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PDA Letter

October 2003

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

Human Drug CGMP Notes, page 22

FDA Releases One Final and Four Draft Guidances

On September 5, 2003, FDA announced one final and four draft guidances in the *Federal Register*. PDA received advance notice and posted these guidances on our Web site (www.pda.org) on September 3, 2003. The guidances are:

- Docket No. 03D-0060, CDER 200399. Guidance for Industry on Part 11, Electronic Records; Electronic Signatures—Scope and Application; Availability. Pages 52779–52781 [FR Doc. 03-22574]
- Docket No. 03D-0382, CDER 1997112. Draft Guidance for Industry on Sterile Drug Products Produced by Aseptic Processing. Pages 52782–52783 [FR Doc. 03-22576]
- Docket No. 03D-0385, CBER 200338. Draft Guidance for Industry: Comparability Protocols—Protein Drug Products and Biological Products—Chemistry, Manufacturing, and Controls Information; Availability. Pages 52776–52777 [FR Doc. 03-22577]
- Docket No. 03D-0386, CDER 2003131. Draft Guidance for Industry on Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical Current Good Manufacturing Practice; Availability. Pages 52777–52779 [FR Doc. 03-22575]
- Docket No. 03D-0380, CDER 2003136. Draft Guidance for Industry: Process Analytical Technology—A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance; Availability. Pages 52781–52782 [FR Doc. 03-22578] ■

—William Stoedter

Building on Our Strengths: Quality, Science and Innovation

2003 PDA Annual Meeting, Courses and Exhibition • November 10–14, 2003

Downtown Atlanta Hilton Hotel on Courtland NE • Atlanta, GA

Steven K. Galson, M.D., M.P.H., Deputy Director of CDER, FDA, to provide an update about CDER for the industry.

Overview

Innovation is the focus of the PDA Annual Meeting. Scientific presentations and interactive Interest Group discussions will highlight cutting edge science and technology.

Participants will benefit from:

- Keynote presentation by FDA's Deputy Director of the Center for Drug Evaluation and Research, Dr. Steven K. Galson
- Pre-Conference: online access to speaker presentations* that you can download in advance
- Roundtable exchange breakfast (choose from a variety of topics)
- Interactive Exhibit Hall and Poster Session
- Networking reception
- Post-conference: complimentary CD-ROM of all conference presentations

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

- 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
- Discuss issues related to cold chain management

Volunteer to facilitate a roundtable discussion on a topic of interest to the industry including: aseptic processing, cleaning validation, environmental monitoring, GMPs, 21 CFR Part 11 and changes to the USP, isolator technology, PAT, quality auditing, rapid methods in microbiology, stability, sterilization, sterility and LAL testing, and more.

Make sure you register today! ■

—Leslie Zeck

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

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

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Important Dates...

- **January 15, 2004—deadline to reserve a hotel room for 2004 PDA International Congress—Basel**
- **January 31, 2004—entry submission deadline for Trainer's Choice Awards**

IN THIS ISSUE...

Neal G. Koller
PDA President

Pacific Rim Chapters Talk Science & Technology With PDA President

In keeping with PDA's objective to build science- and technology-based partnerships with health authorities and industry worldwide, I traveled to the Pacific Rim in July. My trip centered on enhancing the understanding of the value of PDA's Science and Technology, and on creating interactive, mutually beneficial relationships with industry and health authorities. This trip dovetails my previous visits to Europe and Israel where I met with health authorities and members of industry. These international meetings tie into PDA's long-term Strategic Plan of becoming a strong contributor to the international exchange of scientific and technical information and bringing science into the regulatory process worldwide.

My first stop was Japan where I met with the following members of the PDA Japan Chapter Board of Directors: Chapter President K. Mise, Ph.D. (The Organization for Pharmaceutical Safety and Research, The Government Sector); Chapter Chief Secretary K. Kawamura, Ph.D. (Otsuka Pharmaceutical Co.); T. Oba (Japan Red Cross); T. Okugawa (Pfizer Japan); T. Kamikukita (Cuno Co.); Chapter Director and PDA Director Y. Hashimoto (Chiyoda Engineering Co.); D. Murakami (Hori Glass Co.); S. Watanebe (Kyowa Pharmaceutical Co.); and Chapter Secretary M. Nishiyama (Nishiyama Associates). It was a beneficial meeting in which we reviewed the opportunities for strengthening Japan's participation in PDA worldwide, such as in the Science Advisory Board (SAB) and the Regulatory Affairs and Quality Committee (RAQC), to expand the reach of their scientists and technological experts and to bring Japanese science closer to all PDA members. We also considered the activities of the Japan Chapter and reviewed their long-term goals.

From there, I traveled to Taiwan and the Annual Meeting of the PDA Taiwan Chapter. Hui-Po Wang, Director General of the Bureau of Pharmaceutical Affairs at Taiwan's Department of Health, addressed the audience with a presentation comparing the PIC/S GMP Guide with the Taiwan GMPs. Meeting participants later elected a new Board of Directors and discussed the Chapter Annual Report, computer validation issues, 21 CFR Part 11 (electronic records/signatures) and the PIC/S Guide to GMPs Annex 11 on computerized systems. Additionally, I shared lunch with Eric Suen, Deputy Director-General of the National Laboratories of Food and Drugs, Taiwan Department of Health. We talked about the success of the six-module PDA Pharmaceutical Inspectorate Training program held in Italy and its applicability to Taiwan.

Next on the agenda was a meeting with the Taiwan Chapter Board of Directors. The following members attended: Chapter President S.Y. Hsu (Otsuka Pharmaceutical Co.); Past Chapter President S.S. Tsai (PDA Taiwan Chapter); James T.S. Tu (Eli Lilly Suzhou Pharmaceutical Co.); J.S. Lai (Veterans Pharmaceutical Co.); T.M. Cham (School of Pharmacy, Kaohsiung Medical University); C.C. Tsai (China Chemical & Pharmaceutical Co.); Advisor Group member Russell Chen (Tajen Institute of Technology); Advisor Group member S.Y. Lee (PDA Taiwan Chapter); Advisor Group member Y.F. Liu (Wyeth Taiwan Corporation); and Chapter General Secretary T.T. Su (PDA Taiwan Chapter). We discussed the future direction of PDA and possible plans to increase the opportunities for volunteers to pursue their scientific interests within the association.

My next stop was South Korea where Woo-Hyun Paik, Ph.D., Korea Chapter President, introduced me to the Commissioner of the Korea Food and Drug Administration, Chang-Koo Shim, Ph.D. The meeting was a very good one; we discussed PDA's science initiatives and the activities of the SAB, which establishes the strategic perspective for PDA's science and technology efforts and provides science input to the RAQC. Dr. Paik also introduced me to the head of the Korea Pharmaceutical Manufacturers Association, Jeung-Soo Kim, to discuss the structure of PDA, the mission and activities of the RAQC, and PDA's involvement in commenting on official regulations and guidances.

As in Japan and Taiwan, I had a valuable meeting with the PDA Korea Chapter Board of Directors. Among the Board members in attendance were: Chapter President Woo-Hyun Paik, Ph.D. (Chung-Ang University, consultant to the PDA Korea Chapter, and advisor of Boryung Pharmaceutical Co.); Chapter VP Seung-An Kang (Yu Yu Pharmaceutical Co.); Chapter VP Woo-Il Hong (formerly with Yuhan Chemical Co.); Chapter VP Chong-Kook Kim (College of Pharmacy, Seoul); Administration Secretary Jong-Kuk Kim (Pall Korea); Chapter Secretary Jun-Yeon Park (Pall Korea); Auditor Kwang-Soon Kim (Taerim Pharmaceutical Co.); Planning Secretary Young-Il Kim (Korus Korea Pharmaceutical Co.); International Secretary Jong-Dae Lee (Korea Research Institute of Produc-

Dr. Woo-Hyun Paik addresses the Board of Directors of the PDA Korea Chapter.

continues on bottom of page 5

Message from Bob Myers, Chairman of the 2003 Nominating Committee

In light of the current climate of distrust and disappointment with corporate boards around the globe, I would like to take a minute to review how the PDA Board candidate selection process works. Each year, a Nominating Committee is convened to identify well-qualified individuals who are interested in taking on a leadership role within PDA. This Committee is composed of the Immediate Past Chair, the current Chair and the Chair-elect—all individuals with a proven technical track record in the industry as well as in leading PDA. When considering Board candidates, great care is taken to ensure that the future Board and Officers represent the highest technical competency while reflecting the diversity of our membership. Qualifications considered in the nominating process are: significant and well-respected parenteral industry or academic experience; U.S., EU or Japanese regulatory experience; geographical representation; and the type of company represented (manufacturer, consultant, or vendor). The Nominating Committee presents the candidates they recommend to the entire Board of Directors for approval prior to being presented to the membership for an open election. The 2003 Committee was composed of F. Benjamin (Current Chair), N. Mehringer (Chair-elect), and myself.

Prior to the mid-1990's, many of our members felt that PDA was controlled by a small number of people who ran the organization similar to a private club. The Nominating Committee was controlled by the Chair, and individuals selected appeared to be close personal associates who did not necessarily represent the composition of or the best interests of the overall membership. The current revamped Nominating process, as well as term limits on how long an individual can remain on the Board, were instituted under the leadership of Clarence Kemper in the mid-1990's to ensure that PDA is led by a group of technically talented and committed individuals who reflect the diverse views of the membership.

I am very pleased to report that these revised governance processes have been successful. The Board is much more diverse. Seven women now sit as Directors or Officers, the first African American Chairman is now at the PDA helm, and there are Directors from Europe (2), Canada, and Japan. In addition, the first woman Chair was installed a few years ago, and the second will be installed in 2004. In the 2004 slate there was a diverse group of outstanding individuals that represent an excellent cross-section of our membership. For the first time, a European member was nominated. Most importantly, they all have one thing in common: an intense desire/commitment to see PDA progress and maintain its excellent reputation into the future with the organization's interest coming before any personal agenda.

Finally, I want to emphasize how important the recent elections were. I hope each of you voted because this is *your* association. Together we can keep progressing as an association.

As I leave the organization's leadership under the revised process, I am satisfied that the installation of the Board's recommendations for Officers and any four of our Director nominees will ensure we continue to be viewed as the premier scientific and educational organization in the parenteral industry. Please feel free to call me directly at (908) 447-3843 if you have any concerns. Thank you for your time and consideration. ■

—Robert B. Myers
Immediate Past Chair and Chairman of the 2003 Nominating Committee

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President's Message, from page 4

tion and Technology); Editing Secretary Jong-Hwa Oh (sureGMP.com); and Science Secretary In-Koo Chun (Dong-Duck Women's University). They, too, were interested in the PDA peer review system of SAB and RAQC and in learning more about PDA's structures for chapters, membership and committees, as well as the status of overall membership.

The PDA Korean Chapter reached an important milestone by celebrating its fifth anniversary in April 2003. The Chapter publishes the *KPDA Newsletter* quarterly, holds special lectures on pharmaceutical technology three times a year, and published the *FDA CGMP Q&A* (2001), the Korean version of the "Human Drug CGMP Notes" issued by FDA. The Chapter plans to publish a second GMP book, entitled, *Q7A Q&A*.

The Pacific Rim represents an important scientific and regulatory region of PDA. There are exciting opportunities for PDA to improve our science base and to become more involved in regulatory processes. PDA's chapter activities continue to grow in the Pacific Rim. We plan to work more closely with members of industry and regulators there as we expand our platform for scientific dialogue. ■

PDA President Neal G. Koller accepts a gift from Dr. Woo-Hyun Paik, PDA Korea Chapter.

Embracing Nanotechnology

by D. F. Chowdhury, Aphton Corporation

Most of us by now have heard of the term "nanotechnology" in one form or other, ranging from advanced DNA computing to nanobots that will one day run out of control, overtaking the planet, devouring everything in their path and leaving nothing but a blanket of "grey goo," thus signalling the end of mankind. Though some of these ideas are rather farfetched, great technological strides are being made in many fields utilizing what is described as nanotechnology. So how would one define nanotechnology? Depending on whom you ask, you are likely to get a different response. To put it in very simplistic terms, it could be described as technology that allows the precision manipulation of materials down to the submicron range, resulting in systems engineered to meet specific requirements otherwise not achievable through conventional means.

As with most radical technological innovations, those areas of nanotechnology with potentially immediate applications for human beings are likely to attract a tremendous amount of resources because of the potential benefits. This is evident through the numerous specialist companies springing up throughout the world—from the U.S. to the Far East—and the huge government-funded initiatives assisting them. The focus on drug delivery has been an interesting one whereby materials are being manipulated at the submicron level both through conventional technological means and technologies alien to the pharmaceutical industry, originating primarily from the semiconductor industry. This has significant implications for those of us working within the pharmaceutical field. In order to ensure the successful development of these new technological innovations in drug delivery, it will require large multidisciplinary teams to adopt a collaborative approach and address issues relating to manufacture and regulatory compliance, amongst other things, concurrently with their development.

So, how might nanotechnology be of benefit to us in parenteral drug delivery? The therapeutic potential of many molecules currently under development is hampered by factors such as instability of the active constituent, difficulty of passage through biological barriers, inadequate biopharmaceutical profile, and perhaps even technological reasons, i.e., inadequate manufacturing processes. The ability to develop formulations that are engineered at the submicron level has been shown to effectively overcome some of these issues, and a few examples of such systems under research and in commercial development are discussed below.

The ability to target tissue or organs is of greatest importance, especially where the active constituent is either toxic or very expensive to produce, as with many new biologicals. Nanoparticle-based systems are generally good drug carriers that allow better penetration and drug targeting. Their size also allows intravenous administration resulting in instant delivery to the systemic circulation. Nanoparticles for pharmaceutical use were first developed in the mid-1970s by Birrenbach and Speiser[1], and are generally described as colloidal polymeric systems. These systems are in essence based on colloidal science, which thus may not be regarded as an application of emerging nanotechnologies. What is important here is that nanoparticles are systems, which due to their size impart unique properties and pose great advantages to drug delivery. Emerging nanotechnologies allow for more controlled manipulation and production of these systems. This can help enhance their overall performance and ability to deliver therapeutic agents with improved efficacy.

NANOTECHNOLOGY...COULD BE DESCRIBED AS TECHNOLOGY THAT ALLOWS THE PRECISION MANIPULATION OF MATERIALS DOWN TO THE SUBMICRON RANGE, RESULTING IN SYSTEMS ENGINEERED TO MEET SPECIFIC REQUIREMENTS OTHERWISE NOT ACHIEVABLE THROUGH CONVENTIONAL MEANS.

Researchers at the Max Planck Institute in Germany have developed an encapsulation technology[2] that has two different mechanisms—one for storage of compounds and one for the release of the stored compound—with potential applications for a range of therapeutic compounds.

The capsules are prepared by a patented technique labeled layer-by-layer deposition. The layers are built up of charged polymers such as pectins, polyglutamic and hyaluronic acid. Manipulation of the layer properties allows the precise control over its enzymatic degradation. Therapeutic agents may be incorporated into the lumen of the capsule or within any one of its layers, dictating the controlled release profile of the agent from the capsule. Major advantages offered by such a system are their versatility and safety profiles of the materials of construction.

The above example is perhaps based on the more conventional colloidal technologies, but provides an example of how control over the layered structures allows manipulation of drug carrier and release properties. A slight deviation to this is the

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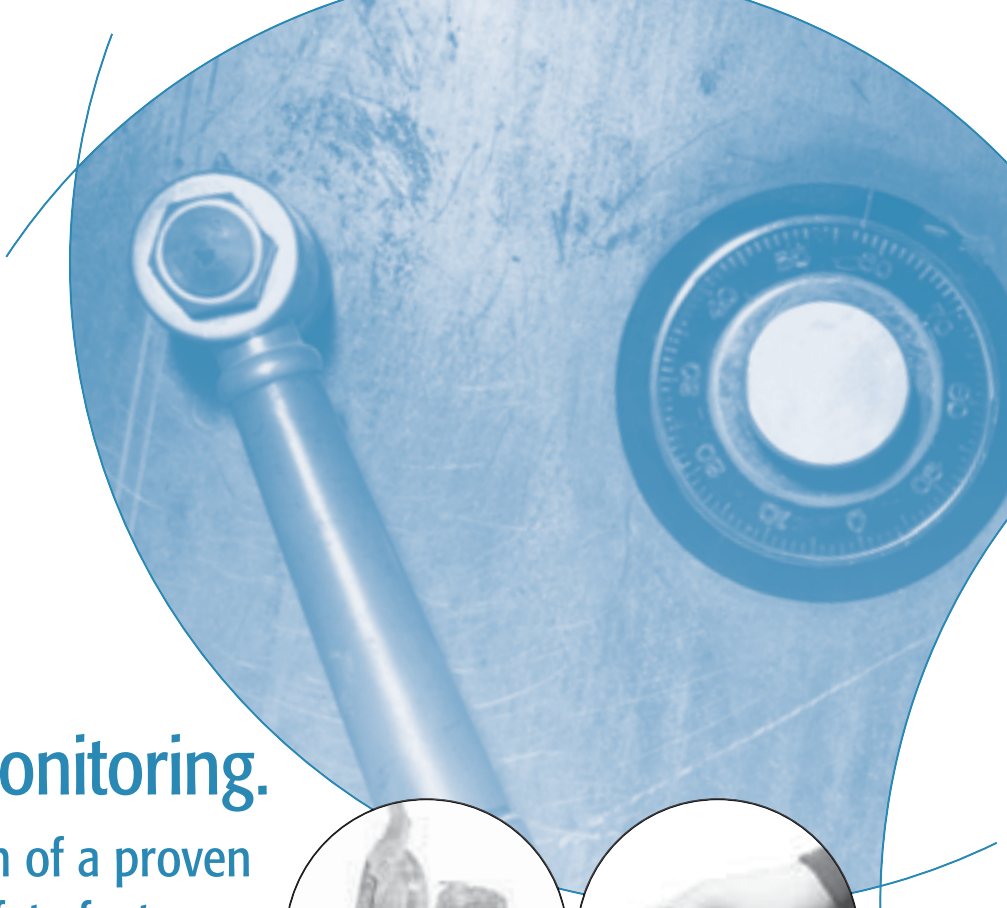

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Embracing Nanotechnology, from page 6

non-invasive nanoshell particles[3], developed by Nanospectra. These particles have the ability to absorb or scatter light at any desired wavelength, even at the level where human tissue is transparent. The particles are in the nanometer-size range that can be optically tuned, and are composed of a dielectric core (e.g., silica) coated with an ultrathin layer (e.g., gold). The nanoshells are embedded in a drug-containing polymer and injected into the body. An infrared laser is directed at the area of injection up to 15 cm away from the site, which causes the nanoshells to melt the polymer and release the drug. This technique could be used to treat, for example, diabetes. Instead of taking an injection of insulin, a patient would use a ballpoint-pen-size infrared laser to heat the skin where the nanoshell polymer had been injected. The heat from the nanoshells would cause the polymer to release a pulse of insulin, precluding the need for regular injections.

Essentially what we are seeing here is that systems are being developed with improved control over drug delivery that could potentially replace traditional parenteral formulations that require very strict dosing regimes.

In addition to the above examples, there are lithographic techniques which have been employed in the semiconductor industry over the last few decades for the fabrication of microprocessors and memory chips. They are now starting to bring a radical change in the field of medical diagnostics and drug delivery. The focus of conventional drug delivery systems has primarily been "top down" technology, whereby bulk materials are processed to produce smaller units. Nanoelectromechanical systems (NEMS) and microelectromechanical systems (MEMS) are miniature mechanical structures that can be fabricated using semi-conductor-based technologies to produce very precise systems and devices providing highly controlled methods of delivering drug to the body. Although this, in essence, is also "top down" technology, it allows for levels of precision and control over dimensions down to the nanoscale, never previously contemplated using existing technologies in the pharmaceutical industry.

The Bio-Capsule For Chronic Disease

Diabetes has posed a challenging healthcare management issue, and is one of the largest causes of death in the West[4]. The rapid rise in blood sugar levels cannot be adequately neutralized by peripherally administered insulin using the mechanism of administration based on existing formulations and technology. The most effective method of treatment is therefore the self-regulation of insulin via the allotransplantation of islet cells into the patient. However, immunorejection by the body and the adverse effects of drug-mediated immunosuppression does not make this a viable option.

Microfabrication, however, has been used to prepare microcapsules (otherwise referred to as biocapsules), which allow the immunoisolation of islet cells for the treatment of diabetes[5]. The device is approximately 2–4mm long and is a planar structure with a reservoir within which the cells are stored. A semi-permeable nanoporous membrane allows the influx of metabolic products such as glucose and insulin. However, it is impermeable to macrophages and antibodies, thus protecting the islet cells. This allows the exit of glucose in a self-regulating manner. The nanopore membrane is produced by the surface micromachining of a thin polymer film on the surface of a silicon wafer, with subsequent etching away of the bulk silicon providing pores (approximately 24.5nm diameter) of very high tolerance and uniformity. Tolerance and uniformity are essential in the process of immunoisolation due to the small differences in size between insulin molecules and those agents deemed toxic to the islet cells.

The chronic nature of diabetes means that improved dosage forms and patient compliance is crucial in minimizing adverse events and in ensuring an efficacious treatment regimen. This is true of other chronic diseases like cancer, spinal cord injury and traumatic brain injury. The treatment of such conditions with conventional dosage forms is susceptible to non-compliance and the associated complications. Apart from the system described above for diabetes, implantable microsystems can be fabricated to provide the appropriate dosing regimen over sustained periods and to avoid those complications associated with poor patient compliance.

A key feature of an implantable drug delivery system is the dosing/dispensing pump. These are prepared via surface micromachining techniques[6]. One such example is the deposition of lead zirconate titanate (PZT) onto the surface of silicon nitride membranes completely sealing a cavity present in the silicon substrate beneath the membrane. It is then possible to cause deflection of the membrane by application of an electric field across the PZT layer. The presence of exit and entry channels with valves will thus create a unidirectional flow of fluid from the reservoir to the external environment, the frequency and volume of which is directly and precisely controlled by the size, direction, and frequency of the applied elec-

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TR-32 Update

Documentum Completes Second Series of Successful Pharmaceutical Industry PDA Audits

by Bonnie Harris, Documentum and Harvey F. Greenawalt, ARC

Independent Industry Audits Demonstrate Documentum's Expertise in Meeting the Specialized Needs of Government-Regulated Industries

Documentum (Nasdaq: DCTM), the leading provider of enterprise content management (ECM), today announced that it has successfully completed two additional PDA Pharmaceutical Industry Software Supplier Quality Audits. The company first announced successful completion of a PDA audit in April of last year. The evaluations, conducted by independent, PDA-sanctioned auditors, verify Documentum's compliance with federal government requirements for companies supplying software solutions to the pharmaceutical industry. The audits took place at the Documentum headquarters in Pleasanton, CA, and at its Customer Support Center in Toronto, Ontario, Canada, which was added through an acquisition completed in early 2002.

"The audit at our Toronto site verifies that the Documentum development life cycle and software development processes have been quickly adopted and fully implemented at this location," said Paul Gray, Director, Corporate Quality Assurance for Documentum.

Audit Requirements

Pharmaceutical companies, medical device, and clinical research organizations must demonstrate that their computer systems are validated and comply with industry regulations, such as the Food and Drug Administration's (FDA) stringent 21 CFR Part 11. The audits required to demonstrate compliance are both time-consuming and costly. Documentum eliminates the need for its customers to conduct their own audits by making audit results of Documentum software available through a centralized repository, providing significant cost and time savings to customers. In addition, prospective customers in these highly regulated industries can access Documentum audit results, bypassing their own lengthy audit process, which in turn, streamlines the procurement cycle, thus enabling them to more quickly select and implement Documentum solutions.

Documentum Helps Companies Meet Regulatory Requirements

Compliance with the FDA's prescribed regulatory requirements for electronic records and signatures (21 CFR Part 11) is one of the most challenging and business-critical issues facing the pharmaceutical, chemical, biotechnology and medical device industries today. The Documentum ECM platform can help companies meet these requirements. In fact, Documentum created its own 21 CFR Part 11 compliant Quality Manual using the Documentum ECM platform.

"This second series of independent assessments confirms that Documentum continues to provide a best-in-class solution for managing the secure generation and delivery of content, from research and development through to commercialization and production," said Dave DeWalt, President and Chief Executive Officer of Documentum. "Documentum is one of the few software companies that have successfully completed three PDA audits, and we'll continue to assist customers in addressing industry regulations, as we've done for more than a decade."

For more information on the official report of Documentum's PDA Audit or to obtain a copy of the report from the Audit Repository Center, contact Harvey Greenawalt, President of ARC, at hgreenawalt@auditcenter.com.

Pharmaceutical Companies Rely on Documentum

With more than 180 customers in the pharmaceutical industry, Documentum is a trusted provider of ECM solutions for companies competing in this highly regulated market. Documentum customers include Acurian, AstraZeneca, Bristol-Myers Squibb, Hisamitsu Pharmaceutical Co., Schering-Plough and Hoffman La Roche.

About Documentum

Documentum is the industry's leading enterprise content management provider, automating the production, exchange and personalization of all types of content, making it easier for the Global 2000 to gain competitive advantage by connecting employees, business partners and customers worldwide. Built on an Internet-scale, XML-enabled and standards-compliant platform Documentum products manage Web content, power portals, enable collaborative commerce, and solve regulatory content challenges. Over 300 partners across all major industries, including high tech, pharmaceutical, healthcare, consulting services, government, manufacturing, financial services, automotive, retail, and consumer goods, build and implement specialized applications using Documentum's content management infra-

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structure. For more information, visit Documentum on the Web at www.documentum.com.

Documentum's Public Relations contact is Bonnie Harris, B3 Communications, at (415) 332-5816 or at bharris@b3communications.com.

For training on PDA Technical Report No. 32, "Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations" and on Auditor Qualification contact Bob Mello, Ph.D., Vice President for Education/Director of the PDA Training & Research Institute, 1450 South Rolling Road, Baltimore Maryland 21227; phone (410) 455-5981; fax: (410) 455-5802; email: mello@pda.org.

Membership

Fifty-six major pharmaceutical/chemical, biotechnology, OTC and medical device companies have become members of the Audit Repository since June of 2000.

Fifteen Suppliers of computer products and services to the industry have become members of the Audit Repository to voluntarily place their audit data in the repository for distribution to their pharmaceutical industry clients.

Auditor Resources

Currently there are 98 PDA Qualified Auditors. The PDA Qualified Auditors represent over 16 countries throughout North America, Europe, and Asia.

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

Availability of Audits

Currently 54 audits are either under consideration, in process or are available for distribution. Thirty audits are available for immediate distribution.

Table 1.0 provides a summary of the 33 audits that are currently available for distribution from the repository.

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

Table 1.0 appears on next page

Supplier Name	Supplier Product
1. Access360, Inc.	enRole 4.0 (Provisioning Software)
2. Agilent Technologies	Cerity for Pharmaceutical QA/QC. Network data system for analytical laboratories
3. Alacris, Inc.	idNexus, Alacris products are designed to simplify identity management and maximize trust associated with Public Key Infrastructure (PKI) implementation and security technologies
4. Applied Biosystems, Inc.	SQL LIMS™ Software—Laboratory Information Management System
5. Automation Tooling Systems, Inc.	Custom programming services for Process Control Software
6. Decision Management International, Inc. (DMI)	Regulus™ Document Authoring (DA) a member of the Regulus™ off-the-shelf solution set
7. Docent	• Docent Learning Management Server; • Docent Content Delivery Server
8. Documentum, Inc.	• Content Authentication Services (CAS); • Documentum eContent Server; • Document Control Manager (DCM); • GXPharma
9. Documentum, Inc.	• Document WebDAV Server; • Document Media Services; • Documentum Digital Asset Manager; • Document Desktop for Macintosh
10. Documentum, Inc.	• Documentum DocApp Installer; • Documentum Administrator; • Documentum Application Builder; • Documentum DeskTop; • Documentum Web site Manager; • Documentum WebTop; • Web Development Kit; • Documentum Workflow Manager
11. Entrust Technologies Ltd.	Digital security technology for enterprise resource systems. Public Key Infrastructure Technology (PKI)
12. Epicentric, Inc.	Foundation Enterprise Server 4.0, which is a tool for coordinating information from disparate sources and for disparate uses
13. First Consulting Group, Inc.	Custom information-based strategy software, operations improvements, management and integration services
14. Fisher-Rosemount Systems, Inc.	Distributed Factory Automation, Delta V product line
15. Foss NIRSystems, Inc.	SLE Near-infrared analysis of chemical and physical properties
16. GE Kaye Instruments, Inc.	Thermal validation systems, monitoring systems, thermocouple references and turbine temperature monitoring equipment—LabWatch™, ValProbe™ and the Validator®2000 systems
17. Inktomi Corporation	Enterprise Search. Providing performance, scalability, and ease-of-use, Inktomi Enterprise Search is a comprehensive information retrieval platform that delivers access to content across the enterprise, regardless of location, language, or file format
18. Innovatum, Inc.	DataThread™—Data audit, workflow, 21 CFR Part 11 and e-signature solution for AS/400 applications, without programming changes
19. Interwoven, Inc.	Web Publication Management
20. Lexign Corporation	Lexign Flow™ EPR Software
21. LoftWare, Inc.	Loftware Print Server (LPS) Lable Printing System
22. MARC Global Systems	Warehouse Execution Systems
23. Merant	PVCS Dimensions & PVCS Replicator Software Configuration Management Tool
24. Mercury Interactive	Test Management Tools: • QuickTest Professional; • Astra QuickTest; • Astra LoadTest; • Astra Fast-Track; • LoadRunner; • LoadRunner TestCenter; • TestDirector; • WinRunner
25. Propack Data GmbH	Enterprise Production Management System, PMX 3.2 with Solutions MES and CTM.
26. Rational Software Corporation	Rational Suite® Enterprise: • Rational ClearQuest (for team-based change request and defect management); • Rational ClearCase (configuration management for smaller development teams)
27. SAP AG	mySAP.com e-business platform, specifically: aspects of Supply Chain Management, Product Lifecycle Management and Business Intelligence relevant to pharmaceutical manufacturing operations (includes product lines: SAP R/3 4.5B and SAP R/3 4.6B/C)
28. Schlumberger	Cyberflex Palmer Smart Card and Cyberflex Access Integration Kit
29. Serena Software, Inc.	Serena ChangeMan Automating the Software Lifecycle
30. Sparta Systems, Inc.	TrackWise®. Training, Configuration, Installation and Support for TrackWise®
31. SSA Global Technologies, Inc.	Mid-Range ERP software for manufacturing, supply chain and financial application domains
32. The Sycamore Group	Custom IT Solutions. Integration suite of COTS products and services to bridge data across multiple internal computer systems, including e-commerce, LIMS, ERP, enterprise databases, mainframes and wireless and portable devices
33. Waters Corporation	Empower™ chromatography software and ConnectionsAQT—HPLC System, SystemComponents, Data Management

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tric field. Pumps may also be linked in series to increase pressure differential and throughput. The high precision and accuracy of these systems and the kinetics of drug delivery far exceed that which has been produced via conventional means, which rely primarily upon the passive diffusion of drug over sustained periods.

Implantable Biosensing Drug Delivery System

ChipRX, a U.S.-based company, is working on an implantable bio-sensing drug-delivery system[7]. Reservoirs of drug are loaded within the device which can then either automatically respond to the patients' needs or be controlled by the physician or patient to deliver the required therapeutic dosage. Another U.S.-based company, MicroCHIPS, is involved in the development of drug delivery systems based on silicon or polymer based chips[8] that consist of up to thousands of reservoirs that can be filled with drugs, chemicals or other reagents. The release pattern of the drug, for example, may be controlled, and complicated dosing regimes achieved by the integration of the system with pre-programmed microprocessors, via remote control or by use of bio-sensors.

Nanoporous Membranes

Being able to control drug diffusion at the molecular level through precision control of the pore size range allows one to attain almost constant blood drug levels, which has obvious benefits. This has been exploited through the development of nanopore membranes created using photolithography, thin film deposition, and selective etching to create silicon membranes with highly uniform pores in the nanometer range. A step up from this is to be able to produce particles in three dimensions, engineered to have very specific sizes and shapes, and even pore sizes and distribution. These can act as drug reservoirs, and may be created using microfabrication techniques with thickness in the range of 1 to 50 micro-meters and in diameters of 1 to 100's of micro-meters.

Essentially what we are seeing here is that systems are being developed with improved control over drug delivery that could potentially replace traditional parenteral formulations that require very strict dosing regimes. Furthermore, "difficult" drugs may be "packaged" and delivered to provide the requisite levels of efficacy. Although the science of fabricating and mass production of such systems may already be well underway, there remain some pertinent aspects that must be addressed concurrently to, if not prior to, huge investments in production technology. These include the assessment of material biocompatibility and the determination of toxicological profiles of novel materials that may be employed. Moreover, manufacture methods and technologies significantly differ from conventional methods, and, as such, qualification and validation will bring to light many new issues that must be handled early on if the benefits are to be realized. Broadly speaking, even though some of the systems are described as implantable devices, this makes little difference to the aseptic processing requirements. A substantial degree of validation will need to be undertaken. This is best approached very early on to avoid the situation whereby a delivery system or formulation is developed that stands no chance of ever being adequately validated to conform to regulatory requirements. It is easy to get excited over innovations without considering all the potential road blocks to the successful launch of the final product. To manage the process, multidisciplinary teams need to be established early on, and must meet regularly to address issues as they arise rather than after the fact. Without managing the project correctly, it may turn out to be nothing more than an expensive academic exercise. Furthermore it would be advantageous to the industry to have a forum to overlook the different types of technologies that are being developed under the banner of "nanotechnology" and the related manufacturing and processing methods such that appropriate professionals in the field can stay abreast of developments to be able to make educated decisions on how to move forward, without unnecessary delays in translating perceived advantages to tangible benefits to the patient in what appears to be a paradigm shift in drug delivery technology.

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Recent Sci-Tech Discussions

Documentation Review and Disinfectants in Clean Rooms

The following remarks are taken from an exchange in the Pharmaceutical Sci-Tech Discussion Group, a PDA-sponsored Online Forum held on the Internet at www.pda.org. PDA Online Forums are free of charge and open to the public. They serve as a platform for exchanging practical, and sometimes theoretical ideas within the context of some of the most challenging issues confronting the pharmaceutical industry. If you are not currently a member of a Discussion Group, we encourage you to visit our Web site at www.pda.org and join.

This month's posting...

Question 1

I've seen several opinions in cleanrooms for leaving disinfectants on walls, ceilings, and floors; however my own experience is not to leave any disinfectants, due to related problems with microorganism growth adapting process and to leave strange substances in cleanroom. Many A-V indicate rinse surfaces after the disinfection process. What is your opinion?

Response 1.1

There is a great article published by McDonnell and Russell that totally refutes the idea that microorganisms build up resistance to disinfectants (G. McDonnell and A. D. Russell, "Antiseptics and Disinfectants: Activity, Action, and Resistance," Clinical Microbiology Reviews, January 1999, p. 147–179, Vol. 12, No. 1.) Here is a link to the article. http://cmr.asm.org/cgi/content/full/12/1/147.

Response 1.2

I have seen an alternating schedule of LpH and Vesphene that was left on walls and ceilings. I have heard that microbial resistance to these agents is a myth, but don't know if that is true or one of the "industry myths" that float around with no substance. I do know that when we used bleach, it is rinsed mainly because it will eat stainless steel, but the other stuff was left on. Hope this helps.

Question 2

We perform an annual review of any documentation that has not been modified within the past year. A lot of times this review process does not lead to any changes or modifications. The revision and effective date remains the same. Some auditors have commented that we should revise the effective date and/or revision after the review even though there have been no changes. I just wanted to know what your thoughts were on this situation. Any comments/suggestions will be greatly appreciated. Thanks in advance for your opinion.

Response 2.1

Document the review through your document change control system. Then, when questioned, you will have documentation of the review and non-revision. It comes down to choosing your method of traceability. If you have 50 SOPs, the suggestion may be feasible; if you have 5,000 SOPs, that's a different situation.

Response 2.2

In my experience, even though changes are not made, the revision and effective date need to reflect that the document has been reviewed.

Response 2.3

Revising the effective date and revision number is not required and is a waste of valuable resources if no changes are needed. The key point is to be able to document that the SOPs have been reviewed by the appropriate persons per your SOP. I have never had a problem with this as long as I had documentation of the proper review by all required persons for each SOP.

Response 2.4

If absolutely no changes are made to the document following extensive review, then I still believe that its history should reflect the review and a comment made in this section that a review of the document relative to the most current regulatory/quality guidelines or rules show it to be compliant with the appropriate regulations as they have been interpreted and executed in May, 2003. Even if no changes were made, this information is important to demonstrate that the review and the "seal of compliance" has been placed on the most recent document. It also demonstrates that the SOP re: annual review of documentation has been followed.

Response 2.5

For sure you need to keep a record that the review has taken place. About 50% of the companies I audit keep logs that the review has taken place but do not reissue the document if nothing has changed. The other 50% reissue the document in its entirety just changing the effective date (to me a colossal waste of time).

Response 2.6

We, too, have a review period of documents, once a year. We are reviewing documents on due dates, and if there is no change felt, then we stamp the documents with "Reviewed—No changes required" along with date of review and reviewed by. Of course there is an SOP governing this requirement. I feel this is sufficient to fulfill the requirement.

Response 2.7

Review of SOP after a certain prefixed time is a must and is a good practice. Most of the time, on an average, about 20–30% of prevailing SOPs do not require any alteration or change. Under this circumstance too, you have to stamp such SOPs reading "Reviewed—No changes required." Changing of effective and revision dates of these SOPs depend on the SOP governing these requirements. What is of main concern is that you must review your SOPs as per prefixed time; usually it's done annually, unless the SOP specifically defines otherwise, or if circumstances/other changes compel you otherwise. ■

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U.S. Regulatory Briefs

Guidance for Industry, 180-Day Exclusivity When Multiple Abbreviate New Drug Applications Are Submitted on the Same Day Recently, there have been a number of cases in which multiple Abbreviate New Drug Applications (ANDA) applicants or their representatives have sought to be the first to submit a patent challenge by lining up outside, and literally camping out adjacent to, a Food and Drug Administration (FDA) building for periods ranging from one day to more than three weeks. Concerns about liability, security, and safety led the property owners to prohibit lines of applicants before the date submissions may be made. This has lent urgency to the question of how the agency deals with multiple ANDA applicants submitting paragraph IV certifications on the same day. There are other periods of exclusivity expiring soon, and FDA believes it is possible there will be multiple ANDA submissions referencing the same listed drug. Because of the seriousness of these issues, it has been necessary to promptly provide information to the industry on how patent challenges may be made to FDA, and how FDA will apply the 180-day exclusivity provisions of the statute to these submissions.

FDA intends to apply a *multiple first applicant* approach to eligibility for 180-day exclusivity by considering all substantially complete ANDAs, amendments, and supplements containing a paragraph IV certification to a listed patent that are submitted to the document room on the same day as being *first applicants*, when no paragraph IV certification to the patent has been submitted on any previous day, as long as the applications comply with the applicable requirements for submission. FDA considers this approach to be an appropriate interpretation of the statutory language and consistent with the goals of the Hatch–Waxman Amendments. This approach will provide all applicants submitting patent challenges on the same day an opportunity to share in exclusivity; it permits submission by U.S. mail, courier, or delivery service; it permits, but does not require, submission in person; it avoids the random aspect of a lottery or mail room date stamp approach; it will prevent disputes over *who's first*, which rely on video and other evidence; and it will preserve the safety and security of the applicants and FDA property and staff.

Exclusivity begins to run, independent of the approval, with the commercial marketing of that drug product or with a court decision on the patent, whichever comes first. Exclusivity will be triggered for all of the first applicants for a specific listed patent by the earlier of commercial marketing by one of the first applicants or by a court decision (regarding the patent as to which the applicant is a first applicant) finding the patent invalid, unenforceable, or not infringed. The commercial marketing trigger will begin exclusivity as to all of the listed patents; a court decision will only begin the running of exclusivity as to the patents addressed in the decision.

During the exclusivity period, FDA may approve any other first applicant's ANDA, but no other ANDAs. Any first applicant whose ANDA is approved after the exclusivity has been triggered will share in the remaining period of exclusivity. Once the 180-day exclusivity period has run, FDA may approve all subsequent ANDAs.

For more information, go to: http://www.fda.gov/cder/guidance/5710fnl.doc.

FDA Announces Docket for Information on Counterfeit Drugs FDA is announcing that it is establishing a docket to receive information and comments on the agency's initiative against counterfeit drugs. Many individuals, vendors, trade and professional associations, consumer groups, and other stakeholders have offered to assist FDA. This action is intended to ensure that there is a venue for information and comments to be submitted to the agency regarding the anti-counterfeit initiative. Counterfeit drugs pose potentially serious public health and safety concerns. They may contain only inactive ingredients, incorrect ingredients, improper dosages, or even dangerous subpotent or superpotent ingredients. In the United States, drug counterfeiting is a relatively rare event. Although FDA believes domestic counterfeiting is not widespread, the agency has recently seen an increase in counterfeiting activities as well as a more sophisticated ability to introduce finished dosage counterfeits into the otherwise legitimate drug distribution channels. FDA has seen its counterfeit drug investigations increase to over 20 per year since 2000, after averaging only about five per year through the late 1990s.

In an effort to protect against the rising occurrence of potentially unsafe counterfeit drugs reaching consumers, on July 16, 2003, FDA announced an initiative to more aggressively protect American consumers from the risks posed by counterfeit drugs. As part of this effort, FDA established an internal task force that will develop recommendations for steps FDA, other government agencies, and the private sector can take to minimize the risks to the public from counterfeit drugs getting into the supply chain. Some of the areas that FDA's task force will explore include the following topics:

- Technology: assess the extent to which new technologies can help assure the authenticity of drugs
- Regulatory/Legislative Issues: evaluate potential regulatory and legislative changes that could be made to strengthen the nation's protections against counterfeiting
- Public Education: recommend ways to educate consumers and health providers on steps they can take to minimize risks associated with counterfeit drugs; will also educate consumers and health professionals about what to look for and what to do if they suspect they

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have received a counterfeit drug
- Industry and Health Professional Issues: identify actions industry and health professionals can take to prevent, detect, and respond to counterfeit drugs

The task force has the following deliverables:
- An interim task force report was released in September 2003. It will include draft recommendations on which interested persons may comment.
- A public meeting to be held in mid-October 2003; the meeting announcement will be published in a forthcoming *Federal Register* and will pose issues for discussion at the meeting.
- A final task force report to be released in January 2004.

Submit written comments and information to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments. All comments submitted to the public docket are public information and may be posted to FDA's Web site (http://www.fda.gov) for public viewing. Please include the docket number 2003N-0361 on all correspondence. The agency encourages interested parties to submit information by November 30, 2003.

For further information, contact: Poppy Kendall, Office of Policy (HF-11), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; (301) 827-3360; e-mail: pkendall@fda.gov.

Submit written comments and information to: Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to: http://www.fda.gov/dockets/ecomments. All comments submitted to the public docket are public information and may be posted to FDA's Web site (http://www.fda.gov) for public viewing. The agency encourages interested parties to submit information by November 30, 2003. The *Federal Register* Notice can be found at: http://www.fda.gov/OHRMS/DOCKETS/98fr/03-21751.htm.

The Food and Drug Administration Announces Withdrawal of Guideline for the Clinical Evaluation of Analgesic Drugs FDA is announcing the withdrawal of a guideline entitled "Guideline for the Clinical Evaluation of Analgesic Drugs," which was issued on December 1, 1992. The guideline is outdated and no longer reflects FDA's current thinking on the development of analgesic drugs. FDA is revising the guideline and will issue a draft for public comment in the future. For further information, contact: Barbara J. Gould, Center for Drug Evaluation and Research (HFD-550), Food and Drug Administration, 5600 Rockville Pike, Rockville, MD 20850; (301) 827-2504.

The Food and Drug Administration Withdraws Draft Guidance on Nucleic Acid Testing of Pooled Plasma FDA is announcing the withdrawal of a draft guidance entitled "Guidance for Industry: Application of Current Statutory Authority to Nucleic Acid Testing of Pooled Plasma" dated November 1999, that was announced in the *Federal Register* on November 26, 1999. In the draft guidance, FDA sought public comment on the development and implementation of nucleic acid testing (NAT) for infectious diseases. The effective date of withdrawal was September 22, 2003.

In a notice published in the *Federal Register* of November 26, 1999 (64 FR 66481), FDA announced the availability of a draft guidance entitled "Guidance for Industry: Application of Current Statutory Authority to Nucleic Acid Testing of Pooled Plasma" dated November 1999. This draft guidance responded to industry's request for guidance in the development and implementation of NAT of pooled plasma in further improving the safety of the nation's blood products. No NAT test kit manufacturers were licensed at that time. A number of manufacturers have subsequently been licensed for NAT, making the request for guidance in the development of NAT testing of pooled plasma for infectious agents now moot. This draft guidance was therefore withdrawn as of September 22, 2003, because it is obsolete.

For further information, contact: Astrid L. Szeto, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448; (301) 827-6210.

The withdrawal notice can be found at: http://www.fda.gov/OHRMS/DOCKETS/98fr/03-21477.htm.

Electronic Human Cell and Tissue Establishment Registration Now Available Form FDA-3356 [Establishment Registration and Listing for Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)] is now being accepted by electronic submission through a secure Web server.

All establishments that manufacture HCT/Ps are required to register with FDA, pursuant to 21 CFR Part 1271. They must register within five days of beginning operation, and annually in December. Registrants must also submit a list of every HCT/P manufactured, and update their HCT/P listing every June and December if there is a change.

HCT/P establishments located outside of the U.S. that import or offer for import HCT/Ps into the U.S., are required to register with FDA. Foreign registrants must provide the name of their United States agent, the name of each importer, and each person who imports or offers for import the registrant's HCT/Ps.

Registrants use Form FDA-3356, Establishment Registration and Listing for HCT/Ps, to submit registration and HCT/P listing information to FDA. The form (and accompanying instructions) may be downloaded to complete and submit by mail. Alternatively, the form can now be submitted electronically. For more information, go to: http://www.fda.gov/cber/tissue/tisreg-esub.htm. ■

—William Stoedter

Meet the Regulator

Paul Stinavage, Ph.D.

Paul Stinavage, Ph.D., is the Senior Microbiology Reviewer for the Center for Drug Evaluation and Research (CDER) in the Office of Pharmaceutical Science at FDA. His primary job function is to review microbiological methods and acceptance criteria, manufacturing controls, and product attributes as described in new and supplemental New Drug Applications (NDAs) and Investigational New Drug Applications (INDAs). He also serves as a major contributor on policy issues regarding sterilizing filtration issues in drug manufacture. Stinavage is a member of the committee that drafted PDA Technical Report No. 26, *Sterilizing Filtration of Liquids*, and he is a member of the United States Pharmacopeia's (USP) Pharmaceutical Waters Expert Committee.

He joined FDA in 1994 as a Staff Fellow under the supervision of Dr. Peter Cooney. His career started at Pall Filters, where he was a Staff Scientist/Microbiology Laboratory Manager in the Scientific and Laboratory Services division of the company. Following his work at Pall, Stinavage worked for Calgon Corporation in the industrial biocides area.

Stinavage earned a B.S. degree in Biology and Chemistry from Marywood College in Scranton, Pennsylvania. He earned his doctoral degree from Cornell University's Graduate School of Medical Sciences. His thesis research was carried out in Dr. Larry Senterfit's laboratory. His thesis initially examined the documented clinical observation that infection led to a decrease in blood glucose control in diabetic patients. The etiology of this observation was also examined in a diabetic animal model. His post-doctoral work was performed in Dr. John Spitznagel's laboratory at Emory University. There he examined the molecular basis for the ability of *Salmonella* to survive in the phagosomes of polymorphonuclear leucocytes.

Stinavage grew up on a dairy farm in northeastern Pennsylvania. He is married with four children: Maria–14, Kristin–13, Andrew–12, and Michael–10. He enjoys vegetable gardening, hunting, and fishing with his children. ■

—compiled by Evelyn Heitman

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Global Regulatory and GMP Briefs

EMEA News

Updating the Notice to Applicants—Medicinal Products for Human Use—Volume 2B

Presentation and content of the dossier—Part 1: Summary of the dossier—Part 1A—1998 edition or Common Technical Document—Module 1—Administrative information: application form—2001 edition.

Application Form:

The application form is updated in section 2.5.1.2 Batch control/Testing arrangements and section 2.5.3. Manufacturer(s) of the active substance.

User Guide for the Application Form:

The application form is updated in section 2.5.1.2 Batch control/Testing arrangements and section 2.5.3. Manufacturer(s) of the active substance.

Commission Communication on Regulation (EC) No 141/2000 on Orphan Medicinal Products

Following the first three years of application of the Regulation on Orphan Medicinal Products, the Commission has issued a Communication which sets out a position on certain matters relating to the implementation of the designation and market exclusivity provisions. This has been done in response to requests for interpretation and clarification.

The Communication is intended to provide guidance to the European Medicines Evaluation Agency, the Member States, the pharmaceutical industry and other interested parties. The Communication considers points in relation to:

- Article 3 (criteria for designation)
- Article 5 (procedure for designation and removal from the Community register on orphan medicinal products)
- Article 7 (Community marketing authorisation)

In addition, the Commission is obliged to draw up detailed guidelines on the application of Article 8 of Regulation (EC) No 141/2000. This obligation is met in part by section D on market exclusivity (Article 8) in the Communication. The Communication is published in the *Official Journal of the European Union* C 178, 29.07.2003, p. 2.

New Application Form for Variation to a Marketing Authorisation for Medicinal Products (Human and Veterinary) to be Used in the Mutual Recognition and the Centralised Procedure.

The new application form for variations to a marketing authorisation should be used from 1 October 2003 and is in accordance with the new Commission Regulations (EC) No 1084/2003 and (EC) No 1085/2003. This application form is self-explanatory and replaces the previous application forms in Volume 2C and 6C of the Notice to Applicants for Medicinal Products for Human Use and Veterinary Medicinal Products. The previous explanatory note on how to fill in the form is therefore redundant and will be deleted. The Application Form in Word 97 format can be found at: http://pharmacos.eudra.org/F2/eudralex/vol-6/newdoc/newvarform_250703.doc. The Application Form in PDF format can be found at: http://pharmacos.eudra.org/F2/eudralex/vol-6/newdoc/newvarform_250703.pdf.

For details on the above news, please visit: http://pharmacos.eudra.org/F2/pharmacos/docs.htm#news.

Australian Therapeutic Goods Administration

Australian Regulation of Prescription Medical Products

August 2003

It is a requirement under the Therapeutic Goods Act (TGA) 1989 (the Act) that medical products to be imported into, supplied in, or exported from Australia be included in the Australian Register of Therapeutic Goods (ARTG). In order for a product to be included in the ARTG, a sponsoring company is required to make an application, which usually consists of a form accompanied by data to support the quality, safety and efficacy of the product.

It is a requirement under the Therapeutic Goods Act (TGA) 1989 ... that medical products to be imported into, supplied in, or exported from Australia be included in the Australian Register of Therapeutic Goods (ARTG).

The TGA requirements for data are based on the European Union (EU) requirements, and TGA accepts data packages in the EU format and the EU version of the international Common Technical Document, www.health.gov.au/tga/docs/html/eugctd.htm. For high priority drugs for important and serious illnesses, which often include drugs to treat cancers, sponsors may, by prior agreement, submit the U.S. dossier.

Within the European system, there are a series of guidelines, most of which have been adopted by TGA, that deal specifically with the issue of data requirements. These guidelines can be accessed from: www.health.gov.au/tga/docs/html/euguideh.htm.

After an application is made, there is an initial short period during which it is assessed on an administrative level to make sure there is compliance with basic guidelines. This is to save time so that applications which are premature or grossly deficient do not end up within the evaluation sys-

tem, causing delays for themselves and other products. This phase is called the Application Entry Process. At the end of this phase, a decision is made to either accept the application for evaluation or to reject it.

Over 99% of applications are accepted for evaluation at this point in time, but many require questions to be asked to further define the indication being sought or to substantiate that information will either be provided in the future or is not required. At this point, companies are also able to flag with TGA additional data that, while not actually required to substantiate the value of the product, but which could enhance the assessment outcome, will be available at a point determined by negotiation. These additional data may then be submitted at that agreed point in time.

Once an application is accepted for evaluation, the different data parts are allocated to the sections that will evaluate them. The chemistry and quality control and laboratory aspects of products are evaluated by the Pharmaceutical Chemistry Evaluation section and the TGA Laboratories Branch. The pharmacological and toxicological aspects of products are assessed by the Drug Toxicology Evaluation section, and the clinical data are assessed by the Clinical Evaluation section, which specialises in those sorts of products. All of these areas may use the advice of experts and contract out either aspects or the entire part of the evaluation process. Evaluation reports are prepared independently by the evaluators.

Following evaluation, the chemistry and quality control aspects of a product are likely to be referred to the Pharmaceutical Sub-Committee (PSC), which is a sub-committee of the TGA prescription medicine Expert Advisory Committee, the Australian Drug Evaluation Committee (ADEC), www.health.gov.au/tga/docs/html/adec/adec.htm. The PSC consists of experts with pharmaceutical manufacturing and other expertise. The PSC reviews the evaluation reports prepared by the quality control evaluators and the questions that are asked of the company and advises on whether these are reasonable or not. The resolutions of the PSC are given to the company, as are the in-process chemistry and quality control evaluation reports.

For all evaluation sections, evaluators may ask questions to clarify issues during the evaluation process or to request data that have not otherwise been submitted. When evaluation reports are finished, they are examined by a senior officer within the section to ensure that they are complete and are of an adequate quality. Evaluation reports are then sent to the sponsoring company. The company is allowed the opportunity to provide corrections or comments on the views expressed within the evaluation report.

The company may also, in the case of the pharmacology, toxicology and clinical evaluation reports, signal to TGA their wish to submit supplementary data to address points raised in these evaluation reports. This intention must be notified soon after receiving the reports, and causes the clock to stop (which monitors the time spent on evaluations) for an agreed period that has been negotiated between the industry and TGA. The supplementary data will be submitted, evaluated, and then the clock will restart.

When all the evaluations are complete, a senior medical officer within TGA prepares a document outlining the key issues on which advice is sought from the independent advisory group, ADEC. This summary is sent to the sponsoring company, which is able to submit a response dealing with issues raised in the summary as well as those not previously addressed in the evaluation report. This response goes directly to ADEC and is not edited by TGA.

ADEC is an expert advisory group appointed by the Minister. The current Chair is Professor Martin Tattersall. The Committee meets every two months and examines applications referred to it by TGA. It also provides advice on matters regarding drug regulation and specifically, on whether new chemical entities should be approved for marketing in Australia or whether

continues on page 21

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products already approved should have their indications varied. The Committee receives full copies of the clinical evaluation report, the toxicology/pharmacology report, a summary of the pharmaceutical chemistry evaluation report and the minutes and resolutions of the PSC, if relevant. Its resolutions are provided to sponsor companies after five working days.

A delegate within TGA is the decision-maker who takes into account the advice of ADEC in reaching a decision to approve or reject a product. Approvals may have conditions associated with them. One of the strengths of the system is the independent checking of the quality of the review process at all levels. This ensures a fair process for all parties involved.

There is confusion sometimes about the availability of medicines in Australia. It is a requirement under the Act that a sponsor initiate an application. It is not possible for TGA to require a company to submit an application. There may be a number of factors that will influence whether a company will apply to have a product registered in Australia. For example, the product may be registered overseas, but a local company might not have a licence agreement. There may also be delays because dossiers may be submitted at different times throughout the world. In the case of medicines for important medical conditions, such as most oncology and HIV drugs, however, TGA will accept either the European or American dossier format to try to expedite early submission in Australia.

It is also possible that a product is approved, but the sponsor company may choose not to supply the product or not to launch it for some time after approval is given. TGA is aware of examples where products have been launched one to two years after TGA approval was actually given.

The time taken to approve a product can vary considerably. This time consists of time spent by TGA evaluating the product, and time spent with the company clarifying questions raised by TGA. In general, the time in calendar days in Australia is made up of around 50% time spent with industry, and 50% time spent with TGA. The TGA and industry are aware of this and are working together to reduce the total evaluation time. The total time is heavily dependent upon the quality of the submission as initially received and on the preparedness of the sponsor to work with TGA. For example, the approval of the anti-cancer drug Glivec, or imatinib, was achieved within five calendar months. This was a very short time, and was the result of the company's preparedness to work with TGA and also to provide information quickly to TGA during the evaluation process.

An international research institute, CMR International, has published some comparisons of the approval times for new chemical agents from different regulatory agencies. It concluded that Australia's performance was similar to those of comparable international agencies, including those in the U.S. and Europe.

TGA has a system of priority evaluation for products that meet certain criteria. These are: (1) that the product should be a new chemical entity; (2) that it is not otherwise available on the market as an approved product; and (3) that the product is for the treatment of a serious, life-threatening illness for which other therapies are either ineffective or not available (that is, the product should offer a significant therapeutic advance). The allocation of a priority review is limited to these circumstances as it is very resource-intensive.

The "European Guidelines" referred to above, www.health.gov.au/tga/docs/html/pmeds_reg.htm#eu#eu, which have been adopted by Australia, allow for the approval of products for certain serious conditions, such as cancer or HIV, based on Phase 2 trials. For example, in the case of serious cancer, there is no requirement for a Phase 3 clinical trial to be submitted in Australia. Nor is there a requirement for a trial for every medicine to be conducted in Australia before a product can be approved. There are, however, requirements that trials be conducted in accordance with international good clinical practice and ethical standards, as well as minimum requirements regarding the quality of trial data.

The time taken to approve a product can vary considerably.

There are some legal exemptions to the requirement for a product to be registered by TGA. These are implemented through the clinical trials systems (CTX and CTN), www.health.gov.au/tga/docs/html/clintrials.htm, and the Special Access Scheme (SAS), www.health.gov.au/tga/docs/html/sasinfo.htm.

TGA has a multi-faceted program for monitoring approved products that are on the market. There is a problem reporting system, a recall unit, and the report of adverse drug reactions is encouraged by the Australian Drug Reactions Advisory Committee (www.health.gov.au/tga/adr/adrac). This subcommittee of ADEC publishes a regular bulletin for doctors, dentists and pharmacists. TGA Laboratories undertake random and targeted sampling of approved products. Sponsoring companies are required to provide regular post-market reports on approved products and to inform TGA of any international concerns related to the safety or effectiveness of a product. ■

—Gautam Maitra

Human Drug CGMP Notes

First Quarter, 2003

A Memo for Food and Drug Administration Personnel on Current Good Manufacturing Practice For Human Pharmaceuticals

Issued by The Division of Manufacturing and Product Quality, HFD-320, Office of Compliance, Center for Drug Evaluation and Research

Project Manager: Brian J. Hasselbalch

Special Report: This document is prepared periodically by FDA for internal use. It is being presented here for informational purposes only; PDA has neither endorsed these comments nor verified the information for accuracy.

This information represents the Food and Drug Administrations' (FDA's) current thinking on Current Good Manufacturing Practice (GMP) for human pharmaceuticals. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Questions

Stability

• What is the regulatory status of the International Conference on Harmonisation (ICH) guidance, "Stability Testing of New Drug Substances and Products"? Is it appropriate to cite on a FDA 483 instances of this guidance not being followed?

Part 11

• What has recently changed with the Part 11 rule covering electronic signatures and records?
• When do you expect to publish the final version of the "Guidance for Industry Electronic Records, Electronic Signatures Scope and Application"?
• When do you plan to finish reexamination and revision of Part 11?
• Can two or more people share the same user name and password to access the computer for a Part 11-regulated function?

Aseptic Fill

• What is the status of the revisions to the aseptic processing guidance?

Equipment Status Labels

• Is it acceptable for a firm to discard equipment status labels?

Stability and Reprocessing

• Is the stability data from a reprocessed batch that was not distributed to be included in the Abbreviate New Drug Application (A/NDA) annual report?
• What do the CGMPs require concerning a production batch that has been reprocessed?

Announcement

• New USP Guidance Available on Unit-Dose Blister Packaging Operations (details within)

General Comments

The CGMP program is being redesigned, as you've no doubt noticed. This time last year FDA field investigators conducting drug process inspections were given a new, systems-based Compliance Program Guidance Manual to follow (7356.002). More recently, warning letters citing CGMP deficiencies now require Center approval; a new dispute resolution procedure for situations arising from inspections is under development; and other program changes covering both the inspection and the application review process are under consideration. The most recent changes are an outcome of an initiative launched last August known as GMPs in the 21st Century. Representatives from CDER, CBER, CVM, ORA, and OC are working together on the various activities of this effort. Other areas of this initiative include (summaries borrowed from existing announcements):

External Studies of Regulatory/ Industry "Effective Practices"

FDA has recently contracted with an outside research firm to identify "effective practices" in industry and other governmental regulators with respect to achieving product quality. Additional studies by outside researchers may also be supported or sponsored by FDA to provide working groups independent research in their topic areas.

Quality Systems

FDA has established a working group to identify areas for improvement in the application of quality management system practices. This could result in changes to both our internal work practices as well as regulations. In the short term, we will work at ways to further apply internationally recognized standards for conformity assessment to FDA business practices. And in the long term, we will implement out internally harmonized systems by seeking ways to harmonize the requirements we impose on industry with comparable requirements worldwide.

Reevaluating Electronic Signatures and Records Requirement

An important activity in which recent progress has been safe is to reevaluate the impact this regulation has had on all affected FDA-regulated commodities, but especially drugs. A multi-disciplined working group has given a great deal of thought to preserving good electronic information management practices while ensuring, in light of industry experience, that the rule does not inhibit valuable innovation and technologies.

Editor's Note: PDA received this issue of Human Drug CGMP Notes through the Freedom of Information Act.

Better Coordination Pre/Post-Marketing Application Reviews

Recognizing that the on-site assessment (i.e., pre-approval and routine CGMP inspections) and off-site review programs are interdependent and both benefits from efficiency, FDA will better define roles and responsibilities to maximize both programs' areas of expertise.

International Activities

This group is to help coordinate FDA initiative activities with regulatory counterparts around the world. Already this group has requested ICH partners to explore if and how regulator and industry practices impact technological innovation. The group is currently exploring ways to best learn from the experiences of counterpart regulators worldwide.

Risk Management and Work Planning

This area of the initiative will have important long-term consequences and a direct impact on the work of field offices. This work group has reviewed the current work planning model with an eye toward better matching our limited resources with high value programs affecting critical products. Improving site selection decision-making is an area currently being addressed. To learn more about this initiative, see the following Web site: http://www.fda.gov/cder/gmp/index.com.

Remember that FDA is now publishing the Human Drug CGMP Notes EXCLUSIVELY for FDA personnel. ("Exclusively" means that the agency is not posting directly for public consumption, but each edition is fully releasable under the Freedom of Information Act.) With the recent promulgation of the Good Guidance Practices, publishing on FDA's INTERnet Web site would require each edition to be subject to extensive internal review and approval. Since the intended purpose of the Notes is to provide agency personnel with timely answers to their CGMP questions, we've decided to publish in-house only. Be assured, however, that every edition now published comes with the Division's seal of approval, as before.

Questions and Answers:

What's the regulatory status of the ICH guidance, "Stability Testing of New Drug Substances and Products"? Is it appropriate to cite on a FDA 483 instances of this guidance not being followed?

While conformance to the ICH guidance is recommended in applicable situations (see below), it is not a requirement. Citing a firm merely because it is not adhering to the ICH recommendations (e.g., temperature and humidity storage) is not appropriate.

However, if a firm commits itself to following the ICH recommended storage conditions, for example, by incorporating these recommendations in its stability testing protocol or in an approved new drug application, it would be appropriate to

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cite on a FDA 483 a failure to conform to the firm's established procedure.

(Remember that the purpose of the ICH guidance [in this case, ICH Q1A(R)] is to address the generation of stability information for submission in drug applications for new molecular entities and associated products, and the other approaches may be used that are scientifically justifiable.)

As always, before considering any FDA 483 citation for not adhering to guidance, it is important to understand the firm's underlying rationale for the approach taken for the drug in question.

References: *Federal Register*, 66 FR 56332, November 7, 2001.

For further information contact: Barry Rothman, HFD-325; (301) 827-9026; rothmanb@cder.fda.gov.

What has recently changed with the Part 11 rule covering electronic signatures and records?

One outcome of the "GMPs for the 21st Century" initiative, which was first announced in August 2002, has been a complete revaluation of the agency's approach to 21 CFR Part 11, Electronic Records; Electronic Signatures. In fact, FDA recently withdrew all draft guidance and a Compliance Policy Guide (CPG 7153.17) so that the agency could reconsider the effect on innovation associated with compliance to the regulation. In February 2003, FDA published a new guidance to industry for comment. The current draft guidance, Electronic Records; Electronic Signatures—Scope and Application (see link below), has several important differences from the previous draft and approach taken. These are:

- In the agency's overall approach to Part 11 they will interpret the regulation narrowly. Only systems that create/maintain electronic records required by a predicate rule (this includes electronic signature records required by a predicate rule) and those systems that create/maintain records to be submitted to the FDA will be held to compliance with Part 11.
- The agency will exercise its regulatory discretion and not normally enforce the validation requirements of Part 11. Validation may still be required by a predicate rule (e.g., 21 CFR 211.68).
- The agency will exercise its regulatory discretion to not normally enforce the audit trail requirements of Part 11. Audits trail may still be required by a predicate rule.
- The agency will use regulatory discretion to not normally enforce the Legacy System requirements of Part 11, as long as the systems were, and still are, compliant with the predicate rule requirement.
- The agency will exercise its regulatory discretion to not normally enforce the Record Copy requirements of Part 11.
- The agency will exercise its regulatory discretion to not normally enforce the Record Retention requirements of Part 11.

Some important aspects of the agency's approach to enforcing this rule have not changed. They have not changed the remaining requirements for Closed Systems (21 CFR 11.10) or any of the requirements for Open Systems (21 CFR 11.20). The electronic signature requirements [21 CFR 11.100(c)], are the same as they were prior to the release of the draft guidance. They have not altered the e-signature certification requirements. There is a related guidance document that provides useful information in this area: Guidance for Industry: Computerized Systems Used in Clinical Trials, April 1999 http://www.fda.gov/ora/compliance_ref/bimo/ffinalcct.doc.

Industry often asks what particular factors play a role in whether Part 11 compliance is required for a new system. FDA thinks the important factors are system functionality, the intended use of the system at the facility, and, of course, the applicable predicate rule(s), which may vary between GxPs ("x" refers to any and all of Good Practices requirements, e.g., "Manufacturing" and "Laboratory"). The agency's current thinking, as explained in the current proposed guidance, is that it all depends on a risk assessment of the criticality of the electronic data being maintained in the database as per the appropriate predicate rules. If the data being retained in the database is 'critical' data as per predicate rule(s), then the system will require Part 11 compliance.

For human drugs regulated by CDER, the predicate rules that may trigger the need for conformity to Part 11 are as follows:

- 21 CFR Parts 210/211, Current Good Manufacturing Practice Regulations (governing the manufacture, processing, packing, testing, and holding of finished dosage forms)
- 21 CFR Part 58, Good Laboratory Practice Regulations (governing the handling of pre-clinical test and clinical test information, test subject tissue testing, and laboratory animals)
- 21 CFR Part 205, Prescription Drug Wholesaler Licensing Regulations (governing the state licensure of wholesale distributors of prescription drugs)

Some other current and useful links to information about Part 11 are as follows:

- 21 CFR Part 11 Electronic Records; Electronic Signatures http://www.accessdata.fda.gov/scripts/cd/rh/cfdocs/cfcfr/cfrsearch.cfm
- Latest Part 11 Guidance: Electronic Records; Electronic Signatures—Scope and Application; http://ww.fda.gov/cder/guidance/5505dft.PDF
- General Principles of Software Validation; Final Guidance for Industry and FDA Staff (FDA, Center for Devices and Radiological Health, Center for Biologics Evaluation and Research, 2002); http://www.fda.gov/cdrh/comp/guidance/938.html.

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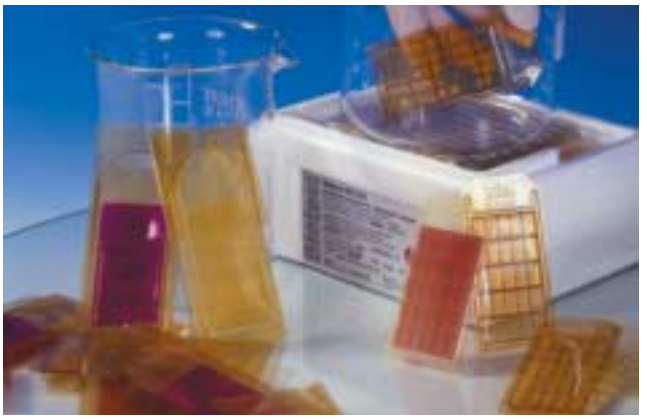

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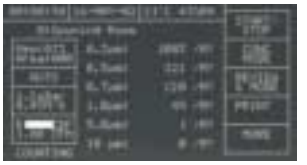

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When do you expect to publish the final version of the "Guidance for Industry Electronic Records, Electronic Signatures Scope and Application"?

At the present time we cannot provide an exact timeframe as to when we will publish the final version but anticipate that it will take between three and six months. The actual date will depend on the public feedback we receive for the draft guidance document, which has a 60-day comment period.

When do you plan to finish reexamination and revision of Part 11?

This will also be closely tied to the feedback the agency receives for the draft guidance document and then to the final version.

Can two or more people share the same user name and password to access the computer for a Part 11 regulated function, or do we require each person to have their own user name and password?

Yes, no. Part 11 does not prohibit the establishment of a common group identification code/password for read-only access purposes. However, such commonly shared codes and passwords would not be regarded, and must not be used, as electronic signatures. Shared access to a common database may nonetheless be implemented by granted appropriate common record access privileges to groups of people, each of whom has a unique electronic signature. Depending on the criticality of the data (as per the predicate rule) and based on a risk assessment and justification, if the access level allows editing of the records, e.g., changes, deletions, or insertions, then each person may be required to have his/her own user name and password, in addition to an electronic signature, if one is to be used.

References: Incorporated above

For further information contact: George Smith, HFD-325; (301) 827-9033; smithg@cder.fda.gov.

What is the status of the revisions to the Aseptic Processing Guidance?

In September 2002, FDA published a concept paper titled Sterile Drug Products Produced by Aseptic Processing. This concept paper is based on the existing Guidance by the same title published in 1987, and is a major step to eventually replace the existing Guidance. The agency published it as a concept paper rather than as proposed guidance to obtain advisory committee input at a meeting held this past October. In addition to adopting the advisory committee recommendations, at the request of the advisory committee, the agency recently discussed this concept paper with a Product Quality Research Institute (PQRI) working group (to learn more about PQRI, please visit their Web site: http://www.pqri.org/). PQRI provided specific recommendations, and FDA is now considering them for incorporation into the draft guidance. The agency anticipates publishing the draft guidance for public notice and comment in the coming months. While a public comment docket has not yet been established for receiving comments on this document, the agency always welcomes FDA staff emails and calls. FDA has been most appreciative of those who have sent in clear, succinct statements of any major "big ticket" issues. You can find the paper on FDA's Web site: http://www.fda.gov/cder/dmpq/index/htm.

One outcome of the "GMPs for the 21st Century" initiative, which was first announced in August 2002, has been a complete revaluation of the agency's approach to 21 CFR Part 11, Electronic Records; Electronic Signatures.

References: Concept Paper, Sterile Drug Products Produced by Aseptic Processing, September 2002.

For further information contact: Rick Friedman, HFD-325; (301) 827-9042; friedmanr@cder.fda.gov.

I once cited a firm for not retaining the labels for determining the status of all equipment after the label was removed. The firm disagreed and claimed that such labels are merely a "quick reference" for manufacturing operations and need not be retained after use. Assuming each major piece of equipment has a unique "Cleaning and Use Log" that is adequately retained, is it acceptable to discard these 'quick reference labels'?

Yes. The CGMP regulations for dosage form manufacturing require the retention of cleaning and use logs for non-dedicated equipment, but no similar requirement exists for retaining what are intended to be temporary status labels. The agency sees no value in requiring such labels to be retained by the firm in addition to the required equipment log or batch record documentation. Examples of these kinds of status labels or tags include "mixing lot ###"; "clean, ready for use as of d/m/y"; and "not clean." The labels, of course, serve a valuable purpose of positively identifying the current status of equipment and the material under process. And it would be appropriate during an inspection to verify that the information on a temporary status label is consistent with the log.

In fact, it is considered acceptable practice to display temporary equipment status information on dry-erase boards or chalkboards. Any status labels should, of course, be legible, readily visible, and associated with the correct piece of equipment. The information on the temporary status label should correspond with the information

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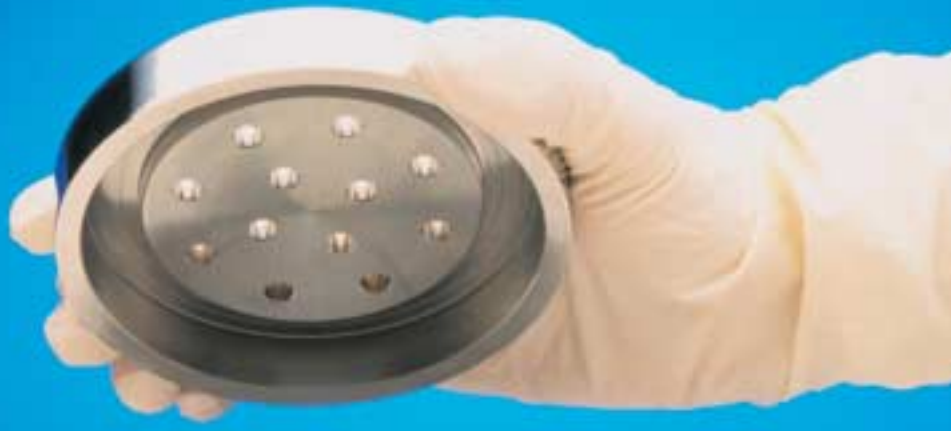

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recorded in the equipment cleaning and use log, or the previous batch record for non-dedicated equipment.

References: 21CFR 211.182: Equipment cleaning and use log.

For further information contact: Brain Hasselbalch, HFD-235; (301) 827-9046; hasseslbalchb@cder.fda.gov.

The CGMPs require that any batch failing to meet specifications be investigated.

Is the stability data from a reprocessed batch that was not distributed to be included in the A/NDA annual report?

No. Firms must include the stability data for a production batch placed on stability in their annual report, whether or not it is released to market, if it represents a distributed batch by the approved process, including an approved reprocessing method (see 21 CFR 314.81). In this case, because the batch was processed differently from the approved manufacturing process, (i.e., the revised process was not approved in the respective A/NDA), and was not distributed, it was not representative of commercially marketed product, and its stability has no bearing on batches made by the established and approved process. Therefore, in this case, the reprocessed batch stability data would not have to be filled in the annual submission to the A/NDA.

This situation arose because the firm chose to reprocess a rejected batch for research and development purposes, perhaps to support a future filing to their approved application for the revised process. Of course, any future application to seek approval for the changed process would be expected to include all relevant stability data and could be audited in a future inspection. And, had stability testing not been performed on the batch in support of the revised process, this would be a violation of the CGMPs.

What do the CGMPs require concerning a production batch that has been reprocessed?

The CGMPs require that any batch failing to meet specifications be investigated. A reprocessed production batch (i.e., intended for commerce) that was never distributed is to be thoroughly investigated to determine the probable reason(s) that the original process failed to produce a batch as intended and to make appropriate corrections to avoid recurrence of the failure. The investigation should extend too all other batches of the same or other products that may be affected by the reasons that the batch failed. For example, if the investigation determines that certain equipment or materials were faulty, the investigation should extend to all other batches or product associated with the use of the faulty equipment or materials. If the reprocessing also failed, an investigation into the cause of the failure might be warranted if, for example, the revised process is one that had been used before.

FDA evaluations of a firm's failure investigations should include a review of the established cause of the failure, its impact on marketed lots, implications for related processes, and the nature and timeliness of corrective action to prevent recurrence.

References: 21 CFR 211.115: Reprocessing; 21 CFR 211.166: Stability testing; 21 CFR 211.192: Production record review; 21 CFR 314.81: Other post marketing reports.

For further information contact: Barry Rothman, HFD-325; (301) 827-9026; rothmanb@cder.fda.gov.

Announcement

New USP Guidance Available on Unit-Dose Blister Packaging Operations

A relatively new guidance on drug blister-packaging operations appears in USP 26, General Information, section <1146> Packaging Practice—Repackaging A Single Solid Oral Drug Product Into A Unit-Dose Container. This section contains guidance that can be valuable for those conducting inspections of drug blister packaging operations. It includes a basic description of blister packaging materials; the process of forming, filling and sealing blisters; and, critical parameters relative to blister packaging operations. The guidance in this section should help focus investigators on the most critical parts of a blister packaging operation. Please remember that some parts of this section are specific to pharmacy dispensers (e.g., "Beyond-Use Date" and parts of "Minimum Requirements"). Investigators should also be aware that this section of the USP is informational only and forms should not be cited for not conforming with any of the guidance in this section unless a violation of 21 CFR Part 211 can be demonstrated.

References: USP 26, General Information, Section <1146> Packaging Practice—Repackaging A Single Solid Oral Drug Product Into A Unit-Dose Container. ■

—William Stoedter

USP Update

by Roger Dabbah, Ph.D.

The U.S. Pharmacopeia (USP) publishes the *Pharmacopeial Forum* (*PF*) on a bimonthly basis, which contains three major elements that are significantly tied in with standards development. One section on adopted revisions contains new or revised monographs that will become official before the publication of the next *USP-National Formulary* (*NF*) or its Supplements. The section is called the "Interim Revision Announcement" (IRA). The July–August 2003 *PF* [Vol. 29(4)] includes the Fourth Interim Announcement to *USP 26* and to *NF 21*. It contains the list of new USP Reference Standards with their date of official implementation, and a list of Reference Standards not yet available for monographs already in *USP-NF*. The IRA became official on August 1, 2003, unless otherwise indicated. Notable in the IRA is the final harmonized Chapter <71>, Sterility Tests, that is to become official January 1, 2004. Publication as an IRA at this time will allow manufacturers to get ready by the implementation date. Also included as an IRA is Chapter <797>, "Pharmaceutical Compounding-Sterile Preparation," and Chapter <1196>, "Pharmacopeial Harmonization," which contains an update on the harmonization progress among the USP, the Japanese Pharmacopeia, and the European Pharmacopeia. The IRA includes a Notice of Postponement of specified revisions to the Prednisolone Monograph that were published in *USP 26, First Supplement*, and originally scheduled to become official on April 1, 2003. It is postponed indefinitely for revisions that will accommodate all approved products.

Another section of *PF* contains proposed revisions of new or existing monographs or general chapters targeted for official adoption. The section is called "In-Process Revision." In the July–August 2003 *PF* there are 72 new or revised monographs targeted for *USP 27, First Supplement*. New monographs include: Allopurinol Oral Suspension, Atenolol Oral Solution, Anthrax Vaccine Adsorbed, Betahistine Hydrochloride, Cyclandelate, Fexofenadine Hydrochloride Capsules, Gemcitabine Hydrochloride, Gemcitabine for Injection, Irbesartan, Irbesartan Tablets, Irbesartan and Hydrochlorothiazide Tablets, Isradipine Capsules, Loratadine, Loratadine Oral Solution, Loratadine Tablets, Nevirapine, Nimodipine, Oxaprozin, Oxaprozin Tablets, Quinapril Hydrochloride, Quinapril Tablets, Valsartan and Hydrochlorothiazide. Revisions of existing monographs are numerous. Highlighted are some of the water monographs where cross-referencing to other water monographs has been deleted, and actual tests to be performed are included in the water monographs. There are 22 new or revised *NF* monographs that are proposed and are targeted for the *First Supplement* of *NF 22*. The new monographs include Alfadex, Low-substituted Carboxymethylcellulose Sodium, Copovidone, Hymetellose, Hypromellose acetate Succinate, Maltose, Vehicle for Oral Solution, Vehicle for Oral Solution, Sugar Free, Vehicle for Oral Suspension, Polyoxyl Lauryl Ether, Polyoxyl Stearyle Ether, Polyoxyl Oleate, Sodium Cetostearyl Sulfate, Anhydrized Liquid Sorbitol, Modified Starch, Pregelatinized Modified Starch, Tapioca Starch, Stearoyl Polyoxylglycerides.

Also under the "In-Process" section is Chapter <386>, "Environmentally Sensitive Preparations," and <429> "Light Diffraction Measurement of Particle Size." Chapter <467>, "Organic Volatile Impurities" also is being revised to make it consistent with the ICH Q3C Guidelines. Revisions to Chapter <601>, "Aerosols-Nasal Sprays-Metered-Dose Inhalers and Dry Powder Inhalers," are proposed and targeted for *USP 27, First Supplement*. The following chapters containing new information are available for the *First Supplement*: Chapter <1136>, "Packaging-Unit of Use," Chapter <1178>, "Good Repackaging Practices," and Chapter <1265>, "Written Prescription Drug Information-Guidelines."

The USP Scientific Conference on Biologicals and Biotechnology Products is scheduled for November 18–21, 2003 in Crystal City, VA. Registration and additional information are available on the USP Web site, www.usp.org. ■

PDA International Congress—Basel

16–20 February 2004

Science, Technology and Regulations in the Global Pharmaceutical Industry

Messe Basel Convention Center • Basel, Switzerland

Congress and Tabletop Exhibits: 16–18 February 2004

Courses: 19–20 February 2004

The pharmaceutical industry has always been identified by its capacity to innovate and discover. Never before has it been so important for pharmaceutical industry scientists and technologists to be informed and up-to-date on changes and developments in technology and regulations which are rapidly being introduced either by academics, industry, or regulators.

This Congress intends to provide a modern, balanced vision of the key aspects of drug and clinical development, manufacturing technologies, biotechnology, applied information technology, as well as the status of worldwide health authority regulations. All of these topics need to be considered for the healthy passage and survival of an industry in a constant state of change and facing new regulatory and cost pressures.

By participating in this Congress, attendees 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
- Discuss issues related to cold chain management

And more…

Session Tracks

- Information Technology
- Manufacturing
- Innovation and Regulation
- Filtration
- Cold Chain Management
- Aseptic Processing
- Quality
- Biotechnology
- Annex 13 and Clinical Trial Directives
- Development

Keynote Speakers:

The New Swiss Agency: Swissmedic
Klaus-Jörg Dogwiler, Executive Director, Swissmedic

Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach, CBER Perspective
Mark A. Elengold, Deputy Director, CBER, FDA

Process Analytical Technologies (PAT)
Ajaz S. Hussain, Ph.D., Deputy Director, Office of Pharmaceutical Science, CDER, FDA

Educational Courses

The PDA Training and Research Institute (PDA-TRI) is the preeminent provider of education, training, and applied research in the field of pharmaceutical, biopharmaceutical, and medical device science and technology. Courses providing in-depth education on technology topics relating to the Congress will be held on 19–20 February following the Congress.

The following PDA-TRI courses are scheduled:

- Clinical Trials Directive & GMP for Investigational Medicinal Products—#415 (19 February 2004)
- Risk Estimation in Aseptic Processing—#402 (19 February 2004)
- CGMPs for Bioprocesses—#461 (19–20 February 2004)
- Ventilation & Airborne Contamination in Cleanrooms—#363 (19–20 February 2004)
- Pragmatic Cleaning Validation—#309 (19–20 February 2004)

Tabletop Exhibits

Tabletop exhibits are strategically located in the foyer area outside the main meeting rooms. Exhibitors are encouraged to invite prospective clients who, although are not attending the conference, may attend the exhibits without charge on Wednesday, 18 February, from 8:30 a.m. to 12:00 p.m. For more information on exhibiting, please contact Nahid Kiani at (301) 656-5900 or via e-mail at kiani@pda.org.

You may register online for this Congress at www.pda.org. ■

—Wanda Neal

Telling Ain't Training

PDA 2004 Biennial Training Conference, Courses, and Vendor Exhibit

May 17–21, 2004

The Westin Rio Mar Beach Resort & Golf Club, Puerto Rico

Featured Speaker Harold Stolovich, Ph.D., to Offer Learning and Performance Solutions

Harold D. Stolovich, Ph.D., is the dynamic featured speaker who has been selected for the PDA 2004 Biennial Training Conference, Courses, and Vendor Exhibit, May 16–19, in Puerto Rico. Harold D. Stolovich & Associates, Inc. (HSA) creates a variety of live training formats that turn the focus of instruction towards the learner, rather than the instructor. HSA engages learners in meaningful practice based on specific learning outcomes. Whether classroom-based large group, or on-the-job small group learning is required, HSA develops courses, workshops, seminars, and conference sessions that are learner-centered, performance-based and highly interactive.

The most valuable lessons are derived from what we experience, not from what we are told.

Dr. Stolovich will present two separate and highly interactive sessions:

Telling Ain't Training

The most valuable lessons are derived from what we experience, not from what we are told. Dr. Stolovich takes a light-hearted, experiential approach to transforming telling (a waste of time) into activities that result in long-term retention and behavior change. Through a series of hands-on exercises, participants will not only have fun learning, but will also acquire some research-based principles for building retention and improved performance.

From Order-Taker to Performance Consultant

Organizationally, training departments are expected to provide training. Training professionals and instructional designers realize that training solutions alone rarely produce desired performance results. When client expectations of performance outcomes are not met, the training is frequently targeted as having been inadequate. How can this situation be changed? This interactive, highly participative session provides models, procedures and tools to help training groups and individuals transition from being order-takers to performance consultants.

Take-Aways

Participants receive a comprehensive participant manual and numerous job aids for use back in the workplace. Participants are also included on a mailing list that provides follow-up information, tools, and support to assist them in developing their training skills beyond the workshop.

Harold D. Stolovitch completed a Ph.D. and post-doctoral studies in Instructional Systems Technology at Indiana University. He has been a teacher, trainer, researcher and consultant for over 40 years. He has been designated a Certified Performance Technologist by the International Society for Performance Improvement (ISPI). Harold has authored more than 100 books, reports, chapters and articles on various aspects of instructional and performance technology. He has produced countless training materials, games, simulations, and other interactive activities using a wide variety of media. Dr. Stolovich retired from the Université de Montréal where, as a full professor, he taught and conducted research in Instructional and Performance Technology. He was recently bestowed the honor of Professor Emeritus. He is also a clinical professor of Human Performance at Work, University of Southern California. He is a consultant to business, industry, government, the military, and the police. Dr. Stolovich is a past President of The Society for Life Science Professionals (ISPE), former Editor of *Performance Improvement Journal*, editorial board member of several human resource and performance technology journals, Co-editor of both award-winning editions of the *Handbook of Human Performance Technology* and Co-author of the award-winning bestseller *Telling Ain't Training*. He received the 2001 ISPI Thomas F. Gilbert Distinguished Professional Achievement award and has won numerous other awards for his contributions to instructional and performance technology, including ISPI's highest award, Member for Life. He is a frequent keynote speaker and presenter for major companies and professional associations.

The complete registration brochure will be available soon.

Don't forget, Trainers' Choice Awards entry submission deadline is January 31, 2004. ■

—Lisa Wade

PDA Web Seminars on Demand

Highlights from the 2003 PDA/FDA Regulatory Conference will become available soon on the PDA Web site, www.pda.org. The selected sessions will include:

1. The FDA Today: Charting a Course for Science, Technology and Innovation, Lester M. Crawford, DVM, Ph.D., Deputy Commissioner, FDA
2. GMPs in Development, Nicholas Buhay, FDA, CDER; Anders Vinther, CMC Biopharmaceuticals A/S; Leslie Osmera, Wyeth BioPharma
3. Current Issues in Aseptic Processing, Rick L. Friedman, FDA, CDER; John Lindsay, Aseptic Solutions, Inc.; Franco DeVecchi, Vectech
4. Using Process Analytical Technologies, Ajaz Hussain, Ph.D., FDA, CDER; Emil Ciurczak, Applied Chemometrics
5. Part 11: What is Current? Where is the Wave Going? Joseph C. Famulare, FDA, CDER; C. Wells Horton, Procter & Gamble; Thomas Quinn, The Hollis Group, Inc.; Laura Robinson, RA Security; David Weitz, Covalent Group

Tell your colleagues who were unable to attend to listen to the program with the synchronized slide presentation for as little as $199* per session, or purchase the full 2-½ day conference on CD for $1,200*.

*Fee is for PDA members only. ■

—Lisa Wade

Highlights from the 2003 PDA/FDA Joint Regulatory Conference will become available soon on the PDA Web site, www.pda.org.

2003 PDA Annual Meeting, Courses, and Exhibition
Building on Our Strengths: Quality, Science, and Innovation

Tour the Georgia Facility of Glass Manufacturer Saint-Gobain Desjonqueres

In conjunction with the PDA Annual Meeting, Saint-Gobain Desjonqueres (SGD), a leading pharmaceutical and cosmetic glass manufacturer, is organizing a plant tour of its molded glass production site in Covington, GA, on Wednesday November 12th at 12:00 noon. Attendees will have the opportunity to witness the dramatic creation of glass from sand and fire!

The event is open to all PDA Annual Meeting attendees. Transportation will be provided from the Hilton Hotel. Space is limited and will be assigned on a first-come, first-served basis.

We hope to see you there!! Please use the registration form below, or go to www.pda.org for more details.

❑ YES! I want to tour Saint-Gobain Desjonqueres on Wednesday, November 12th

Name: _____

Company: _____

Address: _____

City/State/Zip _____ Country: _____

❑ I am staying at the Hilton If not, please tell us where you are staying: _____

Number of people: _____

PDA Training & Research Institute Director's Message

I Love It When a Plan Comes Together

Bob Mello, Ph.D.

Some years ago there was a television show called "The A-Team" in which George Peppard starred as the leader of a team of alleged army deserters that traveled across the country helping the downtrodden beat back the bad guys. The plot was always the same: good folk getting harassed by bullies and delinquents, the A-Team shows up to help, Peppard puts a plans together, successfully vanquishes the bullies and—at the end—he stands, chewing on a big cigar, saying "I love it when a plan comes together."

Well, so do I! Witness the successful completion of the PDA-Blow/Fill/Seal (BFS) Joint Workshop on BFS technology held September 18–19, 2003 at the Cardinal Health facility in Woodstock, IL. This workshop, almost a year in planning, was a joint effort of PDA, the BFS International Operators Association (BFS-IOA) and Cardinal Health Sterile Technologies.

Attendee Grace Gardiner (Aseptic Solutions, Inc.) initiates a BFS product cycle as instructor Martin Haerer observes.

Many of you recognize that the PDA Training & Research Institute offers premier laboratory education courses. Our greatest asset is the facility outside of Baltimore where students can get hands-on training and demonstrations in aseptic processing, cleaning validation, mycology, sterilization, and a host of other areas. While we can offer training in traditional aseptic processing, we are still somewhat limited in our offerings for hands-on training in other forms of advanced aseptic processing. Blow/Fill/Seal technology is one such form.

Bringing this training to our membership is not easy. For example, "small" BFS instrumentation weighs about four tons (8,000 pounds or about 3,600 kilos), and requires several supporting utilities that make it—how shall I say this…'less than portable.'

With the help of the BFS-IOA and the generous donation of Cardinal Health Sterile Technologies' facility and staff, we were able to offer this hands-on training to our membership and to that of BFS-IOA. Due to the interactions of faculty and attendees in and around the BFS equipment at this first-of-its-kind event, registration was limited to 15 attendees. That number was rapidly reached and was extended to 18 attendees (the absolute maximum), and I had to use all my "charm" (?) to extend it to that figure!

The course covered one day of lecture and one day of practical demonstrations of the technology. A tour of the Cardinal Health Sterile Technologies' facility permitted attendees to observe, in real time, how this technology can take all its composite raw materials and turn out finished packaged product in about 18–20 minutes. That is, from formulated product and granules of low (or high) density polyethylene (or polypropylene) to final labeled cases of shrink-wrapped unit cartons of finished product.

Instructors Patrick Poisson (Cardinal Health STG, USA), Dr. Martin Haerer (Holopack Verpackungstechnik GmbH, Germany) and Dr. Anders Löfgren (AstraZeneca, Sweden) each brought their expertise in BFS processing to the group. The international nature of the faculty afforded attendees the opportunity to obtain a balanced US/EU understanding of the technology.

The key to this successful offering, however, was the availability of the Weiler Model 624 BFS machine within Cardinal's Microbial Challenge Facility. This Facility, used for R&D purposes, provided the optimum setting for our hands-on training program. After all, without such a "spare" R&D machine and room, such training would require the shutdown of actual production equipment. That kind of generosity is hard to generate—even with all my "charm"!

We obtained good feedback from the attendees (85% return of course evaluations!), most of whom rated the course as 'outstanding.' We will be assessing all the information received to determine when the course will next be offered.

My thanks, again, to BFS-IOA and especially to Patrick Poisson and all of the Cardinal Health STG staff (Liz Sroka, Mika Nelson, Jennie Krodel, and Kevin Colangelo) for making the event a success.

I Love It When A Plan Comes Together! ■

—Bob Mello, Ph.D.

Attendee Axel Henning (Pharmacia, Belgium) assists instructor Patrick Poisson (Cardinal Health) in installing product filters prior to their steam sterilization-in-place (SIP).

Patrick Poisson (wearing badge) and Kevin Colangelo (both Cardinal Health) familiarize the class with the internal mechanisms of the Weiler 624 BFS machine.

Upcoming PDA Training & Research Institute Education Courses

Courses listed in chronological order

Aseptic Processing 2003 Training Program—Lab **Option 4**: October 27–31, 2003 and November 17–21, 2003; $7,500 members/$7,695 non-members; *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 non-members; *Faculty:* Göran Bringert

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

Aseptic Processing 2004 Training Program—Lab **Option 1**: January 26–30, 2004 and February 23–27, 2004; **Option 2**: March 22–26, 2004 and April 26–30, 2004; **Option 3**: May 24–28, 2004 and June 14–18, 2004; **Option 4**: August 16–20, 2004 and September 13–17, 2004; **Option 5**: October 4–8, 2004 and November 1–5, 2004; $7,800 members/$9,900 non-members; *Faculty:* John Lindsay and David Matsuhiro

These courses will be held at the PDA Training & 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's world headquarters in Bethesda, MD at (301) 656-5900.

PDA Training & Research Institute Location/Lodging Information

Unless otherwise noted, PDA Training & Research Institute courses are held at: PDA Training & Research Institute, UMBC Technology Center, 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 & 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

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

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

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

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

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

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

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

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

Sheraton International Hotel BWI
(410) 859-3300
(410) 859-0565 - 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 www.baltconvstr.com, the Baltimore Convention and Visitors Bureau's Web site.

Transportation to the PDA Training & 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 & Research Institute Thanks the Following...

Sponsors

Abbott Laboratories
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Eisai U.S.A., Inc.
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Genesis Machinery Products, Inc.
GlaxoSmithKline
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IDEXX Laboratories, Inc.
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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
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Cardinal Health
Charter Medical, Inc.
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Contec, Inc.
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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 & 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 two-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 10/03

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 U.S. dollars by a check drawn on a U.S. 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 had a meeting on September 18. The Chapter is planning another meeting on 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, please contact Chapter President Grace Chin by telephone at (416) 422-4056, ext. 230, or by email at grace.chin@snclavalin.com.

Capital Area
For more information about the PDA Capital Area Chapter, 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 presented "Sterile Drug Product Manufacturing Processes—The New Drug Application Review Perspective" on September 17th. The event's featured speaker was Peter Cooney, Ph.D., of FDA. The Chapter's next scheduled meeting will be held on November 19. For more information, visit the PDA Delaware Valley Chapter's Web site at www.pdadv.org.

Israel
The PDA Israel Chapter held a one-day meeting on "Microbiological Issues" in September. 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 will present "A Comparison of Experiences: the Approach of the Pharmaceutical Companies in Italy Towards 21 CFR Part 11", a two-day conference to be held in Milan on 11–12 November 2003. This will be a joint conference to be held with the Italian Affiliate of the Society for Life Science Professionals (ISPE) and with AFI, the Italian Pharmaceutical Association. The meeting follows the issuance of the "Good Practice and Compliance for Electronic Records and Signatures—Part 1 and Part 2" documents, produced jointly by ISPE and PDA, and the latest revision of the Code of Federal Regulations by FDA.

About 20 qualified speakers from various pharmaceutical companies (both multinational and local companies which have one or more manufacturing plants in Italy) will present their company's strategy and plan on addressing the requirements of 21 CFR Part 11.

Sion Wyn, member of the Good Automated Manufacturing Process (GAMP) council and an acknowledged expert in computer system validation and compliance, will participate in the conference as a special guest. Wyn will talk about the new "risk-based" approach of FDA with regard to computers and software validations. For more information, please contact Vincenzo Baselli at vincenzo_baselli@pall.com.

Japan
The PDA Japan Chapter held a meeting entitled, "How to Receive an FDA Inspection" on September 30. The PDA Japan Chapter Annual Meeting will be held 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 held a meeting on September 25. The meeting focused on endotoxin and served as a kickoff for the Midwest Chapter Interest Group, headed by Peter Lee, Ph.D. The Chapter's next meeting will be held November 20. For more information, contact Amy Gotham at PDAMidwest@northviewlabs.com.

Mountain States
The PDA Mountain States Chapter hosted a successful vendor night on September 11.

The Chapter will hold a dinner on November 13 featuring a speaker who is the former Denver FDA Director. For more information, please contact Jeff Beste at cmdjeff@aol.com.

New England
The PDA New England Chapter held a dinner seminar September 24th. The presentation addressed 21 CFR Part 11. The Chapter will have another meeting in December and is planning a social event in conjunction with the PDA Training and Research Institute Boston Course Series in October. For more information, contact Mark A. Staples, Ph.D., at mstaples@glycogenesys.com.

Southeast
The PDA Southeast Chapter held its "Fall Exhibitor Show & Meeting" on September 23. The Chapter is planning a joint meeting with the North Carolina Pharmaceutical Discussion Group, which will be held January 13, 2004. 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
The PDA Southern California Chapter held a meeting on September 18. The topics discussed were "Isolator Design & Validation" and "Aseptic Guidelines". The Chapter will host another meeting in November. For more information about the PDA Southern California Chapter, please visit the Chapter's Web site at www.pdasc.org.

Taiwan
The PDA Taiwan Chapter announced a new listing of officers: as of July 25, 2003, the PDA Taiwan Chapter President-elect is Mr. Shin-Yi Hsu; their Secretary General is Tuan-Tuan Su; and their Chapter Liaison is James T.S. Tu. For more information, please contact Tuan-Tuan Su at pdatc@ms17.hinet.net.

U.K. & Ireland
The PDA U.K. & Ireland Chapter's meeting, "What to Do When Things Go Wrong," was held on September 25–26. Mike Verdi, FDA, and Andrew Bill, MHRA, were the featured speakers. For more information, contact John Moys at john.moys@sartorius.com.

West Coast
The PDA West Coast Chapter is hosting a Chapter dinner meeting on October 9. The title of the program will be "Applications of Failure Mode and Effect Analysis in Bioprocesses". The presenter will be Dr. Robert J. Seely, Corporate Validation, Amgen, Inc. Registration information is posted on the Chapter's Web site at www.istep.com/~randallt/wccpda/. ■

—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.

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PDA
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Company, Colleague & Product Announcements

Hach Ultra Analytics, which provides advanced laboratory and process instrumentation for critical measurements in air, liquid, and gas, has announced the introduction of Long Life Laser technology for its Met One Particle Counter products. Particle counters ensure that damage due to particle contamination is minimized in the manufacture of pharmaceuticals, semiconductors, microelectronics, and hydraulic systems. By applying this technology to its products, Met One has addressed the longevity issues inherent in older particle counters and effectively increased reliability and performance.

This breakthrough technology extends the average service life of the instrumentation's laser to over 10 years. The Long Life Laser is backed by a 3-year standard warranty for most products with a 5-year extended warranty available for some products. Products to incorporate the Long Life Laser will include the Model 4800/4900 and Model 2400/2408 Airborne Particle Counters as well as the Model 3300 Portable Airborne Particle Counter.

Hach Ultra Analytics also announced the availability of the Met One HHPC-2 and HHPC-6 handheld particle counters, which offer simultaneous real-time display of 2 or 6 particle channels. Both models are lightweight and reliable, and serve the needs of environmental professionals who monitor and verify cleanrooms, test filters and track down particle source problems.

The HHPC-6 provides an easy-to-read display for 6 particle channels: 0.3, 0.5, 0.7, 1.0, 2.0 and 5.0 microns. The unit holds 500 samples (2,000 with option EX) in data memory and records date, time, counts, sample volume, temperature and relative humidity (R/H). The included RS-232/RS-485 interface cable and Windows® compatibility software enables easy downloading of data to a computer or printer. The HHPC-6 operates on a long-life rechargeable internal battery or AC.

The portable, palm-size HHPC-2 Hand Held Airborne Particle Counter, with download software and personal computer interface, affords the cost-conscious customer an economical alternative to accurate and reliable instrumentation. Battery- or AC-operated, this 2-channel model has a 0.3 micron sensitivity and stores 100 samples.

For further information contact Ken Szewc at (541) 472-6500, or at kszewc@hachultra.com.

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.

Biotest Diagnostics Corporation, which offers a line of centrifugal air samplers for airborne microbial monitoring, has added a new product to the Biotest line—the RCS Isolator, which is designed for use in cleanrooms and isolators. The RCS Isolator samples 100 liters of air per minute and is controlled via remote keypad or by remote control. It features an integrated rechargeable battery, and the airflow is contained inside the instrument housing. The RCS Isolator provides reproducible results to maintain a contamination control program. For additional information on the RCS product line or any of their other products, please contact Biotest at (800) 522-0090 or visit their Web site at: www.BiotestUSA.com.

Rap.ID Particle Systems GmbH, a company that develops, manufactures, and sells systems for the chemical analysis of micro particles, delivered its Liquid Particle Explorer® to Novo Nordisk of Copenhagen, the largest producer of insulin. The Liquid Particle Explorer® enables users to react quickly to potential particle contamination before incurring substantial damages. "Companies invest in our particle identification to ensure themselves of a cost advantage over the competition in the production of high-quality medication", said Dr. Oliver K. Valet, Managing Partner, who also is responsible for Marketing and Sales at Rap.ID. "Especially in the rapidly expanding field of biopharmaceuticals, our particle identification systems are highly accepted."

According to Dr. Markus Lankers, Managing Partner, "Our customers are the main beneficiaries of the implementation of our quality management systems. Expeditious order processing and the highest demands placed on quality standards for our products and service are important components of the system. Screening of our processes according to ISO-certification is of the utmost importance to our customers." Furthermore, the company reported certification according to DIN EN ISO 9001 in July 2003. For more information, please contact: J. Munhall at Sci-Tec, Inc., 6660 N. High St., Ste. 2A, Worthington, OH 43085, or at: info@sci-tec-inc.com. ■

—compiled by Evelyn Heitman

NEW BOOKS & TRAINING CDs

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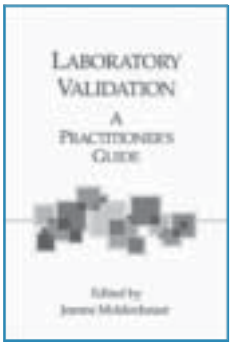
Just Released New Book!

Laboratory Validation: A Practitioner's Guide

Edited by Jeanne Moldenhauer



In recent years, regulatory inspections have focused on laboratory testing performed to assess the quality attributes of a product. In many cases, the testing is so specialized or complex, that the entire responsibility for validation has been transferred to the laboratory personnel. This excellent guide and reference provides an overview of validation from a laboratory perspective.

Divided into three parts, Part 1 includes an overview of many of the laboratory support systems and equipment common to both microbiology and chemistry laboratories. Part 2 is dedicated to systems applicable specifically to the chemistry laboratory, and Part 3 covers the systems applicable to microbiology laboratories. Where the laboratory predominantly performs the test, for example, cleaning and disinfection, requirements are included within the text. While the book offer validation details representative of the most common types of laboratory systems, should you have a system that is not included, the information in these 38 chapters will likely be of great assistance in providing resources for compilation of requirements for other systems. 1,224 pp; hardcover; $250 member/ $309 nonmember **Item No. 17201**

NEW TRAINING CDs

(All of the programs have been developed for pharmaceutical and biopharmaceutical operations: programs may be used for individual or group training.)

A Training Program for a System Audit of the Operation, Control, Qualification, Validation and Design of a WFI System $500 member/$1,495 nonmember **Item No.11012**

Control of Ray Materials for Pharmaceutical and Bio-Pharmaceutical Operations $300 member/$895 nonmember **Item No.11001**

Cross-Contamination in the Production of Pharmaceuticals and Bio-Pharmaceuticals $300 member/$895 nonmember **Item No.11002**

Finishing Operations in the Production of Pharmaceuticals and Bio-Pharmaceuticals $300 member/$895 nonmember **Item No.11004**

Good Manufacturing Practice Regulations, 21 CFR Parts 210-211, Sub-Parts B thru K $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 $300 member/$895 nonmember **Item No.11006**

Quality Assurance Standards for the Manufacture and Control of Injectable Products—A Quality and Compliance Training Program $300 member/$895 nonmember **Item No.11007**

Quality Indicator Reports—A Proactive Management System $300 member/$895 nonmember **Item No.11008**

Shep's Systems Audits© $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 $500 member/$1,495 nonmember **Item No.11010**

Technology Transfer Process for Pharmaceuticals and Bio-Pharmaceuticals $300 member/$895 nonmember **Item No.11011**

The Development Report—A Discussion and Outline for a Development Report $300 member/$895 nonmember **Item No.11003**

Using the FDA Pre-Approval Inspection Compliance Program in Preparing for an Inspection $300 member/$895 nonmember **Item No.11013**

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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**

Introduction to Environmental Monitoring of Pharmaceutical Areas Michael Jahnke; Topics discussed include all aspects of cleanrooms, air handling systems, HAACP and risk analysis along with numerous useful charts, tables and figures. 104 pp; $90 members/$109 nonmembers **Item No. 17182**

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.

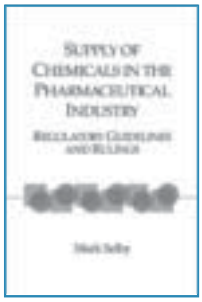
The purpose of the book is to enable novices, busy executives, and hard-pressed colleagues to quickly gain access to excellent global GMP practice and expectations. Beginners will find that it provides a solid prescription in preparation for the constantly expanding global GMPs. Experienced readers will 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. 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**

Technical Report No. 27 Pharmaceutical Package Integrity This report reviews issues of pharmaceutical product package integrity and provides guidance for evaluating the barrier qualities of a pharmaceutical package. It supersedes the previously issued PDA Technical Information Bulletin No. 4, *Aspects of Container/Closure Integrity*. Although it is written to reflect the complexity of all pharmaceutical products and packages, the emphasis throughout the document is clearly on packaging intended for sterile products. The information provided in this guideline is intended to assist users in developing integrity assessment strategies for use during the phases of product life. 1998; 50 pp; $75 members/ $125 nonmembers **Item No. 01027**

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.

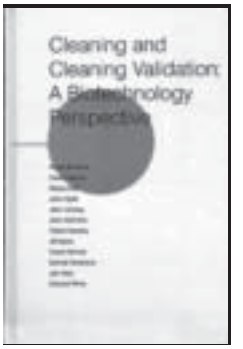
The Archive is updated each year, adding six issues of the *PDA Journal*, all PDA Technical Reports and Monographs, and selected PDA Meeting Proceedings. The archive is a 4-CD set. Archive (contains data through the year 2002); $395 member/$1,200 nonmember **Item No. 01101**

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**

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LTR 10/03

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
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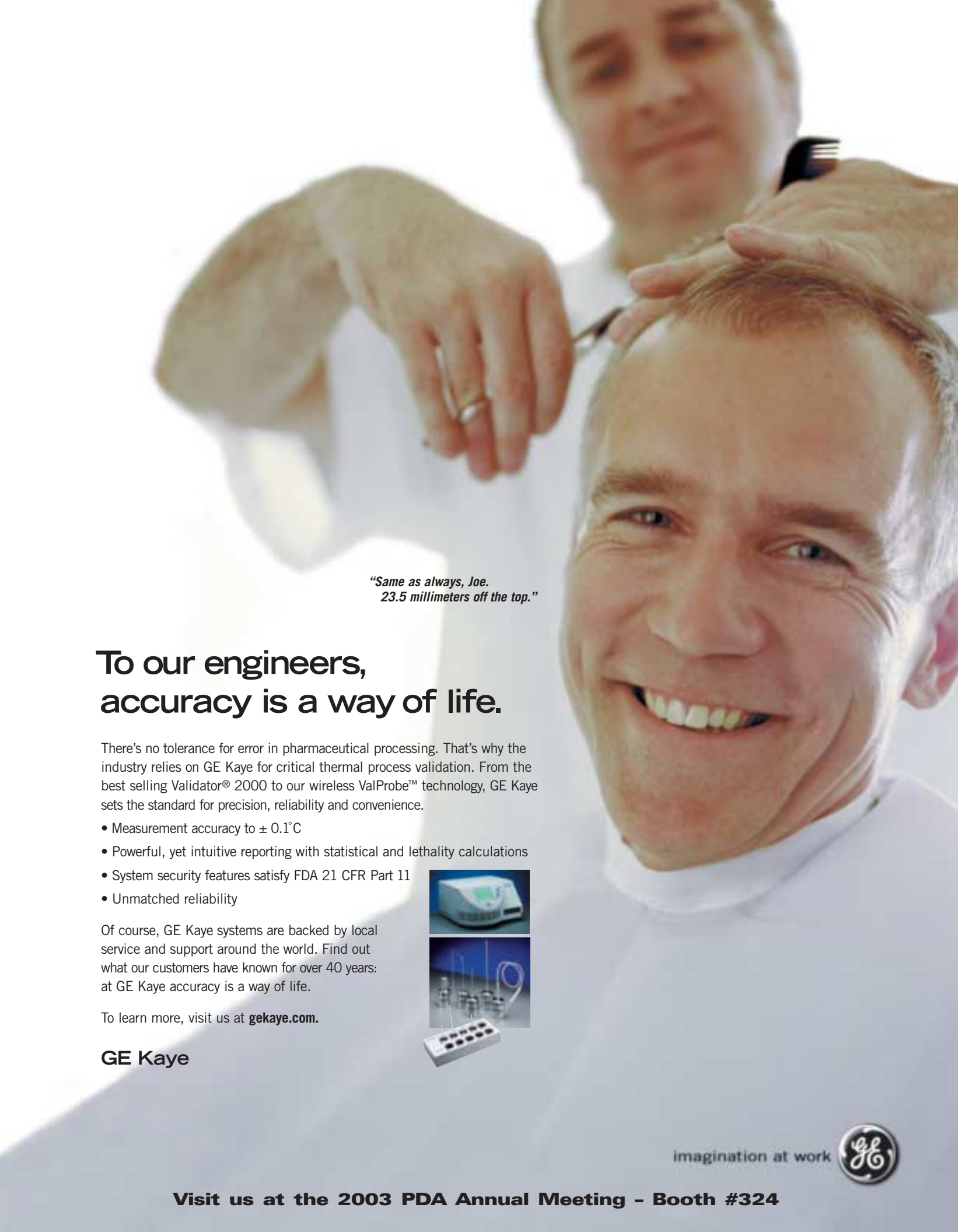

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Calendar of Events

2003

NOVEMBER

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

November 10–14, 2003
2003 PDA Annual Meeting, Courses and Exhibition
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 & 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 & Research Institute Laboratory Course
Aseptic Processing Training Program—Week 2
PDA-TRI Baltimore, MD

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

DECEMBER

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

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

2004

JANUARY

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

FEBRUARY

February 4–6, 2004
PDA Training & Research Institute
Lake Tahoe Course Series
Hyatt Regency Lake Tahoe
Incline Village, NV

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

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

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

MARCH

◆ March 1, 2004
PDA Presents
European Rotational Forums
Location TBA
Barcelona, SPAIN

March 4–5, 2004
PDA Training & Research Institute Laboratory Course
Ensuring Measurement Integrity in the Validation of Thermal Processes
PDA-TRI Baltimore, MD

March 8–12, 2004
PDA SciTech Summit™
Orlando County Convention Center
Orlando, FL

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

◆ March 29, 2004
PDA Presents
Basel Pharmaceutical and Biopharmaceutical Forums
UBS Ausbildungs-und Konferenzzentrum
Basel, SWITZERLAND

◆ Denotes European program/meeting

■ Denotes Pacific Rim program/meeting

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