

The author wishes to thank the chair of his project committee, Robert Wang, and the other two committee members: Larry Gundersen and Gretchen Vik; members of PDA: William Stoedter and Edward Fry, his supervisor Caroline Lee; members of the Pfizer-La Jolla Library Staff: Pam Kubiak and Beth Kilpatrick; David Porter from USP; Pfizer Employee Statistics Expert Min Zhang; and the Pfizer Education Reimbursement Program for funding his education.

The entire thesis can be found on the PDA Web site at http://www.pda.org/membersonly/PDALetterArchive.asp. ■

Possessing all but super hero powers,

the Environmental Monitoring Software System™ (EMSS™) is here to transform the way you handle environmental and water sampling data. EMSS can collect, document and trend data effortlessly, plus give you complete control of all your sampling and testing.

You may not be able to leap tall buildings in a single bound with EMSS, but you'll feel like the hero when you can comply with regulatory requirements ***and*** exceed industry guidelines.

Bring the future of data management to your microbiology lab with EMSS. *For a copy of your 21CFR Part11 assessment, contact your local BD representative today.*

BD

BD Diagnostic Systems
7 Loveton Circle
Sparks, MD 21152-0999 USA
800.638.8663
www.bd.com/industrial

Visit us at the 2003 PDA Annual Meeting—Booth #225

34th R³-Nordic Contamination Control Symposium

Turku, Finland
2–4 June 2003

R³-Nordic, the Nordic Association for Contamination Control, is a non-profit, independent association for the promotion of new technologies in contamination control in the Nordic countries. The aim of their annual symposium is to provide knowledge of contamination control and cleanroom technology dealing with topics in the pharmaceutical, food, and microelectronic industries.

The venue for this year's symposium was Turku Polytechnic in the BioTurku region. A broad range of topics was discussed this year, including: contamination control, cleanroom technology and management, regulations and standards in cleanrooms, cleanroom clothing, isolation applications, air handling, environmental monitoring in production, process design, production hygiene, cleanability, cleaning and disinfection, risk assessment, risk management in packaging material production, quality systems, contamination control, occupational safety, production of pharmaceuticals, biopharmaceuticals, biomedicines, and vaccines.

The format of the program consisted of three sessions that ran in parallel: the pharma session, the food session, and the electronic session. The exhibition presented an excellent forum in which to interact with the participating companies. A fascinating presentation was given on Turku Science Park, which is the core of Southwest Finland's innovation system where research, education, and innovation have become a flourishing business in the field of biotechnology. The expertise of three universities, one polytechnic and the joint effort of numerous stakeholders gave rise to this interactive and innovative community that today hosts a growing number of high technology companies. Today, the Turku Science Park has 180,000 sqm of office, laboratory, and production facilities for companies. By 2009, new construction projects are estimated to double the present capacity. There are currently 250 high technology companies operating in the ten buildings of Turku Science Park. For further details please visit the Web site: www.bioturku.fi.

It was just in October 2002 that I attended the last R³-Nordic annual symposium. I extend my heartfelt thanks to R³-Nordic for inviting PDA President Neal G. Koller and me to this year's event. The next symposium will be held in Helsingor, Denmark from 10-12 May 2004.

For more information about R³-Nordic, visit www.pda.org click on "Links," then scroll down to "Associations." ■

—Gautam Maitra

A3P—Association for Clean and Sterile Products

16th International Congress in Biarritz, France

A3P, the Association for Clean and Sterile Products in the biomedical, cosmetic, food, and pharmaceutical fields, will hold its 16th international Congress on 21, 22 and 23 October 2003. As in each year, special emphasis will be placed on water and air: water as a raw material and as a potential factor of contamination in the pharmaceutical industry. Depending on its various descriptions (water for injection, distilled, ultra filtered, demineralised, steam, or drinkable), water has to meet physical, chemical and bacteriological criteria laid down in the various pharmacopoeia. Water loops and any dead ends are closely examined by inspectors, because water is a critical fluid which can come into contact with our various products.

The issue of air will also be a major focus of this Congress, as it is a vector of contamination as a result of several factors: staff, air filtration systems, etc. This vector must be properly controlled to ensure that it is never a source of contamination for our products. We are all increasingly challenged on this issue, which gives rise each year to comments from the inspectors from the French Health Authority, AFSSAPS, or FDA (regarding such issues as: failure to observe the air class, little or no interpretation of the results of environmental checks, no germ mapping according to the buildings, etc.).

Three topics will be addressed in this upcoming Congress to meet these concerns, two on water and one on environmental control. The first will be addressed through a conference and will cover "EP and USP requirements for measuring conductivity and TOC in pharmaceutical waters". This will be conducted by Xavier Lestienne, société Mettler Tolédo, France. The two others topics will be covered in workshops: Atelier n°2 "Définition des règles et usage en matière de production et de distribution d'eau purifiée en fonction des niveaux requis", in French, with moderators Robert Neri, sociéte BWT; Henry Lérat, société H. Burkhalter; and A3P representative G. Rumpler. Atelier n°5, "Contrôles microbiologiques d'environnement en industrie pharmaceutique: réglementation, nouveaux outils, interprétation des résultats au laboratoire" will also be presented in French, with animateur Véronique Esteve-Daix, from Aventis Pharma; Patricia Lacroix, from Aventis Pharma; and M. Decrulle, from A3P.

For a complete program of the event, please visit www.a3p.asso.fr/enhtml/ev_gb/cong03gb.htm. To register online, visit www.a3p.asso.fr/enhtml/ad_gb/ad1_gb.htm. All of the lectures will be translated simultaneously, and some workshops will be held in English. ■

—Gautam Maitra

Basel Pharmaceutical and Biopharmaceutical Forum

30 June 2003

PDA's second PDA Basel Pharmaceutical and Biopharmaceutical Forum of 2003 occurred on 30 June. Participants from Switzerland, Germany, France, UK, Finland, Sweden, and Turkey took part in the forum. These one-day forums sponsored by PDA offer:

- Salient topics that are important issues regarding manufacturing, GMP, and regulatory concerns;
- At least one European health authority expert who is invited;
- At least two industry experts who are invited, and
- A one-hour panel discussion at the end of the day where attendees discuss their questions directly with experts in the field.

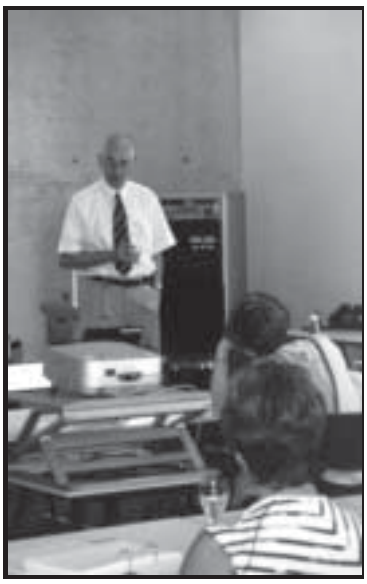
This latest forum featured speakers Dr. Dirk Barends from the Dutch RIVM and Dr. Vinod Shah from the US FDA, CDER Division. Two important participants from industry, Dr. Herald Rettig of Bio Vista, Switzerland, and Dr. Johannes Krämer of PHAST GmbH, Germany, created a very interactive atmosphere, especially during the panel discussion. The main topics of discussion were In-vitro/In-vivo Correlation (IVIVC) and Biopharmaceutics Classification Systems (BCS). The regulatory guidances addressing IVIVC and BCS were created with the purpose of reducing the regulatory requirements either (1) during the development of drug products or (2) when modifying the marketed products.

These one-day forums sponsored by PDA offer salient topics that are important issues regarding manufacturing, GMP, and regulatory concerns.

The fundamentals of the whole concept of In-vitro dissolution were explained at the outset by Dr. Vinod Shah. He explained that dissolution testing is used to assure product quality. Under some conditions, dissolution can be used as a bioequivalence test. He also noted that it helps to establish a procedure for granting Biowaiver. Dissolution assures product sameness under changes pertaining to the Guidance on Scale-up and Post Approval Changes (SUPAC).

The Basel Pharmaceutical and Biopharmaceutical Forum is held four times a year at the same location. The next two Forums will be held on 4 and 5 December 2003. The two-day special program is dedicated to training the European health authority Assessors of the chemistry, manufacture and control part of the marketing application dossier. Please visit our Web site at www.pda.org for more details on these programs. ■

—Gautam Maitra



Dr. Dirk Barends, Institute of Public Health and Environment (RIVM), one of the Forum's speakers.

Dr Harald Rettig, BioVista GmbH, gives a presentation.

L–R: Forum speakers Dr. Johannes Krämer, PHAST Gmbh; Dr. Dirk Barends, Institute of Public Health and Environment (RIVM); Dr. Harald Rettig, BioVista GmbH; and Dr. Vinod Shah, FDA.

PDA SciTech Summit™

March 8–12, 2004 • Courses: March 10–12, 2004

Save the date!

Plan now to be a part of the 2004 PDA SciTech Summit™, the ultimate resource for your company's training and education needs. Send at least *three* representatives from the same corporate site, and the fourth conference registration is FREE *!

Industry and regulatory experts will discuss critical topics such as:

GMPs in Development

- PAT: potential impact on how we develop drugs;
- Risk-(science) based GMPs: the impact on the pharmaceutical development process;
- Comparability protocols: building a foundation during development, and
- Virtual development (outsourcing, contractors and partners).

Sterilization

- Fraction negative;
- Filtration;
- Steam;
- EO parametric release;
- BIs/substrates;
- Ozone;
- Terminal Sterilization Diversity (steam, steam/water, water cascade);
- Liquid peroxide;
- New sterilization methods, and
- Bioburden.

Aseptic Processing

- Concept Paper;
- Annex I;
- "Other" A/P, e.g., manual steps;
- Personnel and media fills;
- Disinfectant rotation, and
- Environmental monitoring.

Manufacturing

- Visual inspection;
- Survey results (terminal sterilization and visual inspection);
- New sterile filling technologies;
- Water;
- DOP elimination;
- Blend uniformity;
- Tablet and capsule validation;
- Machine vision;
- Bar coding, and
- Cleaning.

Biopharmaceuticals

- Cold chain management;
- Multi-product biopharmaceutical facilities;
- Viral safety assurance;
- Using model systems to define expectations and provide performance assurance;
- Understanding and meeting European regulatory expectations;
- Critical process parameters as tools for defining expectations and providing assurance, and
- Expectations and assurance in maintaining validated biopharmaceutical operations.

Part 11 issues

- The new FDA Guidance and
- Auditing suppliers

Strategically co-located with the CleanRooms East Exposition, you will discover cutting-edge expertise and state-of-the-art technology for contamination control and drug manufacturing. Win valuable prizes! Don't miss it!

Contact PDA if you are interested in exhibit or speaking opportunities. Watch the PDA Web site at www.pda.org for updated information on the PDA 2004 SciTech Summit™. ■

—Leslie Zeck

* Must be approved in advance by PDA.

PDA Web Seminars: An Affordable Training Tool

PDA has made available on its Web site four of the most popular presentations from recent conferences. From your desktop, you can affordably and easily view previously videotaped presentations with synchronized PowerPoint presentations. A searchable transcript of the presentation is available for your convenience in accessing key information. The audio conference presentations will have the same features, with the exception of the videotaped speaker.

Each presentation is available 24 hours a day, 7 days a week. Purchase online and watch them at your convenience, on demand. Consider gathering a group of colleagues in your company to view the sessions together, leveraging your return on investment. The registration fee for PDA members is $150, the nonmember fee is $300. Visit www.pda.org, select "Web Seminars," and enjoy one of PDA's newest benefits. ■

—Lisa Wade

2003 PDA Annual Meeting, from cover

PDA Training and Research Institute Lecture Courses at the 2003 PDA Annual Meeting

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

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

November 14
- Managing in a GMP Environment
- Change Control & Documentation

2003 PDA Annual Meeting Exhibitors

AAI 510
Abbott Laboratories, OEM Group. 726
Abbott One 2 One 724
Accugenix 422
AES-Chemunex 925
Afton Scientific Corp. 707
American Pharmaceutical Partners, Inc. 629
American Plastics Technology, Inc. 507
American Stelmi Corp. 621
Applied Biosystems 605
Associates of Cape Cod, Inc. 310, 312
Baxter Pharmaceutical Solutions, LLC 512
BD Diagnostic Systems 225, 227
Ben Venue Laboratories, Inc. 624
Biolog, Inc. 116
bioMerieux, Inc. 529, 531
BioPort Corporation 919
Bioquell Inc. 905
Bioscience International, Inc. 719
BioScreen Testing Services 610
Biotest Diagnostics Corp. 329
BOC Edwards Pharmaceutical Systems 622
Cambrex Bio Science Walkersville, Inc. 720
Cambridge AccuSense, Inc. 606
Cardinal Health 806
Carlisle Life Sciences 224
Celsis Laboratory Group 226
Charles River Laboratories 630
Chesapeake Biological Labs, Inc. 211
Clarkston Consulting 802
Clordisys Solutions, Inc. 202
Comar, Inc. 735
Commissioning Agents, Inc. 611
Compliance Software Solutions Corp. 204
Compli, LLC 819
Contec, Inc. 607
Contract Pharma Magazine 207
Covance 205
CRB Consulting Engineers, Inc. 613
CRC Press 506
Cryovac Sealed Air Corporation 504
CUNO, Inc. 708
Decon Labs, Inc. 705
Dresser-ebro Instruments 304
DSM Pharmaceuticals, Inc. 508
Duoject Medical Systems, Inc. 513
DuPont Contamination Control 305
DuPont Qualicon 125
Ecolab 511
Eisai USA, Inc. 308
EMD Chemicals, Inc. 828
ENV Services 907
Envirocooler 917
Gavin Pharmaceutical Services 627
GE Fanuc Automation 235
GE Kaye Instruments, Inc. 324, 326
Genesis Machinery Products 712
Getinge/Castle, Inc. 713
Grace Engineering & Validation, LLC 218
Hach Ultra Analytics 721, 723
Hollister-Stier Laboratories, LLC 710
INTELITEC Corporation 535, 536
ITW Texwipe 323
Kimble Glass, Inc. 231
KMI, a division of PAREXEL International, LLC 730
la Calhene, Inc. 528
Lancaster Laboratories 516, 517
LearnWright, Inc. 604
Lighthouse Instruments 617
Medical Instill Technologies 812
Meridian Medical Technologies 316
Micron Training 725
Micronova Manufacturing, Inc. 407
MIDI, Inc. 213
Millipore Corporation 429, 431
Minntech Filtration Technologies Group 911
Nicomac, Inc. 334
Nikka Densok USA, Inc. 306
Northview Biosciences, Inc. 129
Novatek International 729
Nuova Ompi S.R.L. 534
Oxoid Inc. 631
Pall Life Sciences 221, 222, 320
Pharmaceutical Technology/Advanstar 628
PharmaSys, Inc. 530
Phoenix Imperative, Inc. 130
PML Microbiologicals 625
PSI 409, 411
Quintiles 734
QUMAS 229
Raven Biological Laboratories, Inc. 608
Remel, Inc. 307
rommelag® USA, Inc. 728
Safety Syringes, Inc. 309
Saint-Gobain Desjonqueres 335, 336
Sartorius Corporation 525, 527
SCA Thermosafe 704
Schering-Plough Corp. 220
Schott Forma Vitrum 634, 635
Schott Scientific Glass, Inc. 636
SCI-TEC Inc. 706
Seidenader Equipment, Inc. 428, 430
SeraCare Life Sciences, Inc. 217
Serail Div. of S.G.D. N. America, Inc. 616
SGM Biotech, Inc. 612
SL Pharma Labs, Inc. 406
Sparta Systems, Inc. 228, 230
Stedim, Inc. 505
STERIS Corporation 210, 212
STS duo TEK, Inc. 816
Usifroid America, Inc. 208
Vectech Pharmaceutical Consultants, Inc. 236
Veltek Associates, Inc. 521, 522, 620
Veriteq Instruments 206
VirTis, an SP Industries Company 122
West Pharmaceutical Services 328, 330

These companies will also be exhibiting at the **2003 PDA Annual Meeting**:

Bioprocess International . . . . . Booth 826

CleanRooms Group . . . . . Booth 234

Eli Lilly & Company . . . . . Booth 824

Hardy Diagnostics . . . . . Booth 913

Kinetics Thermal Systems . . . . . Booth 136

Lighthouse Worldwide Solutions . . . . . Booth 817

2004 PDA International Congress—Basel

Product Life Cycle Management for the 21st Century

Messe Basel Convention Center
Basel, Switzerland

Congress and Tabletop Exhibits
February 16–18, 2004

PDA Training and Research Institute Courses
February 19–20

PDA Training and Research Institute Courses

February 19
- Clinical Trials Directive & MP for Investigational Medicinal Products
- Risk Estimation in Aseptic Processing

February 19–20
- CGMPs for Bioprocesses
- Ventilation & Airborne Contamination in Cleanrooms
- Pragmatic Cleaning Validation

Keynote speaker: Carlo Pini, Instituto Superiore de Sanit, to discuss Biotechnology Inspection Issues; Dr. Ajaz S. Hassain, Deputy Director for CDER, will discuss "Process Analytical Technologies" during the "Innovation and Regulation" session; Mark A. Elengold, Deputy Director for CBER, will discuss "Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach" from the CBER perspective.

Register early for PDA's premier international congress held in Basel, Switzerland. The program has been designed to offer valuable information during the plenary sessions, roundtable discussions, concurrent sessions and panel discussions. Take the opportunity to convene with FDA presenters from CDER and CBER along with industry for discussions on risk assessment, corrective and preventative action programs and further developments in the "Pharmaceutical Manufacturing in the 21st Century" initiatives. Both the European and US perspectives will be openly discussed.

Roundtable Discussion

Start off your morning by joining other colleagues for lively roundtable discussions on topics such as: European and US inspection trends, regulatory training, GMP initiatives, and much more. Please visit PDA's Web site at www.pda.org in the future for additional topics being offered or e-mail neal@pda.org to suggest or facilitate a specific topic.

Congress Highlights

- 21st Century FDA Initiatives: Improving the Control and Effectiveness of Drugs;
- GMP Changes;
- Regulatory Changes;
- Inspections, and
- Clinical Trials Development From Current to Future Manufacturing & Technology Trends;
- PAT Initiatives;
- Contract Manufacturing;
- Biotechnology;
- Isolation Technology or What?;
- Membrane Absorbing Technology;
- Standardization of Nano (Virus) Filters
- New Drug Delivery Technologies—Combination Products;
- Rapid Development of Vaccines vs. Emerging Global Diseases.
- Future Trends of Information and Control System Technology in the Pharmaceutical Industry
- Interpretation of Evolving Regulations;
- Electronic Common Technical Documents (ECTD), and
- Electronic Process Assurance and Control.

Who Should Attend

All individuals interested in the future of pharmaceutical science and technology, including those engaged in manufacturing, production, quality assurance/quality control, engineering and maintenance operations, facility design, product and process development, scale-up, validation, compliance and regulatory affairs, and research and development will derive significant value from participation.

PDA Interest Groups

Take advantage of the informal discussion groups to meet with colleagues to discuss your specific questions and ideas. Interest Groups will be offered each day in the morning or afternoon in conjunction with the scheduled program. More detailed information will be available on our Web site at: www.pda.org.

Exhibits

This Congress will provide a great opportunity to see the latest in pharmaceutical science and technology products and services at the Tabletop Exhibits. The Exhibits will be strategically located in the foyer area just outside the main meeting rooms. Three receptions, two lunches and daily refreshments breaks are scheduled in the exhibit area. Exhibitors are encouraged to invite prospective clients—including those who are not attending the conference—to attend the exhibits without charge on Wednesday, February 18 from 8:30 a.m. to 12:00 p.m. For more information on exhibiting, contact Nahid Kiani at (301) 656-5900 or via e-mail at kiani@pda.org.

Educational Courses

The PDA Training and Research Institute (PDA-TRI) provides unprecedented education, training, and applied research in pharmaceutical sciences and associated technologies. Courses providing in-depth education on technology topics relating to the Congress will be held on February 19–20 following the Congress.

About Basel

Basel, a city of nearly 200,000 people and 2,000 years of history, is located at the elbow of the Rhine on the borders of France and Germany. It is the center of the pharmaceutical industry and the site of major trade fairs. A block of rooms is being held for Congress delegates at the Swissotel Basel, the Hotel Three Kings and the Hotel Europe, which are all conveniently located near the Messe Basel Convention Center. These three hotels are also accessible by tram, bus, and train. Detailed reservation information will be available in future announcements. It is never too early to book your hotel reservations! ■

—Wanda Neal

PDA Training and Research Institute Director's Message

October Course Series to be Held in Boston

Bob Mello, Ph.D.

The PDA-Training and Research Institute (PDA-TRI) is presenting a series of eleven outstanding courses this October 20–22, 2003, at the Radisson Hotel Boston, in Boston, MA. Increase your knowledge base and expand your professional development by obtaining the training necessary to help you perform your job at peak proficiency. Historical Boston is the setting for this array of education offerings. The three-day series offers choices of one-, two-, and three-day courses covering general and advanced compliance and regulatory topics—with a distinct biotechnology slant.

The area's biotech community should be aware of two specific offerings. Dr. David Lansky's course on "Bioassay Development and Validation" covers the fundamental concepts needed to understand the nature, development and validation (including statistical concepts) of bioassays. Joseph Habarta's course "Achieving CGMP Compliance During Development of a Biotechnology Product" will provide attendees with guidance on how CGMP regulations and principles should be interpreted and applied from product development through the final stages of biotechnology drug manufacture and product approval.

For an outstanding introduction to overall "Assay Validation", join Lynn Torbeck as he presents the concepts, definitions, and specific techniques necessary to meet FDA, ICH and USP requirements. Attendees will benefit from Torbeck's background as a statistician to answer their questions on statistical protocol design. Torbeck will also be offering a course entitled "Z1.4 Attribute Inspection Sampling in A CGMP Environment" to provide QA/QC and production personnel with the proper understanding of this standard to ensure its correct use.

Bridge the gap between theoretical GMP and practical compliance by attending Elaine Lehecka Pratt's course "Beyond the GMP/ISO Basics—Practical Strategies for Everyday Compliance." Couple this with another Elaine Pratt course to assist trainers "Maximizing SOPs—An Untapped Resource of Training" to learn new skills, tools, and ideas for using existing facility SOPs to develop a variety of training solutions.

Training experts David Gallup and Richard Sands provide training managers and QA/QC personnel with an outstanding opportunity to learn the knowledge and skills necessary to function as training managers in a pharmaceutical manufacturing facility in their interactive three-day "GMP Training Manager Workshop".

Operations personnel have several exceptional training opportunities. In addition to those already mentioned, join Maureen Reagan as she draws on her 23 years of pharmaceutical manufacturing experience to share with you a fundamental working knowledge of environmental monitoring in her course "Everything You Wanted to Know About Environmental Monitoring But Were Afraid to Ask". Packaging engineers and other operations/QA/QC and development staff will find the course "Parenteral Packaging: Rubber, Glass, Plastic and Metal Seals," offered by the team of Patty Kiang, Diane Paskiet, and Edward Smith to be invaluable in understanding how to evaluate, select and control packaging components for parenteral products.

Corrective and preventive actions are required aspects in today's quality systems within our regulated industry. Register for Ken Peterson's course "Analytical Problem Solving for CAPA Systems" to learn advanced skills in root cause analysis and problem prevention. The common approach to problem-solving and prevention enables participants from different disciplines to work together to resolve problems.

Increase your knowledge base and expand your professional development by obtaining the training necessary to help you perform your job at peak proficiency.

CGMP regulations require that the quality of drug products be reviewed at least annually and, in particular, to assess needs for product changes. Attend Dr. Alan Smith's course "Annual Product Reviews: How to Comply With FDA & ICH Requirements" and learn how to design and implement annual product reviews, determine the presence and adequacy of essential systems to support the reviews, and assure that site and corporate management are adequately appraised of the state of product quality.

As you can see, the content for this outstanding course series presents opportunities for all areas of pharmaceutical and especially biopharmaceutical professional development. Register now and join us in October at the Radisson Hotel Boston. More details and registration information can be obtained at the PDA Web site, www.pda.org. The course series brochure can be obtained online at http://www.pda.org/PDF/TRI-BostonSeries-Bro.pdf. ■

—Bob Mello, Ph.D.

PDA–Blow/Fill/Seal (B/F/S) International Operators Association workshop on B/F/S processing, September 18–19, Cardinal Health Facility, Woodstock, IL.

PDA Italian Inspectorate Training Program Update

by *Carmen Wagner, Ph.D.*

In spite of the heat wave that swept Italy in July, the PDA team responsible for the course on Regulatory Compliance for the Italian Inspectorate continued to work hard to ensure the successful delivery of Module 3: Inspection Processes, Skills and Related Topics. Module 3 was presented on 1–4 July 2003 and was well received by the Italian Inspectorate. The real-life case studies added an important practical dimension to the course and provided the opportunity to discuss several inspection techniques and skills used by European Inspectors. Module 3 was taught by Dr. Joerg Neuhaus of the German Federal Inspectorate, Cologne, and was facilitated by Dr. Carmen M. Wagner, Ph.D., course Director. Dr. Robert J. Mello, Ph.D., Vice President of Education and Director of the PDA Training and Research Institute (PDA-TRI), who was present for a portion of the training period, contributed as well.

Flavio Paoli presents his group's case study results.

Special credit for making the project successful goes to Dr. Carlo Pini, Instituto Superiore di Sanita, Rome, who has worked long and hard with Wagner and the team of instructors to continue to make sure that the course objectives and goals were being met. Drs. Pini and Wagner have implemented a few modifications to the original proposal to continue to tailor the course to the inspectors' specific needs. The project is the culmination of efforts by the Italy PDA Chapter, leaders Antonino Giannetto, SIFI; and Vincenzo Baselli, Pall Italia, to further enhance PDA's growth and effectiveness in Italy and Europe. The PDA effort is lead in the US by the PDA-TRI (Robert J. Mello, Ph.D.), with support of the PDA Europe Office (Gautam Maitra) and the continuing support of Giannetto and Baselli from the PDA Italy Chapter.

The course will continue in September, November and December with modules on GMP Considerations for Different Product Types and Systems, GMP Compliance—Special Topics, QC Laboratory Operations and Regulatory Compliance, respectively. PDA is honored to be the international organization selected to design and direct the course. Watch the *PDA Letter* for future updates. ■

Claudia Signoretti, Guiseppe Pimpinella, Luisa Stoppa, Carlo Pini, and Lorenzo Margheriti analyze data provided for their case study exercise.

Maria Antonietta Antonelli, Lorenzeo Ciceroni, Elisabeth Montesoro (foreground) and the other inspectors working on case studies.

Upcoming PDA Training and Research Institute Education Courses

Courses listed in chronological order

PDA Computer Products Supplier Auditor Process Model: Auditor Training—Lecture September 30–October 1, 2003; $1,350 members/$1,545 nonmembers; *Faculty*: Charles Waite

Environmental Mycology Identification Workshop—Lab October 2–3, 2003; December 4–5, 2003; $2,000 members/$2,195 nonmembers; *Faculty:* John Brecker

Designing, Operating and Controlling High Purity Water Systems for Regulatory Compliance—Lab October 8–10, 2003; $2,500 members/$2,695 nonmembers; *Faculty:* Bob Livingston

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

Aseptic Processing 2003 Training Program—Lab **Option 4**: October 27–31, 2003 and November 17–21, 2003; $7,500 members/$7,695 nonmembers; *Faculty:* John Lindsay and David Matsuhiro SOLD OUT

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

These courses will be held at the PDA Training and Research Institute (PDA-TRI) in Baltimore, MD, unless otherwise noted. **For course content information**, call PDA-TRI directly at **(410) 455-5800**.

For registration information, call PDA Global Headquarters in Bethesda, MD at **(301) 656-5900**.

PDA Training and Research Institute Location/Lodging Information

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

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

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

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

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

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

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

Holiday Inn Inner Harbor **
(*Special Rates for our course attendees*)
(410) 685-3500
(410) 727-6169 – fax

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

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

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

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

* no on-site restaurant

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

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

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

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

PDA Training and Research Institute Thanks the Following...

Sponsors

Abbott Laboratories
Alma, Inc.
Becton Dickinson Microbiology Systems
Berkshire Corporation
bioMerieux Vitek, Inc.
Biotest Diagnostics Corporation
Bonfiglioli Pharma Machinery
Bristol-Myers Squibb Company
Charles River Endosafe
Chemunex, Inc.
Comar, Inc.
DuPont Pharmaceutical Co.
Dycem Ltd.
Eagle Picher
Eisai U.S.A., Inc.
Electrol Specialties Company
Environmental Monitoring Technologies
General Econopak, Inc.
Genesis Machinery Products, Inc.
GlaxoSmithKline
Helvoet Pharma
IDEXX Laboratories, Inc.
Interpharm
Kimberly Clark Corp.
KMI, a division of PAREXEL International, LLC
La Calhene, Inc.
Larson Mardon Wheaton
Micro Diagnostics
Micronova Manufacturing, Inc.
MIDI Laboratories, Inc.
Millipore Corporation
M.W. Technologies, Inc.
Nalge Co.
Pacific Scientific Instruments
Pall Corporation
Particle Measuring Systems, Inc.
PML Microbiologicals
Raven Biologicals, Inc.
Research Equipment Services
Rhone-Poulenc Rorer
Sartorius AG
Siemens Building Technologies, Inc.
SGM Biotech, Inc.
STERIS Corporation
Veltek Associates, Inc.
VWR Scientific Products
West Pharmaceutical Services
Wilco AG
Wyeth-Ayerst Laboratories

Contributors

Amgen, Inc.
Atlantic Technical Systems
Automated Liquid Packaging, Inc.
Berkshire Corporation
Bioscience International
Cardinal Health
Charter Medical, Inc.
Cole-Parmer
Contec, Inc.
Corning, Inc.
Cotter Corp.
DuPont Tyvek
Eli Lilly & Company
Fedegari
Kaye Instruments, Inc.
National Instrument Co., Inc.
Neslo, Inc.
Perfex Corporation
Pfizer, Inc.
Sievers Instruments, Inc.
Technovation

2004 Aseptic Processing Course Dates

The 2004 dates for the PDA Training and Research Institute (PDA-TRI) 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 offering (or Option, as it is called). In response to the overwhelming registration requests for the four Option dates in 2003, PDA-TRI has added a fifth Option date to this series in 2004. This extremely popular 2-week course sells out rapidly, so we urge you to register early. Check our Web site at www.pda.org; the registration information will be available soon.

The 2004 dates are as follows:

Option I

Week 1 January 26–30, 2004
Week 2 February 23–27, 2004

Option II

Week 1 March 22–26, 2004
Week 2 April 26–30, 2004

Option III

Week 1 May 24–28, 2004
Week 2 June 14–18, 2004

Option IV

Week 1 August 16–20, 2004
Week 2 September 13–17, 2004

Option V

Week 1 October 4–8, 2004
Week 2 November 1–5, 2004 ■

——Bob Mello, Ph.D.

R

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

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

Membership Number

Job Title Company

Business Address

City State/Province ZIP+4/Postal Code

Telephone Fax E-mail

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

LTR 09/03

2. Indicate the course(s) you'd like to attend (please print). Individuals registering at the nonmember rate receive one full year of PDA membership. Nonmembers registering for multiple events need only pay the nonmember fee once. (If you do **NOT** want to become a PDA member, please check here ❑).

COURSE TITLE	COURSE #	DATE	LOCATION	PRICE (member or nonmember)	PRICE (govt. member or govt. nonmember)
				TOTAL :	$

3. Please check the appropriate box:

❑ **Check** enclosed ***Charge:*** ❑ MC/EuroCard ❑ VISA ❑ AMEX

Account Number_____ Exp. Date _____

Name _____
(exactly as it appears on credit card; please print clearly)

Signature_____ Date _____

Payments must be made to PDA in US dollars by a check drawn on a US bank, or by American Express, MasterCard, EuroCard, or VISA.

Payment must be included to be considered registered.

4. Return completed form with payment made to:

PDA
P.O. Box 79465
Baltimore, MD 21279-0465 USA
USA Fax: (301) 986-1093 (credit cards only)

Federal Tax I.D. #52-1906152

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. 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 $55.00 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.*

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

Chapter News Update

Australia

The PDA Australia Chapter is pleased to announce that another successful meeting was held on July 24. This meeting was attended by 71 people, and the topic, "Avoiding Cleaning Validation", was well received. Ken Dibble, Chapter President, stated "It opened the eyes of quite a few validation people—some of whom had not thought of disposable manufacturing much before." The PDA Australia Chapter has two upcoming meetings on September 18 and November 27. For more information, please contact Ken Dibble at ken_dibble@millipore.com.

Canada

The PDA Canada Chapter has wrapped up its meetings for the year. Individuals interested in helping out within the Canada Chapter may contact Chapter President Grace Chin at grace.chin@snclavalin.com.

Capital Area

For more information, please contact Bob Mello, Ph.D., at rjmello1@aol.com.

Central Europe

For more information about the PDA Central Europe Chapter, please contact Erich Sturzenegger at erich.sturzenegger@pharma.novartis.com.

Delaware Valley

The PDA Delaware Valley Chapter will present "Sterile Drug Product Manufacturing Processes—The New Drug Application Review Perspective" on September 17, featuring speaker Peter Cooney, Ph.D., of the FDA. A unique marketing opportunity has been provided by the Delaware Valley Chapter of PDA through their vendor exposition, which will be held during the dinner meeting. The Chapter's next scheduled meeting will be on November 19. For more information, contact Art Vellutato, Jr. at Artjr@sterile.com.

Israel

The PDA Israel Chapter is planning a one-day meeting on "Microbiological Issues" in September, and the Chapter's Annual Meeting is scheduled for December. For more information, please contact Karen S. Ginsbury at kstaylor@netvision.net.il.

Italy

The PDA Italy Chapter boosted their membership dramatically through their Congress on "Sterile Manufacturing Practices in the Third Millennium: A Regulatory and Industry Perspective" on June 23–25 in Milan. The Chapter brought 51 new members to PDA, increasing their membership by 25 percent through this one event. For more information, please contact Vincenzo Baselli at vincenzo_baselli@pall.com.

Japan

The PDA Japan Chapter will feature "How to Receive an FDA Inspection" on September 30. Their Annual Meeting is slated for October 28–29. For more information, please contact Hiroshi Harada at van@bcasj.or.jp.

Korea

For more information about the PDA Korea Chapter, please contact Jun Yeon Park at jun_yeon_park@pall.com.

Metro

For more information about the PDA Metro Chapter, please contact Frank R. Settineri at frank_settineri@chiron.com.

Midwest

The PDA Midwest Chapter is planning meetings for September 18 and November 20. For more information, contact Amy Gotham at PDAMidwest@northviewlabs.com.

Mountain States

The PDA Mountain States Chapter has scheduled a Vendor Night for September 11 and a Speaker Dinner for November 13. These will be the last two events of 2003 for the Chapter. The September 11th event will be held in conjunction with the local chapter of the Colorado Biotech Association. The speaker for the November dinner will be a former Denver FDA Director. For more information, please contact Jeff Beste at cmdjeff@aol.com.

New England

The PDA New England Chapter has not finalized its schedule for the fall. Their plans will likely include dinner seminars in September and December and potentially a social event in conjunction with the PDA Training and Research Institute's Boston Course Series in October. Visit the PDA Web site at www.pda.org for more information, or contact Mark A. Staples, Ph.D., at mstaples@glycogenesys.com.

Southeast

The PDA Southeast Chapter's next meeting will be September 23. They are also holding elections this fall. Elected offices include: President, Vice President, Treasurer, and Secretary. (Reminder: only PDA members may serve as Chapter Officers.) For more information, contact Mary Carver at mary_carver@eisai.com.

Southeast Asia

For more information about the PDA Southeast Asia Chapter, please contact K. P. P. Prasad at Prasadk@labs.wyeth.com.

Southern California

For more information about the PDA Southern California Chapter, please contact John Spoden at spoden_john@allergan.com.

Taiwan

The PDA Chapter in Taiwan has been in operation since 1997 and has 483 members, 80 percent of whom are from the pharmaceutical industry sector. For more information, please contact Tuan-Tuan Su at pdatc@ms17.hinet.net.

UK & Ireland

Plans are in effect for the PDA UK & Ireland Chapter's upcoming meeting on September 25–26, "What to Do When Things Go Wrong". Mike Verdi from FDA and Andrew Bill from MHRA will be presenting at this Conference and Exhibition, alongside several other featured speakers. The Conference will be held at the Britannia International Hotel at Canary Wharf in London, near the EMEA Headquarters. For more information, contact John Moys at john.moys@sartorius.com.

West Coast

The PDA West Coast Chapter is planning to host a Chapter dinner meeting in September. The PDA West Coast Chapter has been active for many years and welcomes participation from all people in the San Francisco Bay biotech community. They target professionals involved in pharmaceutical, academic, biotechnology, and government organizations with a desire to learn more about issues facing the industry and an interest in networking opportunities. For more information, please contact Randall Tedder at randallt@istep.com. ■

—compiled by KiKi Coffman

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.

International Chapters

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

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

Central Europe Chapter
Contact: Dr. Erich Sturzenegger
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@pall.com
Web site: http://www.pda-it.org

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

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

US Chapters

Capital Area Chapter
Areas Served: MD, DC, VA, WV
Contact: Robert Mello, Ph.D.
PDA-TRI
Tel: (410) 804-2284
Fax: (410) 455-5802
E-mail: rjmello1@aol.com
Web site: www.pdacapitalchapter.org

Delaware Valley Chapter
Areas Served: DE, NJ, PA
Contact: Art Vellutato, Jr.
Veltek Associates, Inc.
Tel: (610) 983-4949 x110
Fax: (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: (908) 730-1222
Fax: (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: (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: (303) 832-8100
Fax: (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.
GlycoGenesys, Inc.
Tel: (508) 870-0007 x140
Fax: (508) 870-0224
E-mail: robert_pazzano@vtsinc.net

Southeast Chapter
Areas Served: NC, SC, TN, VA, FL, GA
Contact: Mary Carver
Eisai, Inc.
Tel: (919) 474-2149
Fax: (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: (714) 246-5834
Fax: (714) 246-4272
E-mail: spoden_john@allergan.com
Web site: http://www.pda.org/chapters/Web-site-SoCal/SoCal-index.html

West Coast Chapter
Areas Served: Northern California
Contact: Randall Tedder
Tel: (415) 841-0373
Fax: (415) 841-1961
E-mail: randallt@istep.com

PDA
An International Association For Pharmaceutical Science And Technology

Company, Colleague & Product Announcements

Ben Venue Laboratories, Inc. celebrated the dedication of the latest expansion of its Bedford, Ohio pharmaceutical manufacturing facility. The new facility represents an addition of 162,000 square feet, and a capital investment of $82 million. The company has spent over $150 million dollars in the last three years at its Bedford facility on further expansion and improvements. "Ben Venue continues to grow to position itself to supply the expanding market for injectable pharmaceuticals," said Thomas Russillo, President and COO. The new facility includes two continuous filling lines with robotic traying that can accommodate either lyophilized (freeze-dried) or liquid products. It also includes six new 400 square-foot lyophilizers with clean-in-place/steam-in-place capability, new sterilization equipment, and a 10,000 unit per hour packaging line. Ben Venue Laboratories, Inc. is a subsidiary of Boehringer Ingelheim Corporation based in Ridgefiled, CT, and is a member of the Boehringer Ingelheim group of companies, headquartered in Ingelheim, Germany. For further information, go to www.boehringer-ingelheim.com.

BD Diagnostic Systems, Sparks, MD, announced the availability of the first edition of the new *Difco™ & BBL™ Manual.* In keeping with the previous *Difco™ Manual's* history of excellence in providing microbiologists worldwide with technical and product information, the revised *Difco™ Manual* has now been incorporated with BBL™ products. Essentially two popular, separate BD publications have been combined into one. The new *Manual* replaces the *Difco™ Manual (*11th edition) and the *Manual of BBL™ Products and Laboratory Procedures* (6th edition). A comprehensive guide to the entire BD line of Difco™ and BBL™ brand media, the new *Difco™ & BBL™ Manual* includes dehydrated culture media (DCM) and prepared, plated, tube, and bottled media. Each manual comes with a CD-ROM, which contains the entire contents of the book in electronic form, with a search feature included.

The *Manual* contains a description for each medium, including the medium formulation, relevant information concerning the history, ingredients and usage of each medium, and recommended quality control organisms and expected results. The *Manual* also features icons denoting media listed in "official" and "standard methods" publications and the BD catalog numbers for all packaging configurations. A Reference Guide contains tables for industrial and clinical applications, along with flowcharts delineating media and reagents for identification of food pathogens. For more information, please call 1-800-638-8663; the *Manual* can also be ordered through Amazon.com, using the book's title and ISBN 0-9727207-7.

Particle Measuring Systems, based in Boulder, Colorado, recently announced the release of their IsoAir sensors, which make aerosol monitoring trouble-free and cost-effective. They are compact and simple to install, and they provide unparalleled performance in a chemically resistant, easy-to-disinfect stainless steel box. IsoAir features 0.5 and 5.0 channels for GMP. It has Ethernet and/or 4-20 mA output. It is controlled by Facility Net software, which provides advanced reporting features, as well as alarm paging for instant responses to particle events. IsoAir has an optional internal pump or can be used with an external vacuum source. System validation documentation is also available. For more information, visit www.pmeasuring.com.

BioReliance Corporation announced that it has developed a sensitive assay for the detection of mycoplasma for inclusion in its quantitative PCR[1] (Q-PCR) technology platform. This new test is ideal for tissue-based products, biopharmaceutical products with a short shelf life, or process development samples that may be incompatible with the traditional 28-day culture medium or cell-based mycoplasma testing. Q-PCR testing is an alternative for biologicals that need a faster mycoplasma detection method. The Q-PCR assay is targeted to 60 species of mycoplasma, including the eight most common contaminants: *M. arginini, M. fermentans, M. hominis, M. hyorhinis, M. laidlawii, M. orale, M. pirum,* and *M. salivarium.* These eight species constitute approximately 95% of mycoplasma contamination in cell culture.[2] Says Dr. Allan Darling, Vice President of US Biologics Testing at BioReliance, "The launch of this assay highlights our continued commitment to the biopharmaceutical industry to provide state-of-the-art testing services to ensure the safety of biological products." For more information, visit the BioReliance Web site at www.bioreliance.com. ■

[1] The Polymerase Chain Reaction (PCR) process is covered by U.S. patents No.s 4,683,195 and 4,683,202 owned by Roche Molecular Systems, Inc. and F. Hoffman-LaRoche Ltd.

[2] McGarrity, G.J. and Kontani, H. Cell culture mycoplasma. In: The Mycoplasma: pathogenesis of mycoplasma diseases, Vol IV. Razin S. and Barile MF, eds. New York; Academic Press; 1985; p. 353–390.

—compiled by Evelyn N. Heitman

Send announcements on personnel changes and new products . . .

to **Evelyn Heitman** via e-mail at heitman@pda.org or mail a hard copy to PDA global headquarters at 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814.

NEW TRAINING CDs

at PDA ... your source for scientific, technical and regulatory information.

A Training Program for a System Audit of the Operation, Control, Qualification, Validation and Design of a WFI System This program covers quality assurance and regulatory standards for Water for Injection (WFI) systems used in the production of injectable pharmaceutical and biopharmaceuticals. Quality specifications, sampling programs and operational parameters for WFI systems are identified and discussed. 70-minute presentation with 111 slides. $500 member/$1,495 nonmember **Item No.11012**

Control of Ray Materials for Pharmaceutical and Bio-Pharmaceutical Operations This program discusses the need for adherence to standard operating procedures (SOP's) to assure good raw materials are available for production operations. The SOP and documentation requirements for the ordering, receipt, sampling, assay, release, storage, use and final accounting for the disposition of each lot of raw material are discussed in depth. 21-minute presentation with 54 slides. $300 member/$895 nonmember **Item No.11001**

Cross-Contamination in the Production of Pharmaceuticals and Bio-Pharmaceuticals This program identifies and discusses six key causes or sources of cross-contamination in the production of pharmaceuticals, they are: buildings, employees, raw material handling procedures, manufacturing and controls, laboratory controls and equipment. The way by which these avenues of cross-contamination can be prevented or eliminated are discussed. 22-minute presentation with 43 slides. $300 member/$895 nonmember **Item No.11002**

Finishing Operations in the Production of Pharmaceuticals and Bio-Pharmaceuticals This program identifies and discusses four main objectives of finishing operations. The importance of six key areas involved in finishing operations are identified and discussed. Five criteria in finishing operations that must be met before a batch may be released for distribution are identified. 25-minute presentation with 51 slides. $300 member/$895 nonmember **Item No.11004**

Good Manufacturing Practice Regulations, 21 CFR Parts 210-211, Sub-Parts B thru K Plain Language GMP Summaries with Discussions of FDA Intent These ten GMP training programs are presented on one computer CD, or they may be purchased separately. These programs are summaries of the regulations with discussions of FDA intent and their current interpretations. A review section at the end of each training session may be used for individual or group testing or may be used for open-book testing or discussions. $300 member/$895 nonmember **Item No.11005** (single program); $1,500 member/$4,500 nonmember **Item No.11014** (Set of 10 programs)

Managing an FDA Inspection in Your Facility-Establishing a Proactive System for Managing an FDA Inspection–A Quality and Compliance Training Program This training program was developed by Dick Shepherd. He used his 39 years of experience from being on both sides of an FDA inspection to develop the philosophy and procedures which are discussed and outlined in detail in this training program. 45-minute presentation with 61 slides. $300 member/$895 nonmember **Item No.11006**

Quality Assurance Standards for the Manufacture and Control of Injectable Products—A Quality and Compliance Training Program The program discusses and outlines standards for the production and control of injectable products. It includes terminal sterilization and aseptic sterilization standards. The information in this program may be used for training auditors, production and quality personnel, and in the development of production, control and quality standards and specifications. 30-minute presentation with 36 slides. $300 member/$895 nonmember **Item No.11007**

Quality Indicator Reports—A Proactive Management System A Quality and Compliance Training Program The program discusses FDA's intent on quality reports and the requirements for a quality report system. The program outlines and discusses the objectives, report distribution, policies and procedures, report frequency and report format. Information to be included in the report is listed and discussed in depth. 20-minute presentation with 45 slides. $300 member/$895 nonmember **Item No.11008**

Shep's Systems Audits © Programs Designed to Train Auditors in Conducting Systems Audits of Pharmaceutical and Bio-Pharmaceutical Operations. Quality and Compliance Training Programs There are 21 individual programs in Shep's Systems Audits©. Each program contains key points which he has identified over the years to evaluate the effectiveness of operational quality assurance systems. Each of the individual programs are presented as slides without narration in order for individual companies to tailor the content to cover their individual operations. $300 member/$895 nonmember **Item No.11009** (single program); $1,500 member/$4,500 nonmember **Item No.11015** (Set of 10 programs)

Team Biologics Inspection Program for Bio-Pharmaceutical Operations, FDA Compliance Program 7341.001 This plain language training program outlines with related narration the current minimum requirements for the production and control of bio-pharmaceutical products as outlined in FDA Compliance Program 7341.001. This is the compliance program that FDA's Team Biologics is currently using in evaluating bio-pharmaceutical production and control operations. The training program is presented in five sections which covers the seven major sections of the Compliance Programs. This includes FDA-483 observations that FDA has identified as "significant deviations". 11-minute with 35 slides. $500 member/$1,495 nonmember **Item No.11010**

Technology Transfer Process for Pharmaceuticals and Bio-Pharmaceuticals This is a regulatory compliance technical training program which discusses and outlines a system for the successful transfer of technology and products. Areas covered include: objective of technology transfer: keys to technology transfer: managing the transfer: management team: policies and procedures: responsibilities: documentation: operations—transferring and receiving sites. 50-minute presentation with 56 slides. $300 member/$895 nonmember **Item No.11011**

The Development Report—A Discussion and Outline for a Development Report The information that needs to be included in a development report is outlined and discussed in detail. The program discusses how the development report became a required document for Pre-Approval Inspections. It discusses in detail three different formats that may be used for a development report. There are no FDA regulations on a format for a development report. 28-minute presentation with 54 slides. $300 member/$895 nonmember **Item No.11003**

Using the FDA Pre-Approval Inspection Compliance Program in Preparing for an Inspection This program discusses and outlines the requirements of the FDA Pre-Approval Compliance Program: the program was developed to assist a company in preparing for a successful Pre-Approval Inspection using the Compliance Program requirements and current industry standards. 48-minute presentation with 105 slides. $300 member/$895 nonmember **Item No.11013**

NEW TRAINING CDs

(All of the programs have been developed for Pharmaceutical and Biopharmaceutical Operations: programs may be used for individual or group training.)

For complete descriptions, visit our Web site, www.pda.org.

PDA-DHI Press Best Sellers

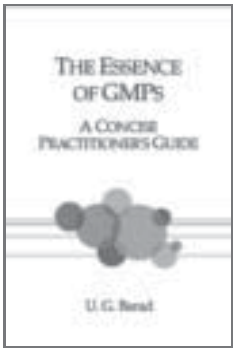
Do You Have Your Copy Yet?

Does Your Librarian?

Commercial Off-The-Shelf Software Validation for 21 CFR Part 11 David Nettleton and Janet Gough; Validation clearly is a requirement for regulatory compliance. Every indication is that the regulations will focus more and more on the electronic generation of data, data control, and data transfer. The goal of this book is to provide guidance for validating commercial, off-the-shelf (COTS) computer software that generates data or controls information about products and processes subject to binding regulations. This book provides the practical information needed to ensure an understanding of the FDA-issued guidance as they develop systems that will enable them to go partially or fully electronic; hardcover; 118 pp; $185 members/$229 nonmembers **Item No. 17200**

Electronic Records and Electronic Signatures Compliance Assessment Chris Reid and Barbara Mullendore; Provides practical guidance on the interpretation of 21 CFR Part 11 and the steps you need to take to address current and future compliance issues. This quick guide is designed to help you identify ERES business benefits, establish policies, procedures, and processes that ensure compliance, and define and evaluate system requirements. This excellent resource and reference also contains invaluable appendices containing examples of warning letters, a valuable list of records specifically identified in predicate rules, numerous examples of electronic records relating to specific system types, and very extensive sets of ERES assessment questionnaires. This guide is a must-have for everyone concerned with any aspect of ERES regulation. 58 pp; 2001; $90 member/$109 nonmember **Item No.17177**

JUST RELEASED



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 policies (prevention of contamination) that are the requirements of non-sterile pharmaceuticals. This section is followed by complete coverage of sterile products, and the book culminates with a complete glossary in part four.

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**

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. It is hoped that this book will demystify the field of microbiology by describing it plainly and systematically from various scientific, technical, and functional perspectives. 900 pp; $240 members/$299 nonmembers; 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 a subject matter expert and has a minimum of 10 years of hands-on experience in the topics discussed. The authors use this experience to identify practical ways to perform research, development, validation, and production activities associated with steam sterilization. Many of the chapters include sample standard procedures or protocols that may be used as templates to generate documents for your facility. Other chapters outline and explain the requirements. The book also provides guidance for those individuals who are responsible for the oversight of these processes or those who wish to update their knowledge. While written primarily for the pharmaceutical industry, much of the content may be applicable to the food and cosmetic industries as well. While this book does not specifically address the bulk drug industry, certain information may be applicable to bulk drug 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**

Supply of Chemicals in the Pharmaceutical Industry: Regulatory Guidelines and Rulings Mark Selby; This informative guide highlights the areas of legislation that suppliers of all chemicals involved in the synthesis and supply of healthcare products should be aware of, and offers details and comparisons of current issues in Europe, the United States, Canada, Australia, Japan and other countries worldwide. Topics include help in deciding how the legislation may apply to you if you manufacture chemicals, pharmaceuticals, or medical devices or are engaged in R & D related to these efforts. The book describes the chemical supply in global terms, discusses supply of new substances, offers specific cases such as export only, R & D, and clinical trials, provides information about worker health, communication of hazard, and control of pollution, and provides details about lab testing, also complete with examples of test guidelines. The book contains a useful glossary. If you supply any type of healthcare product, it is very likely that at some stage chemical supply legislation has an impact; failure to recognize the importance of such legislation may delay or prevent supply. 160 pp; $185 members/$229 nonmembers; hardcover **Item No. 17204**

Good Practice and Compliance for Electronic Records

Published jointly with ISPE

Part 1—Good Electronic Records Management (GERM): Electronic Information Assurance for the Regulated Industry—Guide to Current Good Practice for Electronic Records and Signatures 2002; 104 pages; $95 PDA members/$190 nonmembers **Item No. 19003**

Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures 80 pages; $95 members/$190 nonmembers (English) **Item No. 19001**

Also available in German and Spanish. For more information, visit www.pda.org.

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**

Technical Report No. 1 Validation of Steam Sterilization Cycles This is a comprehensive, straightforward approach toward validation procedures for steam sterilization cycles. There is no known similar treatise. This report was produced by a Task Force of the PDA Research Committee and is primarily the work of R. Michael Enzinger. 1978; 36 pp; $75 member/$550 nonmember **Item No.01001**

Technical Report No. 3 Validation of Dry Heat Processes Used for Sterilization and Depyrogenation This report presents a review of validation for processes that use dry heat to achieve sterilization and/or depyrogenation. Various theories, sterilization variables, engineering and microbiological studies relative to validating dry heat sterilizers are discussed. 1981; 55 pp; $75 member/$550 nonmember **Item No.01003**

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**

To Order, use Form on Page 44.

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.

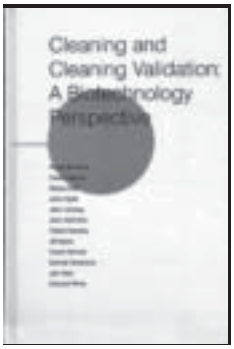
The Archive is updated each year, adding six issues of the *PDA Journal*, all PDA Technical Reports and Monographs, and selected PDA Meeting Proceedings. The archive is a 4-CD set. Archive (contains data through the year 2002); $395 member/$1,200 nonmember **Item No. 01101**

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**

PDA Books

Cleaning & Cleaning Validation: A Biotechnology Perspective Authors: Roger Brunkow, David DeLucia, George Green, Shane Haft, John Hyde, John Lindsay, Jill Myers, Robert Murphy, John McEntire, Karen Nichols, Ray Prasad, Brenda Terranova, Jon Voss, Caroline Weil, and 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 is an analysis of the risk-to-benefit scenarios associated with the various forms of product manufacturing, an analysis of change-over programs, equipment considerations and material transport as they are affected by multi-product manufacturing strategies. 1995; 190 pp; $125 members/$320 nonmembers **Item No. 13002**

PDA Publication Order Form

S

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

Name _____ Member No. _____

Company _____

Address _____

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

Tel: _____ Fax: _____ E-mail: _____

Payment type: ❑ Check drawn on a US bank ❑ MasterCard ❑ VISA ❑ AMEX ❑ EUROCARD

LTR 09/03

Mail to: PDA
P.O. Box 79465
Baltimore, MD 21279-0465 USA

Fax: (301) 986-1093 (credit cards only)

Questions? Call (301) 656-5900 x133 or e-mail *info@pda.org*.

Credit Card # _____ Exp. _____

Name _____
(exactly as it appears on credit card; please print clearly)

Signature _____

Item No.	Title	Qty.	Price	Total

Payment
Payments must be made in US dollars, by a check drawn on a US bank, or by credit card.
Federal Tax I.D. #52-1906152
Please allow 4–6 weeks for delivery on some items.

Subtotal	
Shipping & Handling	
5% Tax *(MD Residents Only)*	
TOTAL	

Shipping
Domestic US orders are shipped via UPS Ground. Second-day and next-day air service is available. Call or e-mail for prices.

Shipping & Handling Rates for the US, Puerto Rico & Canada

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

International orders: Please add 20%, minimum $18.00, maximum $150.00. Items are sent priority air, with delivery in 6–8 weeks, but express service is available for some countries; please call for details.

PDA USE:
Date: _____ **Check:** _____ **Amount:** _____ **Acct:** _____

M

Return your completed PDA membership application, with payment made to: **PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA** or fax it to: (301) 986-1093. *(Credit cards only.)*

Member Info

Please type or print clearly

Last Name _____

Mr.❍ Ms.❍ Dr.❍ First Name _____ MI_____

Job Title _____

Company _____

Address _____

City _____ State/Province _____

Country _____ Zip+4/Postal Code _____

Business Phone: _____ Fax: _____

E-mail: _____

LTR 09/03

Member Profile

Business Environment (check only one)

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

Professional Interest (check all that apply)

- ❑ Aerosols
- ❑ Analytical Chemistry
- ❑ Biologicals
- ❑ Biotechnology
- ❑ Computers
- ❑ Engineering
- ❑ Formulation Development
- ❑ GMP Compliance/Inspection Trends
- ❑ Liquids
- ❑ Maintenance
- ❑ Manufacturing/Production
- ❑ Microbiology
- ❑ Ointments
- ❑ Ophthalmics
- ❑ Packaging
- ❑ Parenterals
- ❑ Quality Assurance/Quality Control
- ❑ Regulatory Affairs
- ❑ Research
- ❑ Solid Dosage Forms
- ❑ Sterilization/Aseptic Processing
- ❑ Training
- ❑ Validation

Membership dues are non-refundable and non-transferable.

Payment (US Dollars Only)

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.*

❑ **Individual Membership ... $195**

❑ **Government Agency Employee Membership ... $80** *You must be an employee of a government agency to qualify for this rate.*

Please check the appropriate box:

❑ **Check** enclosed **Charge:** ❑ MC/EuroCard ❑ VISA ❑ AMEX

Account Number _____ Exp. Date _____

Name _____

Signature _____ Date _____

(exactly as it appears on credit card; please print clearly)

Federal Tax I.D. #52-1906152

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

◆ Denotes European program/meeting

■ Denotes Pacific Rim program/meeting

December 8–9, 2003
PDA Presents
◆ **Basel Pharmaceutical Forums**
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

2004

JANUARY

January 26–30, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 1
PDA Training and Research Institute, Baltimore, MD

FEBRUARY

February 16–20, 2004
◆ **2004 PDA International Congress—Basel**
Messe Basel Convention Center
Basel, SWITZERLAND

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 8–12, 2004
PDA SciTech Summit™
Courses: March 10–12, 2004
Orlando County Convention Center
Orlando, FL
PDA Training and Research Institute
Lecture Courses: March 10–12, 2003

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

APRIL

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

MAY

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
■ **2004 PDA Pacific Rim Congress—Singapore**
Congress: May 17–19
Courses: May 19–21
Tabletop Exhibits: May 17–19
The Ritz Carlton Millenia
SINGAPORE

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

AUGUST

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

SEPTEMBER

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

OCTOBER

October 4–8, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 1
PDA Training and Research Institute, Baltimore, MD

NOVEMBER

November 1–5, 2004
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA Training and Research Institute, Baltimore, MD

Information on these conferences and courses will be posted on the PDA Web site as it becomes available.

Visit often to get the latest information!

www.pda.org.

"Same as always, Joe.
23.5 millimeters off the top."

To our engineers, accuracy is a way of life.

There's no tolerance for error in pharmaceutical processing. That's why the industry relies on GE Kaye for critical thermal process validation. From the best selling Validator® 2000 to our wireless ValProbe™ technology, GE Kaye sets the standard for precision, reliability and convenience.

- Measurement accuracy to ± 0.1˚C
- Powerful, yet intuitive reporting with statistical and lethality calculations
- System security features satisfy FDA 21 CFR Part 11
- Unmatched reliability

Of course, GE Kaye systems are backed by local service and support around the world. Find out what our customers have known for over 40 years: at GE Kaye accuracy is a way of life.

To learn more, visit us at **gekaye.com.**

GE Kaye

imagination at work

Visit us at the 2003 PDA Annual Meeting—Booth #324

Calendar of Events

2003

OCTOBER

October 2, 2003
◆ **EC GMP Annex 1 Sterile Products Forum**
Langen, GERMANY—Metro Frankfurt

October 2–3, 2003
PDA Training and Research Institute Laboratory Course
Environmental Mycology Identification Workshop
PDA Training and Research Institute, Baltimore, MD

October 8–10, 2003
PDA Training and Research Institute Laboratory Course
Designing, Operating and Controlling High Purity Water Systems for Regulatory Compliance
PDA Training and Research Institute, Baltimore, MD

October 13–14, 2003
◆ **2003 Taormina International Conference and Tabletop Exhibits—a Conference for Decision-makers Responsible for Strategy, Implementation and Management of Quality Assurance and Regulatory Compliance**
Managing for Quality in a Cost-Focused Environment
Conference: October 13–14
Tabletop Exhibits: October 13–14
Grand Hotel Timeo & Villa Flora
Taormina, Sicily ITALY

October 13–15, 2003
PDA Training and Research Institute Laboratory Course
Cleaning Validation
PDA Training and Research Institute, Baltimore, MD

October 20–22, 2003
PDA Training and Research Institute
Boston Course Series
Radisson Hotel Boston, Boston, MA
PDA Training and Research Institute Lecture Courses:
October 20
Beyond the GMP/ISO Basics–Practical Strategies for Everyday Compliance
Bioassay Development & Validation
October 20–21
Parenteral Packaging: Rubber, Glass, Plastic and Metal Seals
Everything you Wanted to Know about Environmental Monitoring, but were Afraid to Ask
October 20–22
GMP Training Manager Workshop
October 21
Maximizing SOPs–An Untapped Resource of Training
Assay Validation
October 22
Achieving CGMP Compliance during Development of a Biotechnology Product
Z1.4 Attribute Inspection Sampling in a CGMP Environment
Analytical Problem Solving for CAPA Systems
Annual Product Reviews: How to Comply with FDA & ICH Requirements

October 21–23, 2003
◆ **A3P 16th International Congress**
Congress: October 21–23
Exhibits: October 21–23
Bellevue Congress Hall
Biarritz, FRANCE

October 27–31, 2003—**SOLD OUT!**
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 1
PDA Training and Research Institute, Baltimore, MD

October 28–29, 2003
■ **PDA Japan Chapter Annual Meeting**
Location: TBA

NOVEMBER

November 6–7, 2003
PDA Training and Research Institute Laboratory Course:
Ensuring Measurement Integrity in the Validation of Thermal Processes
PDA Training and Research Institute, Baltimore, MD

November 10–14, 2003
2003 PDA Annual Meeting, Courses and Exhibition
Building on Our Strengths: Quality, Science and Innovation
Annual Meeting: November 10–12
Courses: November 13–14
Exhibition: November 10–11
Downtown Hilton Atlanta on Courtland NE
Atlanta, GA
PDA Training and Research Institute Lecture Courses:
November 13
Designing, Monitoring & Validation of Pharmaceutical Manufacturing Ventilation Systems
Auditing Techniques for CGMP Compliance
November 13–14
Basic Concepts in Cleaning and Cleaning Validation
Computer-Related Systems Validation
A Practical Approach to Aseptic Processing and Contamination Control
November 14
Managing in a GMP Environment
Change Control & Documentation

November 17–21, 2003—**SOLD OUT!**
PDA Training and Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA Training and Research Institute, Baltimore, MD

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

DECEMBER

December 4–5, 2003
PDA Training and Research Institute Laboratory Course
Environmental Mycology Identification Workshop
PDA Training and Research Institute, Baltimore, MD

◆ Denotes European program/meeting

■ Denotes Pacific Rim program/meeting

Be sure to watch **www.pda.org** for conference and course updates!

continues on page 46