Volume XXXVII, No.9

PDA Letter

September 2001

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

Streamlining the CMC Regulatory Process for NDAs and ANDAs, page 20

Training Courses at Annual Meeting Focus on Compliance

This December's Annual Meeting in Washington, DC brings together scientific and technical professionals from every aspect of the pharmaceutical industry. To meet the educational needs of this membership, the PDA-Training and Research Institute (PDA-TRI) has put together a group of high impact courses to be offered in conjunction with the conference. Organizations sending participants to the courses will be rewarded with improved compliance in the topic areas offered.

The lineup of courses for this conference offers something old and something new. Four of our most well respected faculty will be presenting topics of interest to a wide range of individuals. Renee Galkin will be presenting two separate one-day courses. The first is "Auditing Techniques for CGMP Compliance," a course which has not been offered since last June in New Jersey. This is a foundation course for any person who has to conduct an audit in the pharmaceutical industry. Galkin will follow this up with a new offering entitled "Change Control and Documentation."

Regulatory changes related to electronic records in the past couple of years have had an immense impact on those of us responsible for computer sys-

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PDA Publishes Two Technical Reports

Two new PDA Technical Reports will be sent to all members as supplements to the September/October 2001 issue of the *PDA Journal of Pharmaceutical Science and Technology*. They are *TR 13: Revised, Fundamentals of an Environmental Monitoring Program,* and *TR 34: Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products.* Each of these reports is summarized below.

PDA Technical Report No. 13, Revised

Fundamentals of an Environmental Monitoring Program

This report identifies 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.

The document is designed to serve as a source of information on clean room environmental test methods, and although some non-viable particulate and endotoxin testing data are included, its primary focus is microbiological control. The concepts for sterile product manufacturing are the most stringent application, but these concepts can also be applied to non-sterile product manufacture. The focus is environmental monitoring as it relates to facility control and compliance and the document was compiled to aid in setting up a program that is meaningful, manageable and defendable.

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Important Dates...

- The Extractables Puzzle Poster Abstracts—October 12, 2001, page 28
- 2002 PDA Spring Conference Abstracts—October 12, 2001, page 32
- Hotel Cutoff Date for PDA's Annual Conference—November 9, 2001, page 33

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Fry

An FDA Perspective on Equipment Cleaning Validation

At a recent non-PDA conference an FDA field investigator made a presentation on cleaning validation that appeared to articulate new CGMP requirements. The presentation, which was distributed to the audience, suggested that the concept of establishing cleaning limits and acceptance criteria for cleaning validation using maximum allowable carryover (MAC) limits "conflicts with current Good Manufacturing Practices (CGMP) and may, in fact, be so inherently contrary to CGMP that drugs associated with this practice become violative under Federal law." The MAC formulas in PDA's *Technical Report 29: Points to Consider in Cleaning Validation,* were specifically suggested to be unacceptable.

The concern that the focus of cleaning validation should be on cleanliness rather than setting tolerances for contamination is understandable, but the presentation appears to contradict well-established and well-accepted cleaning validation principles. As far as is known, cleaning validation practices as set forth in PDA's *Technical Report 29* have been accepted by FDA during many inspections worldwide. In addition, PDA has never received any official commentary from FDA that the methods in the Technical Report are unacceptable.

Maximum allowable carryover limits are used by many companies for determining cleaning acceptance criteria for product to product carryover. Recognizing that detectable residues will often be unavoidable in production equipment that is not purely dedicated to a single product, PDA's *Technical Report 29* sets forth scientifically defensible rationales for establishing necessary carryover limits. In the Technical Report, the MAC limit is defined as "the maximum amount of carryover from one product to the next that will not produce a therapeutic dose, corrected with a safety factor." The Technical Report states that the MAC limit is determined from the mathematical calculation:

$$\text{MAC} = \frac{\text{Single Therapeutic Dose of Product A (x) Batch Size of Product B (x) Safety Factor}}{\text{Largest Daily Dose of Product B}}$$

In order to clarify FDA policy, PDA Staff Russell Madsen, Bill Stoedter and I held a telephone conference with Brian Hasselbalch, Compliance Officer in CDER's Division of Manufacturing and Product Quality on July 30, 2001. Hasselbalch explained that CDER recognizes that CGMPs do not require equipment surfaces be absolutely free of residual contamination, and that CDER generally would not support enforcement of zero tolerance in cleaning validation. FDA has not endorsed or at this point rejected outright any particular specification-setting concept. Manufacturers are cautioned that setting cleaning specifications by MAC alone may be objectionable, since equipment must be subjected to a validated cleaning procedure and be visually clean [the PDA Technical Report does not advocate using MAC alone.]

Hasselbalch added that the presentation referenced above does not necessarily convey agency policy, and that the FDA Good Guidance Practice regulations, which became effective last year, govern how CGMP guidance is now disseminated. Future internal communication to the FDA field is being considered to further clarify cleaning validation requirements.

Any member having a question or comment on this issue should contact Bill Stoedter at (410) 455-5806. ■

—by Edmund Fry

International Calendar

2001

OCTOBER

October 24–26, 2001
A3P 14th International Congress
Espace Bellevue
Biarritz, France
INFORMATION AND REGISTRATION:
Frédéric Estassy
A3P Services – Le Gros Moulin – F-45200
Amilly – France
E-mail: info@a3pservices.com
Tel: +33 (0)2 38 071 – Fax: +33 (0)2 38 071 072
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2002

FEBRUARY

February 11–13, 2002
Basel 2002: PDA International Congress, Courses and Exhibition
Adding Value to the Pharmaceutical Industry—Leveraging the Future
Basel Convention Center
Basel, Switzerland
For Exhibit Information Contact:
Nahid Kiani, PDA
(301) 986-0293 ext. 128
kiani@pda.org

Contact PDA or go to www.pda.org for additional details on PDA events

TR 32 UPDATE

by Harvey Greenawalt, Audit Repository Center

Since the issue of TR 32 in January of 2000 the audits are being scheduled and implemented at an average rate of two per month. This effort is made possible by contributions from Pharmaceutical Industry Subscribers and Participating Suppliers to the PDA's licensed audit repository administered by Audit Repository Center (ARC).

All of the Pharmaceutical and Biotechnology Companies and Suppliers who initially subscribed to ARC and the PDA Process have renewed their subscriptions for 2001–2002. Currently seven Pharmaceutical and Biotechnology Companies and five suppliers subscribe to the process.

Benefits of the Application of the PDA Process Model and ARC in the Subscriber Environment, as provided to ARC by subscribers are presented below.

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

Pharmaceutical Companies who are Subscribers have reported that using the PDA Process and membership to the repository have resulted in the enhancement of their System Life Cycle (SLC) practices and Part 11 implementation.

Nearly all SLC practices in use today involve the acquisition of Commercial-Off-The-Shelf (COTS) products. The PDA program has established a standard way of performing organizational assessment of suppliers whose marketplace products are used in critical business operations that are either regulated or that impact the company's high risk computing base. The PDA Process has allowed subscribing companies to focus a handful of internal resources to be knowledge workers in analyzing supplier capability rather than high cost data collectors in executing audits. Data collector roles are fulfilled by PDA qualified external third party services. The end result is the ability to manage over 60 audits per year using qualified services strategically located around the world without leaving the comforts of home.

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

Subscribers to the PDA Process have recently realized a benefit with regard to Part 11 that was not initially obvious to the Subscribers. The benefit? The Part 11 Record keeping burden may be reduced, as the process, tools and auditor qualifications are external to the FDA regulated company.

Subscribers have reported the following benefits:

- 50% reduction in cost of doing audits;
- 400% increase in the number of audits that can be managed by a single individual;
- Enterprise-wide sharing of audit information;
- Standardization of method for analysis and consistent look and feel to reports;
- Seamless integration with acquisition and SLC practices; and
- Fulfillment of Part 11 expectations with regard to computer validation and the use of COTS products.

Auditor Training & Qualification

One hundred eight auditors have been qualified under the purview of PDA to implement the process defined in TR 32. Representatives of pharmaceutical companies, suppliers and third party consultant groups have attended auditor training. Roughly 10 percent of the auditors qualified reside in Europe and one auditor resides in Japan. Forty-eight percent of the auditors are from pharmaceutical industry companies with the remainder coming from consultancy groups.

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

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

Several Pharmaceutical companies have requested training sessions on-site for their personnel. These sessions have been delivered on the company's facility by PDA-TRI.

The next auditor-training course is scheduled at PDA-TRI in Baltimore, MD on October 11–12, 2001.

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

Availability of Audits

Currently, 14 audits are available for distribution from the repository. Additionally, 27 audits are either in process or planned to be implemented within the next six months.

For more information about the audit repository visit ARC's Web site at www.auditcenter.com or www.pda.org.

Table 1.0 provides a summary of the 14 audits that are currently available for distribution from the repository. ■

Table 1.0 Audits Currently Available in ARC.

	SUPPLIER	PRODUCT
1	Accraply, Inc.	Label Applicators, Automatic Labeling Systems, & Custom Designed and Self Adhesive Material Application Systems
2	ActionPoint	Input Accel Document Imaging LIMS
3	Applied Biosystems	SQL*LIMS – Laboratory Information Management System including the QA Stability & Schedule Modules
4	Decision Management International, Inc. (DMI)	Regulus™ Document Authoring (DA) a member of the Regulus™ off-the-shelf solution set.
5	Etrails.com, Inc.	Electronic Data Capture – EDC Electronic Patient Diaries – EPD Electronic Trail Management – ETM
6	Fanuc Robotics North America	Robotic Controllers & Communications
7	First Consulting Group, Inc.	Custom information based strategy software, operations improvements management and integration services
8	Infinity QS International (Lyle-Kearsley, Inc.)	Infinity QS Statistical Process Control Software
9	Merant, Inc.	PVCS Dimensions & PVCS Replicator Configuration Management Systems
10	Precision Solutions	Custom Development, SLE-Capture of check weight data Custom Software Programming
11	Qumas, Ltd. (Participating Supplier)	Qumas-Doc: Electronic Records Document Management Systems
12	SSA Global Technologies, Inc.	Mid range ERP software for manufacturing, supply chain and financial application domains
13	Supply Chain Logic, Inc.	General use COTS Asset Tracking/Delivery Systems
14	Sparta Systems, Inc.	Track Wise Software

US Regulatory Briefs

Address for written comment to FDA unless otherwise indicated:
Dockets Management Branch (HFA-305)
FDA
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Buehler named Director of the Office of Generic Drugs. Effective July 15, 2001, Gary J. Buehler officially assumed the position of Director, Office of Generic Drugs. He was appointed the Acting Director upon departure of Doug Sporn in March 2000. Buehler previously held the position of Deputy Director, Office of Generic Drugs, CDER, FDA since May of 1999. Buehler has worked for the FDA since 1986. Prior to joining the Office of Generic Drugs, he was Senior Regulatory Project Manager for the Division of Cardio-Renal Drug Products. He also served as Chair of CDER's Medication Errors Subcommittee and was a member of the Commissioned Corps Awards Committee. The Office of Generic Drugs, part of FDA's Center for Drug Evaluation and Research (CDER), employs over 130 scientists, professionals and support staff with expertise in areas such as chemistry, medicine, microbiology, biopharmaceutics, pharmacy, statistics and information technology. These employees are responsible for assuring that only safe, effective, high-quality and equivalent generic products are approved for use. More information can be found at www.fda.gov/cder/ogd.

A Tour of the FDA from your computer. *A Tour of FDA* is the first of many Web-based courses to be offered as part of the FDA's Office of Regulatory Affairs University or "ORA U." These courses will be accessible to thousands of federal, state and local regulators and employees of regulated industries worldwide. This first offering provides basic information about FDA and is coupled with quizzes to test your knowledge. The Web-based course initiative is made possible through the Cooperative Research and Development Agreement (CRADA) between FDA and EduNeering, Inc. The tour can be found on the FDA Web site (www.fda.gov) under "More FDA News" or by going directly to: www.eduneering.com/fda/courses/fdatour/welcome.html. To use this course, you must have the Shockwave plug-in installed. If you do not have Shockwave, it can be downloaded at the tour site for free.

New guidance for industry: S7A Safety Pharmacology Studies for Human Pharmaceuticals. The Food and Drug Administration (CBER and CDER) have jointly issued the ICH (International Conference on Harmonization) document, S7A. This guidance was developed to help protect clinical trial participants and patients receiving marketed products from potential adverse effects of pharmaceuticals, while avoiding unnecessary use of animals and other resources. This guidance provides a definition, general principles and recommendations for safety pharmacology studies. Pharmacology studies have been performed worldwide for many years as part of the nonclinical evaluation of pharmaceuticals for human use. There have been, however, no internationally accepted definitions, objectives or recommendations on the design and conduct of "safety pharmacology studies." The term "safety pharmacology studies" first appeared in the ICH *M3 Timing of Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals* and *S6 Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals* as studies that should be conducted to support use of therapeutics in humans. Details of the safety pharmacology studies, including their definition and objectives, were left for future discussion. This guidance generally applies to new chemical entities and biotechnology-derived products for human use. This guidance can be applied to marketed pharmaceuticals when appropriate (e.g., when adverse clinical events, a new patient population or a new route of administration raises concerns not previously addressed). The entire document can be found on the Internet at: www.fda.gov/cder/guidance/index.htm.

FDA starts new scientific journal. The inaugural issue of the *Regulatory Research Perspectives: Impact on Public Health* is making its debut with a review written by the Division of Microbiology, National Center for Toxicological Research, (NCTR) Jefferson, Arkansas. The objective of the journal is to provide a vehicle for FDA scientists to communicate important information to each other and to the Agency, with the hope of generating collaborations within the global community. It is hoped that each center will submit manuscripts for publication through their respective editorial board members. Initially, the plan is to publish quarterly. Volume 1, Issue1, can be found at: www.fda.gov/nctr/science/journals/default.htm.

The FDA has created an Antibiotic Resistance Web Page. FDA has created a new Web page that brings together sources of information on the growing problem of disease-causing microbes that have become resistant to drug therapy. Tuberculosis, gonorrhea, malaria and childhood ear infections are just a few of the diseases that have become hard to treat with antibiotic drugs and are becoming an increasing public health problem. One aspect of the dilemma is that bacteria and other microorganisms that cause infections are remarkably resilient and can develop ways to survive drugs meant to kill or weaken them. This *antibiotic resistance*, also known *as antimicrobial resistance* or *drug resistance,* is due largely to the increasing use of antibiotics. The Antibiotic Resistance Web Page can be found at: http://www.fda.gov/oc/opacom/hottopics/anti_resist.html.

The Humanitarian Device Exemption (HDE) and the Humanitarian Use Device (HUD). A Humanitarian Device Exemption (HDE) is an application that is similar to a premarket approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD). As defined in the Federal Food, Drug and Cosmetic Act

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Regulatory News from page 8

(the act), a HUD is a device that is "intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States." In the final regulation however, FDA added the qualifying phrase "per year" to the defining criteria. As the agency explained in the preamble to the final rule, FDA believes that "a point prevalence definition would be considerably more restrictive and provide less of an incentive for the development of such devices." FDA also added the phrase "or is manifested" to the definition of a HUD "to establish that a HUD designation may be appropriate in cases where more than 4,000 people have the disease but fewer than 4,000 manifest the condition." Therefore, the final definition of a HUD is a device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or is manifested in fewer than 4,000 individuals in the United States per year.

The FDA is seeking comments on a draft guidance requiring sponsors to disclose financial agreements made with clinical investigators. Financial Disclosure by Clinical Investigators (OMB No. 0910-0369). Respondents are sponsors of marketing applications that contain clinical data from studies covered by the regulation. These sponsors represent pharmaceutical, biologic and medical device firms. Applicants will be required to submit, for example, the complete list of clinical investigators for each covered study, not employed by the applicant and/or sponsor of the covered study, and either certify to the absence of certain financial arrangements with clinical investigators or disclose the nature of those arrangements to FDA. Steps taken by the applicant or sponsor to minimize the potential for bias must also be reported. The clinical investigator will have to supply information regarding financial interests or payments held in the sponsor of the covered study. FDA has said that it has no preference as to how this information is collected from investigators and that sponsors/applicants have the flexibility to collect the information in the most efficient, least burdensome and effective manner. The sponsors of covered studies will be required to maintain complete records of compensation agreements with any compensation paid to non-employee clinical investigators, including information showing any financial interests held by the clinical investigator, for a time period of two years after the date of approval of the application. This time is consistent with the current record-keeping requirements for other information related to marketing applications for human drugs, biologics and medical devices. Currently, sponsors of covered studies must maintain many records with regard to clinical investigators, including protocol agreements and investigator resumes or curriculum vitae. The draft guidance can be found in the *Federal Register*: July 25, 2001 (Volume 66, Number 143) Pages 38712-38713. Submit written or electronic comments on the collection of information by **September 24, 2001**. Electronic comments on the collection of information to can be submitted to: http://www.acessdata.fda.gov/scripts/oc/edockethome.cfm. Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with Docket Number 01N-0308.

Human Drug CGMP Notes

The FDA will no longer be publishing Human Drug CGMP Notes for the public. Because of the "Good Guidance Practices" that the agency must follow, it was decided that the internal review process required prior to publication would be too lengthy, making it difficult to get the notes published in a timely manner. The FDA will continue to publish Human CGMP Notes for internal use on the closed FDA intranet system.

—William Stoedter

International Briefs

Note: All EMEA and CPMP guidance documents can be accessed at the EMEA Web site, www.emea.eu.int/.

Information Package for Certification of Medicinal Products issued by the EMEA. In June, the EMEA released a new revision of *Information Package for Certificates of Medicinal Products issued by the European Agency for the Evaluation of Medicinal Products* (EMEA/14400/01 Rev. 4, June 15, 2001). The purpose of this document is to provide a brief and easily understandable summary of the procedures for authorization and certification of medicinal products in the European Union. Definitions and references are included.

Investigation of Bioavailability and Bioequivalence. In July, the CPMP adopted the revised *Note for Guidance on the Investigation of Bioavailability and Bioequivalence* (CPMP/EWP/QWP/1401/98, July 26, 2001). The objective of this guidance is to define, for products with a systemic effect, when bioavailability or bioequivalence studies are necessary and to formulate requirements for their design, conduct, and evaluation. This Note replaces the previous guideline adopted in December 1991 and will go into effect January 2002.

Plasma Master File. In July, the CPMP released for consultation a draft *Contribution to Part S 2.3 of the Structure of the Dossier for Applications for Marketing Authorisation – Control of Starting Materials for the Production of Plasma-Derived Medicinal Products* (CPMP/BWP/2053/01 draft – III/5272/94 rev 1, July 26, 2001). This document provides a draft of the Plasma Master File (PMF), to be included as part of the dossier whenever a human plasma-derived product is used in a medicinal product either as an active substance or as an excipient. The draft discusses the content of the PMF and how it should be used in-

cluding annual updates. The deadline for comments is end of December 2001.

EU Influenza Vaccine Recommendation. In March, the EMEA issued *Final EU Recommendation for the Influenza Vaccine Composition for the Season 2001/2002* (CPMP/BWP/844/01, March 29, 2001). The Ad Hoc Influenza Working Group of the BWP determined that the final selection of virus strains for the manufacture of the influenza vaccine for 2001/2002 should consist of a trivalent vaccine containing: an A/Moscow/10/99 (H3N2)-like strain; an A/New Caledonia/20/99 (H1N1)-like strain; and a B/Sichuan/379/99-like strain. Based on cross reactivity and growth in eggs, the group also identified which strains are acceptable for the purpose of vaccine manufacture. Annex I lists the sources of reagents for vaccine standardization.

CPMP Oral Explanations. CPMP released in July, a draft *Guidance to Applicants on CPMP Oral Explanations* (CPMP/2390/01, July 31, 2001). The CPMP is considering the streamlining of its centralized procedure in several areas to reinforce the efficiency of the procedure and to improve the quality of the scientific CPMP Opinions. This document provides the Applicant with guidance on a number of action points in preparation of and following a hearing with the CPMP in order to optimize the efficiency of Oral Explanations. The deadline for comments is **October 15, 2001**.

Fee Reductions for Orphan Medicinal Products. In July, the EMEA released *EMEA Public Statement on Fee Reductions for Designated Orphan Medicinal Products* (EMEA/4042/01/Rev1, July 26, 2001). This document lists the fee exemptions for 2001 subject to the availability of funds, and provides the procedure for requesting fee reductions for eligible Orphan Medicinal Products. On advice from the Committee for Orphan Medicinal Products, protocol assistance is now considered a priority by the EMEA when establishing a policy on fee reductions.

Evaluation of New Anti-Fungal Agents. The CPMP released in July the *Concept Paper on the Development of a Committee for Proprietary Medicinal Products (CPMP) Points to Consider Document on the Evaluation of New Anti-Fungal Agents for Invasive Fungal Infections* (CPMP/EWP/134301, July 26, 2001). This document highlights the major problems encountered in the clinical evaluation of new agents for invasive fungal infections. These same issues often cause difficulties in data interpretation for regulatory authorities as well as problems in providing clear and consistent scientific advice to sponsors during drug development. The CPMP is proposing that a *Points to Consider* document should be developed to address these problem areas. A draft could be released for consultation 2/3Q2001.

Test Procedures and Acceptance Criteria for Herbal Drug and Medicinal Products. In July, the CPMP and CVMP released *Note for Guidance on Specifications: Test Procedures and Acceptance Criteria for Herbal Drugs, Herbal Drug Preparations and Herbal Medicinal Products (Formerly CPMP/HMPWP/19/99),* (CPMP/QWP/28280/00, EMEA/CVMP/815/00, July 26, 2001). This document, which goes into effect January 2002, provides general principles on the setting and justification of a uniform set of specifications for herbal drug preparations (herbal drugs) and herbal medicinal products to support applications for marketing authorizations. This publication should be read in conjunction with the Note for Guidance on quality of herbal medicinal products (CPMP/QWP/2819/00 and EMEA/CVMP/814/00).

Quality of Herbal Medicinal Products. The CPMP and CVMP released in July *Note for Guidance on Quality of Herbal Medicinal Products (formerly EMEA/HMPWP/9/99)* (CPMP/QWP/2819/00, EMEA/CVMP/814/00, July 26, 2001). This document describes the special problems of herbal medicinal products and the differences between medicinal products containing chemically defined active substances. Guidance for assuring consistent quality for products of herbal origin, including method of preparation, control of starting materials, control and stability tests, is included. The effective date for this Note is January 2002. ■

—James C. Lyda

Introduction to Europe Authorities

Introduction

What is EDQM? What is the CPMP? These questions, and similar ones, are not uncommon in today's global pharmaceutical regulatory environment. (EDQM is the European Agency for the Evaluation of Medicinal Products and the CPMP is the Committee for Proprietary Medicinal Products.) As the European Union, and all of Europe, has continued to evolve in recent years, the changes and new procedures have come to be of more and more importance to pharmaceutical companies around the world. Gone are the days when tracking FDA's regulatory and compliance actions were all that was needed to keep out of harm's way. This is true for several reasons.

First, there has been a striking amount of change in Europe in recent years. While FDA can boast a history of almost 100 years as an organization, the EMEA did not even come into existence until 1995. Similarly, while the United States Pharmacopeia (USP) can trace it's first monographs to the 1820s, the European Pharmacopoeia (*Ph. Eur.*) was only created in 1964. (Incidentally, that extra "o" in Pharmacopoeia is not a typo.). By any measurement the amount of regulatory change in Europe has been astounding.

Another factor is the amount of activity. While FDA continues to publish guidances and regulations, the USA 'notice and comment' system has bogged down many FDA initiatives in recent years; e.g., the 1996 GMP revisions, which are still not finalized, and the revised aseptic processing guideline, which has not seen a first public release after years of talk and drafts. Perhaps the system has become too cumbersome?

In Europe, on the other hand, there has been the release of one Note for Guidance and GMP revision after another. For example, GMP Annex 1 on sterile products was revised in 1996, and just last month the guidance on media filling was revised (albeit with no public comment.) There is a palpable sense of momentum and decisiveness in the public releases of the EMEA and the European Commission. There have been comments by observers that this is possible today because the affected industry and scientists have not organized themselves to demand a more transparent process. Whatever the reason, the EU regulatory train has clearly left the station and is accelerating.

Third, is the decision-making process itself. There is a consensus building, even political, aspect to the drug regulatory process in Europe. The composition of the EMEA Management Board and the CPMP, with representatives from each member state in the European Union, are examples of this. Authority is distributed based on the political realities in Europe. Examination of the structure of the regulatory system reveals a very different philosophy and culture from the FDA. Negotiation, compromise and attention to protocol are necessary aspects of the consensus building process in Europe. The system is admirable because it works better than one might anticipate. The result is a culture of decision making quite different from the historical FDA experience. Failure to recognize and accept this can be costly, as more than one multinational has found. Many people also sensed that FDA had to come to terms with this during the last 10 years of ICH work.

Following is the first of several articles outlining the major European organizations or bodies involved in drug approval, registration, quality standards and inspection. Some of these organizations, such as the EMEA, have authority only in the 15 member states of the EU. Others, such as the European Pharmacopoeia, affect European countries, which are not yet members of the EU. Others, such as the PIC/S, have no real authority of their own and include member countries outside of Europe. The descriptions of each of the organizations are based on their own publications. The European Commission—Enterprise Directorate, the European Pharmacopoeia and PIC/S will be addressed in separate articles over the next few months in this section of the *PDA Letter*.

European Agency for the Evaluation of Medicinal Products

Executive Director—Thomas Lönngren
Location—Canary Wharf, London, UK
(See attached organizational chart)

Overview of the European authorization system

Registration procedures

The European pharmaceutical regulatory system is based on three complementary procedures for the registration of medicinal products:

(1) the **Centralized procedure** is mandatory for certain biotech-derived medicinal products and optional for other innovative products: a pharmaceutical company, established in the EU, submits a marketing authorization application to the European Agency for the Evaluation of Medicinal Products (EMEA). Drawing on scientific advice of the highest possible quality, the Agency coordinates, through the 15 Member States, a single scientific evaluation of the application. The applicant then obtains a single marketing authorization, valid throughout the EU.

(2) the **mutual recognition procedure** is the main route for non-biotech products: a pharmaceutical company established in the EU, which has obtained a marketing authorization in one EU

Member State, applies to one or more other Member States to recognize it, in accordance with the mutual recognition principle.

(3) the **national procedure**, is used to authorize medicinal products for local use in individual Member States.

Introduction to EMEA

In 1995 a new European system for the authorization of medicinal products came into operation. After several years of cooperation between national competent authorities at European Union (EU) level, the EU Council adopted three directives and a regulation in June 1993 which together form the legal basis of the system.

The European Agency for the Evaluation of Medicinal Products (EMEA) was established by Council Regulation (EEC) No 2309/93 of July 22, 1993 (OJ L 214, 24.8.1993, p. 1) and London was chosen as its seat by decision of the Heads of State and Government on October 29, 1993.

The Agency is located in Canary Wharf between the City of London and City Airport. The Agency occupies the third, fourth, fifth and seventh floors of 7 Westferry Circus, covering an area of about 7,000 square metres.

Protection of human and animal health

The European system for the authorization of medicinal products for human and veterinary use is designed to promote both public health and the free circulation of pharmaceuticals. Access to the European market is facilitated for new and better medicines — benefiting users and European pharmaceutical research.

In the case of veterinary medicinal products, consumer and animal health is protected through the fixing of maximum residue limits in food-producing animals.

The European procedures

The European system offers two routes for authorization of medicinal products:

The centralized procedure is compulsory for medicinal products derived from biotechnology, and available at the request of companies for other innovative new products. Applications are submitted directly to the Agency in London. At the conclusion of the scientific evaluation undertaken in 210 days within the Agency, the opinion of the scientific committee is transmitted to the Commission to be transformed into a single market authorization applying to the whole European Union.

The decentralized procedure (or mutual recognition procedure) applies to the majority of conventional medicinal products and is based upon the principle of mutual recognition of national authorizations. It provides for the extension of a marketing authorization granted by one Member State to one or more other Member States identified by the applicant. Where the original national authorization cannot be recognized, the points in dispute are submitted to the EMEA for arbitration.

The European Commission adopts the final decision in both cases with the assistance of a standing committee or in the event of serious disagreement between the Member States, by the Council of the European Union. Purely national

Web Sites For European Drug Regulatory Information

EMEA - History and Description (New site this year)
http://www.emea.eu.int/aboutus.htm

EMEA Documents for Download
http://www.emea.eu.int/index/indexh1.htm

EMEA What's New (Recommended)
http://www.emea.eu.int/index/indexwn1.htm

European Commission - Enterprise Directorate (New site this year)
http://pharmacos.eudra.org/F2/home.html

European Commission - GMP Documents for Download
http://pharmacos.eudra.org/F2/pharmacos/gmp_doc.htm

European Commission - What's New
http://pharmacos.eudra.org/F2/pharmacos/docs.htm#news

Pharmaceutical Inspection Cooperation Scheme (PIC/S) Documents for Download
http://www.picscheme.org/index.htm

European Pharmacopoeia (Ph. Eur.)
http://www.pheur.org/

European Federation of Pharmaceutical Industries and Associations (EFPIA)
http://www.efpia.org/

authorizations remain available for medicinal products to be marketed in one Member State.

"A network agency"

The European system is based on cooperation between the national competent authorities of the Member States and the EMEA. The EMEA acts as the focal point of the European system, coordinating the scientific resources made available by Member State national authorities, including a network of some 2,300 European experts. The principal scientific bodies of the EMEA are the Committee for Proprietary Medicinal Products (CPMP) and the Committee for Veterinary Medicinal Products (CVMP). Staff of some 200 people now ensure the link with the CPMP, CVMP and over 4,000 officials in the Member State national competent authorities.

The partnership between the EMEA, national authorities and the European Union institutions is crucial to the successful functioning of the European authorization procedure.

An information technology network (funded by the European Commission and supported by the Joint Research Centre) links all partners and allows rapid exchange of adverse drug reaction reporting and drug safety information. This network is supplemented by the use of video- and teleconferencing.

As a technical agency, the EMEA is able to provide support to the Commission for the performance of harmonization tasks in both the European and international arena. The EMEA is currently involved with central and eastern European countries and international harmonization work with Japan and the United States (ICH and VICH). The EMEA will implement third-country mutual recognition agreements with Australia, Canada, Japan, New Zealand, Switzerland and the United States.

EMEA mission statement

To contribute to the protection and promotion of public and animal health by:

- mobilizing scientific resources from throughout the European Union to provide high quality evaluation of medicinal products, to advise on research and development programs and to provide useful and clear information to users and health professionals;
- developing efficient and transparent procedures to allow timely access by users to innovative medicines through a single European marketing authorization; and
- controlling the safety of medicines for humans and animals, in particular through a pharmacovigilance network and the establishment of safe limits for residues in food-producing animals.

Accountability and transparency

Members of committees, European experts and inspectors are nominated by Member States who guarantee their scientific competence. Their independence and integrity of members and experts is assured through public declarations of interest. When acting for the EMEA, they do so independently of their nominating authority.

EMEA has used the growth in Internet technologies to disseminate information on its work, in particular by making evaluation reports public. Regular consultation with all interested parties is an important aspect of the EMEA activities.

As a decentralized agency of the European Union, the EMEA is required to follow the budgetary and financial rules of the EU. These are supervised and enforced by an independent financial controller reporting to the EMEA Management Board and also by the European Court of Auditors. The Court of Justice of the European Communities exercises jurisdiction over the EMEA for the application of Community law.

Structure of the EMEA

Managing Board EMEA—Two representatives per Member State, two from Commission, two appointed by European Parliament (Total 34)

Secretariat/EMEA staff—About 200 employees (see organizational chart, page 15)

Scientific Committees—The scientific expertise of the EMEA resides in the committees comprised of member scientists and regulatory experts from each of the Member States. In total over 4,000 individuals from across Europe may be involved in the scientific deliberations of the EMEA.

Committee for Proprietary Medicinal Products (CPMP, human drugs), includes

Quality Working Party (QWP)
Safety Working Party (SWP)
Efficacy Working Party (EWP)
Biotechnology Working Party (BWP)

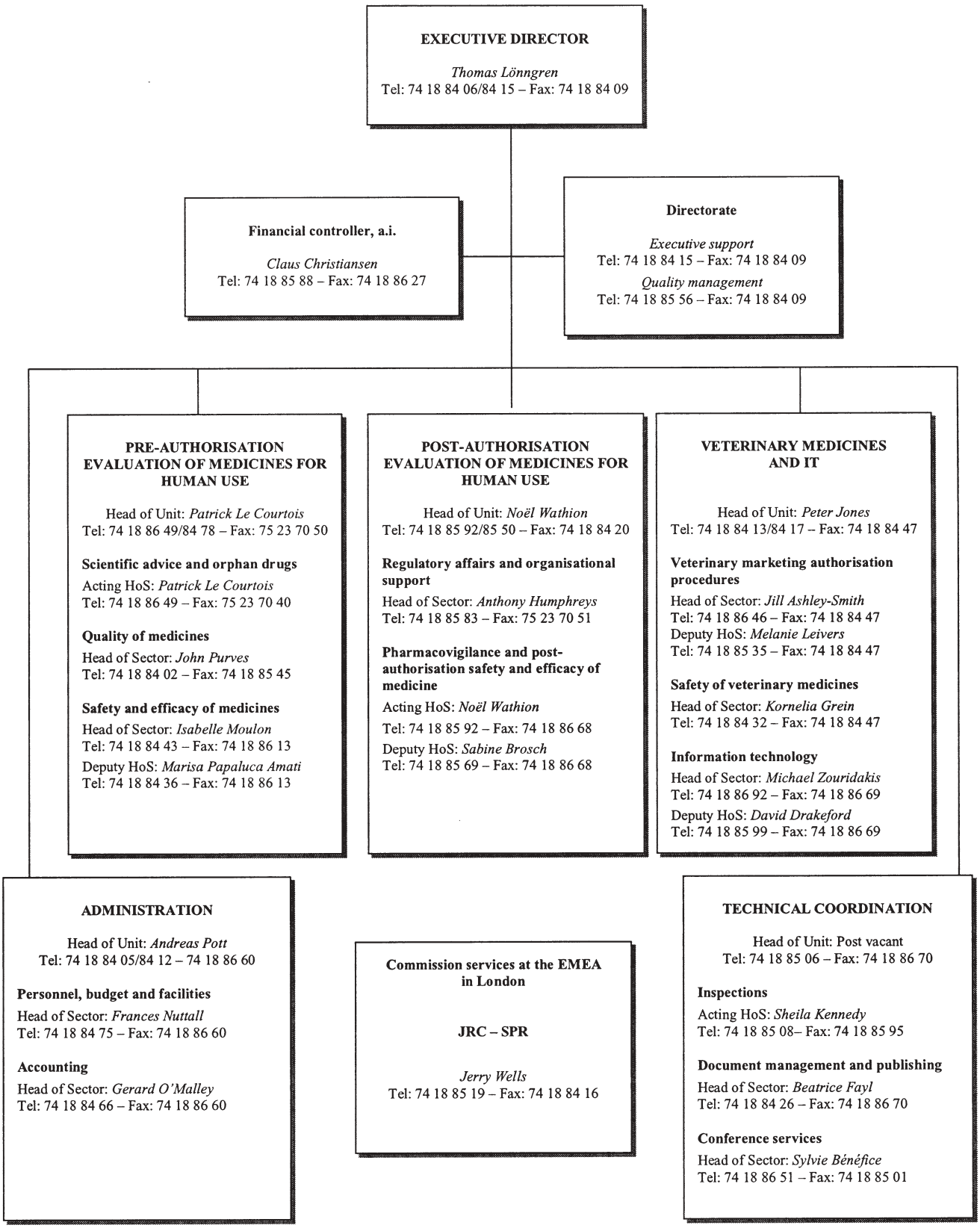
Committee for Veterinary Medicinal Products (CVMP)

Committee for Orphan Medicinal Products (COMP)

Next month: ***the European Pharmacopoeia—EDQM.*** ■

—James C. Lyda

EMEA Organizational Chart



PDA and ISPE to Co-publish Series on Good Practice and Compliance for Electronic Records

by George Grigonis, Merck & Co., PDA Part 11 Task Group Leader

Computer technology has changed the framework of business in every industry, transforming the way businesses operate internally, as well as the way they interface with customers and external businesses. Many companies today see computer technology as vital to delivering products and services to the marketplace.

The pharmaceutical industry is just one of many industries transformed by computers and software. Industries involved in commerce and trade are not the only entities affected: governments, in their desire to stay current while reducing cost of operation, have also been transformed. Governments need to serve the general public, not just in delivery of public services, but also in the regulation of commerce. This government transformation has led to the creation of new laws and government programs that rely upon computers and web technologies.

Computer technologies serve two fundamental purposes. First, they fulfill functions for automation and control in the management of human workflow and real-time process control. Second, they facilitate information management. It is in this area, electronic information management, that the rapid pace of computer technologies has presented challenges to information reliability, authenticity, and long term accessibility and usability. The rapid growth of computer technology has rendered much electronic information, created just a decade ago, inaccessible to modern computers.

On the other hand, the proliferation of technology has facilitated an explosion of electronic information that can easily be created and changed without leaving a trail of evidence. This is the greatest challenge for electronic record authenticity and trustworthiness. The vital attributes inherent to paper records are not always designed into electronic technologies unless they have been engineered in from the start.

The regulated industries are presently faced with having to re-evaluate record life cycles from a number of perspectives as they evolve to electronic business processes. They need to have their electronic records trustworthy and reliable, both for business reasons and for fulfilling regulatory obligations. Tightly coupled to electronic records is the use of electronic signatures as the principal enabler for transactions executed in electronic business environments.

The US Food and Drug Administration (FDA) has taken a bold step in establishing one of the first regulations to define the conditions under which the Agency will accept information and authentication in electronic form, constituting operational records and signatures as defined by predicate laws predating the electronic age. With this move the Agency has not only propelled itself into the electronic age, but it has created a need for industry to adapt an existing computing infrastructure to the new ways of electronic government and electronic commerce.

The FDA is but one example of how governmental changes affect electronic information. The main stream of activity continues to produce a number of directives and laws that are affecting governments, private industry, and the general public globally. The rules for authentic and trustworthy electronic information undoubtedly will play an increasingly important role in the engineering, operation, and use of computer technologies as our dependency on them increases for the management of electronic records.

PDA and the International Society for Pharmaceutical Engineering Good Automated Manufacturing Practices Forum (ISPE GAMP Forum) have operated two separate initiatives, but with close cooperation, to deliver industry guidance relative to electronic information and emerging governmental regulations. Both initiatives produced work products from different perspectives; however, the approaches are complementary and, collectively, they cover the broad issues that are associated with electronic records and signatures. The work products of both initiatives will be co-published as a series for the benefit of practitioners involved in electronic records management programs in FDA-regulated companies.

The compilation, known as *Good Practice and Compliance for Electronic Records*, will be published in three volumes. The first to be released (late September) will be *Part 2 – Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures*. This document was produced by a Special Interest Group of the GAMP Forum (pharmaceutical companies, suppliers, consultants and the Medicines Control Agency in the UK) in order to promote a better understanding of *21 CFR Part 11*. It aims to provide

industry and its suppliers with practical guidance on how to comply with the rule, while highlighting and addressing common issues of concern. The manuscript provides a management process for achieving and maintaining compliance with *21 CFR Part 11* in manufacturing environments. Specific guidance is provided for both new and existing systems in addition to the role of suppliers in supporting this approach. Appendices provide information, examples, templates, checklists and a lifecycle for the management of electronic documents that are useful when implementing *21 CFR Part 11* compliance programs. A Glossary and References List are also included.

The remaining volumes are expected to be published by late 2001/early 2002. They are: *Part 1 – Good Electronic Records Management (GERM)*, and *Part 3 – Models for Systems Implementation and Evolution*. ■

TO ADVANCE ORDER A COPY OF *Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures*, use the order form on page 44 of this issue of the *PDA Letter*.

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Streamlining the CMC Regulatory Process for NDAs and ANDAs

by Paulette F. Kosmoski, Director, Regulatory CMC, Reliant Pharmaceuticals Inc.

An AAPS workshop cosponsored with FDA was held in June on streamlining the CMC regulatory process for NDAs and ANDAs. The workshop attracted approximately 400 attendees with over 70 FDAers attending. At the workshop, opportunities were presented to:

- review the FDA categorization of post-approval changes as reflected in the Guidance on Changes to An Approved NDA or ANDA;
- share industry experience with using the "Changes" guidance and identify parts of the guidance that may warrant revision; and to
- discuss FDA's new initiative to reduce the CMC information/data to be included in original regulatory submissions and supplements.

Breakout sessions were held serving as platforms for brainstorming, exchanges of information and ideas for further discussions. Out of these sessions, summary reports were generated to provide FDA with proposals to consider in the revision of the "Changes" guidance. Subsequently, FDA will form a working group to initiate the revision process based on the workshop report, comments submitted to the docket and FDA's own experience.

The development of strong science-based, rational and creative initiatives were central to the workshop in order to meet the regulatory challenges from a global perspective and to ensure product efficacy and safety are maintained.

Outlined below are summary highlights of key issues identified in the summary recommendations to FDA as well as some important discussion points.

- It was generally agreed upon that improvements are still needed to the "Changes" guidance and *21 CFR 314.70* must be revised to be consistent with FDAMA 116.
- There exist conflicts in reporting mechanisms between the "Changes" guidance and in SUPACs.
- The "Changes" guidance does not provide recommendations on specific information that should be developed to assess the effect of change. As progress continues on refining the existing SUPACs and developing new SUPACS, it is hoped that they can supplement areas not covered under the "Changes" guidance.
- There is a perceived need to clarify the relationship and hierarchy between the SUPACs and the "Changes" guidance.
- One issue that provoked lively discussion revolved around the issue of automatic extension of expiry dates for drug products on the basis of pilot data submitted in the Annual Report if you filed your stability protocol stating this in the approved submission.

Summary Recommendations—Proposals

Components and Composition/Manufacturing Site Changes

- FDA stated that a change in source of API should be reported as a PAS. Concern was expressed that if the materials are used in another approved application and all solvent/impurities are known, consideration should be submitted as a CBE-30. There was expressed interest in allowing this change to be submitted in a lesser filing category, such as CBE, if there is an approved comparability protocol, which should provide more regulatory relief.
- Changes of non-release rate controlling coating composition using certified colorants and GRAS or compendial components should move to a lower filing category of CBE-30 than PAS.
- The "two-year rule" for satisfactory site GMP inspection has been removed unless the manufacturing process has been discontinued for more than two years for that type of operation; the site was never inspected for that type of operation or failed a GMP inspection. However, firms are hesitant to use the CBE-30 category for qualified site changes due to possible uncertainty of current GMP status of the involved facility. Moreover, there may still be a risk, because the filing may spark an inspection.

Tests and Acceptance Criteria

- Establishing a new regulatory analytical procedure that provides increased assurance of drug substance/drug product quality, but is otherwise not a USP monograph procedure, should fall into a CBE-30 category to encourage innovation and improvement. Along these same lines, allow any loosening of an acceptance criteria change as a result of improvement in analytical procedure to be downgraded to a CBE or AR; there should be no penalty for good science.
- As suggested by ICH Q6A, allow tentative acceptance criteria when a new test or analytical procedure is approved with a commitment to tighten or loosen the analytical control as more data is collected. Meeting tighter acceptance criteria can challenge known manufacturing

and analytical capability, especially since batch manufacture experience may be limited with perhaps none at commercial production scale.
- Allow a lower filing category for changes instituted to conform to ICH guidelines.

Manufacturing Process

- All changes to the drug substance after the final intermediate should not be treated the same as multiple steps after the final intermediate can have varying impact. PAS should be restricted to changes in critical parameters.
- Remilling a drug substance to meet particle size specifications and recrystalization of a drug substance to improve purity should be categorized as a CBE-30 instead PAS.
- Changes in the imprint/embossing/debossing a series of characters and codes of a modified release dosage form should not be arbitrarily a PAS; it should depend on the nature of the MR dosage form.
- Change in shape of an immediate release tablet should not require a PAS despite of the change in appearance specifications.

Sterile Drug Products and Drug Substances

- A change in sterilizing filter pore size with serial filtration should be a CBE-30 filing category instead of PAS.
- Replacing the filling process with barrier technology should be reported as a CBE-30 instead of PAS.
- AR should be the filing mechanism for the transfer of a terminally sterilized product to a different facility on the same site.
- AR should be the filing mechanism for the reporting of a change in site to manufacture prefilled syringes used with the drug product.
- AR should be the filing mechanism for reporting a change in contract manufacturer for packaging components.
- The change in container shape and size should allow a lower filing category than a PAS with the use of pre-approved protocols to qualify the container change.
- Definition of a change in the sterilizer load in terms of order of magnitude and/or significance should be provided to allow for a downgrade of the filing category.

Labeling

- To add or strengthen storage recommendation should be a CBE filing category.
- Falling into AR category would be changes in logos, label trade dress, the name of a corporate identity and prominence on labels, for example. ■

PDA Seeks Volunteers for New S&T Activities

PDA's Science Advisory Board, under the direction of Jim Agalloco, has proposed several areas for the association's involvement. Once initiated, the following projects would likely result in the development of technical reports.

- Procedures for Developing a New Sterilization Method
- Water Systems and Survey on Water System Practices
- Filter Extractables and Filter Integrity Test Methods

If you are interested in participating in or leading one of these new activities, please send an e-mail to Russell Madsen, PDA's Senior VP Science and Technology, at madsen@pda.org, or send a fax to him at (301) 986-0296.

Steam Quality Issues Key to TM 1 Revision

Steam quality issues were the subject of a meeting of a PDA task force steering committee on July 25, outside of London. The meeting was held to determine the best way to resolve differences in steam sterilization validation and control approaches in Europe and the US.

The revision process for PDA *Technical Monograph No. 1: Validation of Steam Sterilization Cycles*, has been underway for about four years and is in currently in draft 11. The last few drafts have been on the PDA Web site for availability to all PDA members. Emerging steam quality issues have held up completion of the document. The other major outstanding technical areas, primarily aspects of overkill cycle and standard cycle can be worked out. Steam quality is the key issue requiring resolution.

The committee noted that existing European guidance usually does not reference US guidance sources and TM 1 does not always reference European guidance documents. The committee believes that TM 1 should be international in scope, addressing any differences in approach. References should contain the necessary information for the reader to find the technical information relative to the expected or applicable validation approach.

The Europe group has prepared porous load guidance for insertion into the draft TR and has decided that the issue of steam quality is applicable to porous loads only. They defined porous load to mean that steam is in direct contact with the surface to be sterilized.

Limits for steam quality (e.g., 3.5% non-condensable gas) are artificial limits and there is no available data to show the actual range and effects. PDA is considering research into steam quality that may be able to give some scientific basis for the numbers and limits. There is no guarantee that the results of such research is will be accepted by all, including the regulators.

It was agreed to revise the porous load section to:

- Reference HTM 2010 (or EN 285)
- Note that values are arbitrary, but established, regulatory expectations

The committee also decided it would be helpful to develop a parallel comparison of what is required for porous load vs. what is required for terminal sterilization of drug products in final containers. This will help to reduce the confusion and misuse of the porous load guidance.

PDA hopes to have a final draft available for public comment by November 2001. The target for publication of the revised TM 1 is July 2002. ■

—Russell E. Madsen

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Sterilization of Oil Solutions

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

This month's posting…

Dear Forum,

Our company is manufacturing parenteral oil injections. During the formulation, sunflower oil is first heated to 120°C for 2 hours. Then the active substance (a hormone or vitamin) is dissolved in the oil and the solution is filtered through a 0.45 micron-rated cartridge into a sterile tank from which it is filled. After filling some of the products are autoclaved at 100°C for 30 min and some at 120°C for 30 min. There is disagreement in our department whether such terminal heating is of any use. Some people argue that 100°C or 120°C have no effect on microorganisms in oil solutions. Therefore they think that the solutions should be filtered through a 0.2 micrometer filter and filled aseptically. The other group thinks that filtration through a 0.45 micrometer filter is enough because of low bioburden and that the above mentioned temperatures must have some killing effect. They say that it is better to heat the solutions at least slightly than not to heat them at all. What do you think about this? Could anybody give me some references on the D and z-Values for different microorganisms in oil solutions? Any input will be welcome.

Response 1

Steam sterilization of oil is difficult. I tend to agree that the times and temperatures quoted are having little or no effect on any potential contaminants. The oil takes much longer to reach sterilization temperature than water or media. Final filtration through a 0.2 μm filter for aseptic fill would be the best case unless the product can be terminally sterilized by some other means like gamma or e-beam. We have tested silicone oil for sterility after gamma sterilization. I don't know what that would do to the hormone or vitamin.

Response 2

0.45 μm membrane filters are not considered as sterilizing filters because they do not have a log reduction value (LRV) of 7 per square cm with Brevundimonas dimunita as the test organism. When 0.45 μm membranes are tested with this organism an LRV of 4 or 5 will be obtained. I remember but cannot give exact information that 0.45 membranes are tested with Serratia marcescens as the test organism. However, bacterial spores are much larger than these organisms, therefore using a 0.45 μm membrane will give a considerable reduction of the spore count; changing to a smaller pore size may not increase the efficiency and may cause problems due to lower flow rates.

Some references for heating in oil:

G. Molin. Dry heat resistance of Bacillus subtilis spores in contact with serum albumin, carbohydrates or lipids. *J. Appl. Bacteriol.* (1977) 42, 111–116.

LH Ababouch et al. Thermal inactiviation kinetics of Bacillus subtilis spores suspended in buffer and in oils. *J. Appl. Bacteriol.* (1995) 78, 669–676.

D and z-values can be found in AD Russell Destruction of bacterial spores by thermal methods. In: Disinfection, preservation and sterilization Russell, Hugo and Ayliffe (Eds.). Blackwell Science, p 640–656.

Response 3

You may want to discuss filtration issues with your filter supplier (if they can provide any technical support).

Response 4

If you are making product for Europe, you should check the decision tree, which includes a dry heat cycle.

Response 5

The decision tree can be found in the Annex to the Development Pharmaceutics guideline on the EMEA Web site—look under the Quality Working Party, Adopted guidelines.

Response 6

The 120°C temperature is intended for steam sterilization and is effective due to the transfer of energy from the steam to the substance being sterilized as the steam condenses on cooler surface. Heating oil to 120°C would amount to a marginal dry heat cycle and the effectiveness would have to be determined with resistant challenge or-

ganisms. The filtration through a 0.45 micron filter is not sufficient for sterilization. 0.22 micron is typical. Without validation to support what you are doing, the product would not be considered sterile according to US requirements.

If the product is not capable of withstanding a validated terminal sterilization cycle you would have to filter with a 0.22 micron filter and perform an aseptic fill. Leave the post-fill heat cycle in the process to provide an additional margin of safety.

Response 7

First off, sounds like you have a "bioburden reduction cycle," rather than a sterilization cycle. If you had a true sterilization cycle, there would be no argument by your peers. Sterility (to whatever level) would be proven and not argued about.

As for your friend's comments that heating in oil has no effect on the reduction of bacteria, they are not completely correct. I would rather have heard that the cycle is "meaningless" than "It does nothing." Our microbiologist friends will have to help us with determining whether or not it would actually *help* the lethality, and whether or not you actually need to validate the cycle using water, rather than oil. Irregardless of all this, here is the bit on D-Value and z-Value and why it makes no difference what medium you are sterilizing in. D-Value and z-Value are based upon experimental data showing, expressing what the actual lethality of the cycle is. (My validation friends may argue with me on the use of the D-value term here, and use "in product D-value," but let that slide for a moment). We package the death curves into nice little terms like D-value, which is the actual time in minutes it takes for the sterilization cycle to reduce the bacterial population by one log.

As for your filtration…well, as a subscriber pointed out earlier, 0.45 doesn't cut it for sterility. It will, certainly, reduce your population. We call the .45 filter a "clarifying" filter. We use the 0.45 filter in our processes as well but then terminally sterilize those same solutions before we let anyone use them.

I would be willing to bet our fellow peers would suggest (and I know the FDA would) that you should go with the terminally sterilized solution wherever possible. Aseptic fill should be your last resort. This would be true business-wise as well as with respect to our friendly regulatory agencies. You will need to deal with a myriad of other complications ($$$) if you try to fill aseptically. If you are concerned about your hormone or vitamin being degraded by the heat, you will need to perform heat degradation studies (vary temp or time of the cycle with respect to concentration), but I would still feel that it would be a small price to pay compared to the long-term commitments and risks of an aseptic fill. ■

—compiled by Russell E. Madsen

Company, Colleague & Product Announcements

Phoenix Imperative® Inc., a full-service engineering, validation and compliance company that supports the pharmaceutical and biotechnology industries, is pleased to announce the addition of James E. Taylor to their team of professionals. Taylor will fill the position of South East Regional Operations Manager. Taylor's 30-plus years of engineering/construction/validation experience is expected to support the company's efforts corporate wide. For the last 15 years he has provided services focused on clients required to demonstrate compliance with CGMP. "We are very excited about Jim coming aboard. I look forward to working with him in building our presence in the southeast region," said Richard F. Geoghegan, Jr., President/CEO/Chairman. "Additionally, Jim brings a tremendous experience base to support our corporate engineering and validation services," Geoghegan continued. For more information, contact Dee Phillips at (302) 366-0855 or visit www.phoeniximperative.com.

Propack Data, worldwide supplier of Enterprise Production Management software (EPM), announced the release of its new PMX software version 3.2. The new releases of the Clinical Trial Management solution (PMX CTM) as well as the Manufacturing Execution System solution (PMX MES) are now be available. PMS CTM Release 3.2 enables you to access clinical trial documentation and materials online. As a result, the management of enterprise-wide clinical trials is enormously facilitated. Planning and administration of clinical trials are realized with the help of a new site concept on a worldwide basis. Every location is given direct online access to all centralized and decentralized data, while a sophisticated rights management allows control over user and access permissions and ensures secure data exchange via the Internet. The new release of PMX MES, on the other hand, specifically enhances its previous version's warehouse and asset management functions. Due to the fact that load carriers are managed in accordance with their respective status, an even higher degree of transparency is achieved in the areas of material and plant management. A number of warehouse journals informs users about the current inventory, thereby ensuring permanent traceability. PMX users gain full control over the material flow as a whole, since a minute and detailed information exchange is guaranteed. Propack Data provides a component-based out-of-the-box Manufacturing Execution System (MES) PMX for the pharmaceutical and other and regulated industries that is designed to help customers reduce operating costs, shorten cycle times and improve product quality in their production operations. For more information, contact Nadine Heier at +49/(0)7 21/96 50-759 (nah@propack-data.com) or visit www.propack-data.com.

STERIS Corporation, a provider of infection and contamination prevention, microbial reduction, and therapy support systems, products, services and technologies to health care, scientific, research, food and industrial customers throughout the world, has introduced the STERIS VHP® M1000 Modular Continuous Biodecontamination System. This vaporized hydrogen peroxide system consists of three modules that can be conveniently integrated with an HVAC system and the customer's isolators, rooms and production filling equipment. Benefits include continuous operation and short cycle times. The VHP M1000 provides an environmentally safe way to optimize an aseptic manufacturer's production potential. For more information, contact Robin S. Baum at (440) 354-2600 or visit www.STERIS.com.

Document Control Systems, Inc. announced the release of MASTERControl v.6.0 FDA Edition—validation-ready document control software with 21 CFR Part 11 Compliance. In addition to powerful time-based routing, approval, escalation, full audit trail capabilities and management of the document for its entire life cycle (available in previous versions of MASTERControl FDA Edition) electronic signatures can now be manifest right on the first or last page of an approved document. The electronic signature meets the requirements for FDA *21 CFR Part 11* by providing information such as the time, date and intent or meaning of the person's signature. Other new features include more flexible document watermarking capabilities for better management of "uncontrolled" documents, and more secure viewing options that give system administrators the power to allow certain individuals or departments limited viewing rights on documents that pertain only to them. Document Control Systems, Inc. develops and manufactures client/server and Web-based software designed to address manufacturing, engineering and FDA document collaboration, control and approval processes, including validation and *21 CFR Part 11* compliance. For more information, contact Jason Clegg at (800) 825-9117 or jclegg@mastercontrol.com. ■

—compiled by Joseph G. Bury

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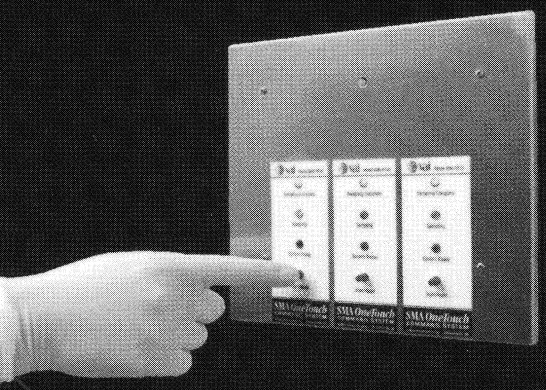

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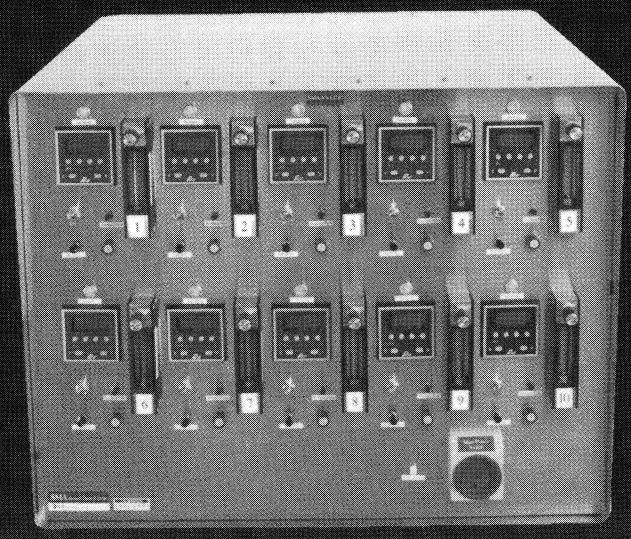

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The Extractables Puzzle: Putting the Pieces Together

Resolving Analytical, Material, Regulatory and Toxicology Issues to Find Solutions

November 12–13, 2001 • Doubletree Hotel • Rockville, Maryland

This conference, designed to determine the state-of-the-art in extractables science, will be of value to analytical chemists, formulators, material scientists, material and component suppliers, packaging scientists, regulatory affairs professionals, toxicologists, and CMC and DMF writers.

Representatives from FDA CBER, CDER and CDRH will participate in panel discussions covering the four disciplines that are necessary for the assessment of extractables: analytical chemistry, material science, toxicology and regulatory affairs. At the conference, participants will discuss 3–4 case studies that will be introduced at the beginning of the meeting and developed during breakfast breakout sessions on the morning of the second day of the meeting. A survey of current practices will be conducted from among Forum registrants and other PDA members, with a presentation of survey results at the Forum. Each registrant will receive a "regulatory sourcebook" with includes a comprehensive reference list of key documents and a compendium of definitions of important terms.

Gordon Hansen, of Boehringer Ingelheim Pharm. Inc., and Chair, IPAC-RS, will present the luncheon address, *An Integrated Strategy for the Determination and Qualification of Leachables and Extractables in Orally Inhaled and Nasal Drug Products.* ■

Poster abstracts are being sought for presentation during the Monday, November 12 reception.

Guidelines for submission of poster abstracts:

1. Abstract is limited to approximately 100 words in length, using a 1 to 1.5-inch margin.
2. Include the following information on the abstract:

   PDA 2001 Extractables Conference
   November 12–13, 2001, Rockville, Maryland.
3. Include a concise title that engages and stimulates interest.
4. Include primary contact name, address, telephone and e-mail information. Also include names and credentials of all abstract authors.
5. Submit ***electronically*** with file saved in Microsoft Word or Rich Text format **by October 12, 2001** to: royal@pda.org.

The Survey

Conference participants and visitors to the PDA Web site (www.pda.org) are invited to complete an anonymous survey of their current extractables practices. The survey questions cover the four dimensions of the conference (regulatory, toxicology, materials, and analysis). Results will be tabulated and presented at lunch on the second day of the conference. This survey will not be published.

—Leslie Zeck

To register for the conference, visit PDA's Web site at www.pda.org.

Training Workshop

ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (APIs)

FDA, in collaboration with PDA, Pharmaceutical Research and Manufacturers of America (PhRMA) and the Generic Pharmaceutical Association (GPhA) announce a workshop training series on Q7A Guidance. The ICH Q7A document, the first GMP guidance jointly developed between regulators and industry, is intended for use worldwide. It impacts any manufacturer who manufactures in, or intends to supply into, the ICH regions (US, Europe, Japan). The workshop will be offered in the follow locations and will contain identical subject matter:

Chicago, IL: October 22–24, 2001
Princeton, NJ: November 7–9, 2001
Newport Beach, CA: February 25–27, 2002
San Juan, Puerto Rico: April 8–10, 2002

This three-day workshop, the only training to be officially co-sponsored by the US Food and Drug Administration (FDA), will provide training of FDA personnel alongside industry participants. The faculty is comprised of both regulators and industry representatives who served as members of the ICH Expert Working Group that developed the document. Substantial time has been allotted for question and answer sessions.

Highlights

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

Training will be presented by the following members of the International Conference on Harmonization (ICH) Q7A Expert Working Group:

John DeFoe, Pfizer Inc.
John A. Eltermann, Jr., FDA, CBER (invited)
Steven Fairchild, Quantic (former EMEA)
Betsy P. Fritschel, Johnson & Johnson
Stephanie Gray, GlaxoSmithKline (former FDA)
Lothar Hartmann, F. Hoffmann-La Roche Ltd.
Max Lazar, Hoffmann-La Roche Inc (retired)
Edwin Rivera Martinez, FDA, CDER
Joseph Phillips, Quintiles (former FDA)
Paolo Romagnoli, European Generic Medicines Association

Who Should Attend

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

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

Learning Objectives

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

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

—Leslie Zeck

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

www.fda.gov/cder/guidance/index.htm
www.emea.eu.int/pdfs/human/ich/410600en.pdf
www.ifpma.org/ich5q.html#gmp

PDA/FDA Viral Clearance Forum

October 1–3, 2001 • Hyatt Bethesda • Bethesda, MD

The upcoming PDA/FDA Viral Clearance Forum will feature 45 cutting-edge scientific and technical presentations on the state-of-the-science in viral clearance issues for biologics. Twenty posters featuring the latest technologies will be displayed in two evening receptions. The conference will bring together representatives from international regulatory agencies, academicians, pharmaceutical/biotechnology manufacturers, manufacturers of enabling technologies and contract testing organizations (CTOs).

Regulatory presentations will address the following topics:

- *Virus Validation of Filtration Procedures*, Hannelore Willkommen, Paul-Ehrlich-Institut, Germany;
- *The Choice of Viruses for Validation of Viral Clearance*, Mahmood Farshid, Ph.D., CBER/FDA; and
- *Evaluation of a Quantitative Product-Enhanced Reverse Transcriptase Assay to Monitor Retrovirus in mBb Cell-Culture*, Kurt Brorson, Ph.D., CBER/FDA.

Industry presentations will cover such issues as:

- *Inactivation of Infectious Pathogens and Leukocytes in Labile Blood Components*, Laurance Corash, M.D., Cerus Corporation;
- *Virus Safety of Plasmaderived Biologicals and Blood Components: Overall Process Validation—Industry Perspective*, Albert Groener, Aventis Behring;
- *A Summary of the Challenges and Solutions to Interpreting the ICH Guideline for Viral Safety Evaluation in Various Specific and Complex Situations*, Holly Hutchins, Amgen Inc.;
- *Validation of the Clearance of Five Model Viruses in the Acrinol Immunoadsorption, Alcohol Precipitation, and Acrinol Clarification/Silica Gel Chromatography Process Steps of the SS ATGAM Manufacturing Process*, Robert L. Garlick, Ph.D., Pharmacia Corporation;
- And many more…

Don't miss this opportunity to interact with the experts from FDA and industry to discuss current guidance, critical issues and approaches to viral clearance issues for biologics.

Participation in this conference is limited and is nearly *sold out*. Ensure your ability to take part in the discussions with leading regulatory representatives by registering today.

For additional information, or to register for this conference, visit PDA's Web site at www.pda.org. ■

—Leslie Zeck

Did You Get the News?

As a new member service, monthly PDA e-Updates will be sent to keep members apprised of activities, deadlines and other important issues. However, more than 30% of the PDA membership does not have an e-mail address on file. Members may add or update their e-mail addresses (as well as other contact information) by sending this information by e-mail to info@pda.org.

E-mail updates on time-senstive issues will be released as needed. Be assured that we are taking every measure to use this communication vehicle judiciously (we won't bury you in e-mails). And, if you do not wish to receive the PDA e-Update, you may exercise an "opt out" at any time (opt out must be performed by direct link from the e-mail). ■

Basel 2002

PDA International Congress, Courses and Exhibition

Adding Value to the Pharmaceutical Industry: Leveraging the Future

Convention Center Basel, Switzerland

February 11–13, 2002 Congress and Exhibition
February 14–15, 2002 Courses

Make your plans now to attend PDA's prestigious International Congress, Courses and Exhibition in Basel, Switzerland. The event that will attract more than 500 professionals and scientists from across the globe working in the parenteral, sterile products, biotechnology and related fields. *Adding Value to the Pharmaceutical Industry: Leveraging the Future* will feature a multi-track format of topics important to the industry. Regulatory and industry experts will discuss the latest science and technology related to regulatory issues, compliance strategies, harmonization issues, validation, biotechnology and more.

The Program Planning Committee (see photo) met in London in July to review and select abstracts for presentation and to develop an agenda for the conference. Presentations will address such topics as:

- *Method of Increasing Test Range and Accuracy of Bioindicators—Bacillus stearothermophilus Spores*;
- *Simulation of Multistep Aseptic Production by Media Challenge Test*;
- *Validation of Rapid Microbiological Test Systems*; and
- *ICH Harmonised Tripartite Guideline—Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients*.

Exhibits

Anticipated attendance of 500 scientists from Europe, US, Asia and other global regions will make this a premier event, allowing pharmaceutical science and technology suppliers to meet key contacts. For information on exhibiting and/or sponsoring an event, contact:

Nahid Kiani
PDA
7500 Old Georgetown Road, Suite 620
Bethesda, MD, USA 20814
Tel: (301) 986-0293 x128
Fax: (301) 986-0296
E-mail: kiani@pda.org

The full agenda and a list of papers to be presented for this conference are available on PDA's Web site at www.pda.org. ■

—Leslie Zeck

The program committee includes: (seated, L-R) Lisa Skeens, Baxter Healthcare, Co-chair, and Nigel Halls, GlaxoSmithKline (UK), Co-chair. (Standing, L-R) Leslie Zeck, PDA; Bengt Ljungqvist, Royal Institute of Technology, Sweden; Tom Berger, Abbott; Keith Wickert, Pall Life Sciences; Hiltrud Horn, Knoll; Bernard Kronenberg, Bakrona Basel; James Agalloco, Agalloco & Assoc; Russell E. Madsen, Jr., PDA. Not pictured: James C. Lyda, PDA Europe; Jennie Allewell, Cell Therapeutics, Inc.; Martine Palliere, Aventis Pharma, France; Paolo Verardi, GlaxoWellcome SpA, Italy; and Janette Waterhouse, Quintiles, UK.

ANNOUNCEMENT AND CALL FOR PAPERS

2002 PDA Spring Conference, Courses and Exhibition

Environmental Monitoring and Aseptic Processing: Reaching a Common Understanding of the Regulatory and Technical Requirements

March 11–15, 2001 • Rosen Hotel, Orlando, Florida

This year's Spring Conference will focus on Environmental Monitoring and Aseptic Processing. Abstracts outlining the latest science and technology in following issues are being sought:

- Airflow velocity measurements;
- Surface monitoring of sterile product contact surfaces during aseptic filling operations;
- Alert and action level excursions during microbial monitoring of aseptic filling operations;
- Environmental monitoring during manufacturing;
- Identification requirements for environmental and sterility test isolates;
- Media fill acceptance criteria and duration;
- Gowning qualification and frequency of requalification;
- Resolving disagreements about 483 items and filing requirements; and
- HEPA filters.

Abstracts of papers not previously published or presented at scientific meetings are sought for this meeting that will attract 500+ international scientists for high-level education and networking. Accepted abstracts will be non-commercial in nature and describe new work and significantly contribute to the body of knowledge of pharmaceutical science and technology.

ABSTRACTS MUST BE RECEIVED BY

OCTOBER 12, 2001

FOR CONSIDERATION.

Abstract Instructions:

1. Abstract is limited to approximately 100 words in length, using a 1 to 1.5-inch margin.
2. Include the following information on the abstract:
   2002 PDA Spring Conference
   March 11–13, 2002—Orlando, Florida.
3. Include a concise title that engages and stimulates interest.
4. Include primary contact name, address, telephone and e-mail information. Also include names and credentials of all abstract authors.
5. Include a brief, two-paragraph bio for each prospective presenter on the same page as the abstract (please submit only one document).
6. Submit ***electronically*** with file saved in Microsoft Word or Rich Text format **by October 12** to: pda@outsources.com.

Presenters of selected abstracts agree to submit copies of their presentation slides or overheads by **February 1, 2002** for inclusion in the conference notebook to be distributed on site. ■

—Leslie Zeck

The 2002 PDA Spring Conference will feature Tabletop Exhibits.

For Information on securing space for your Tabletop display, contact

Nahid Kiani at

Phone: (301) 986-0293 ext. 128 or

E-mail: kiani@pda.org.

www.pda.org

Training Courses continued from cover

tems. This is nowhere more evident than in the area of "Computer Related Systems Validation," a long-standing PDA course taught by John Voss and Sam Clark. Participants in this course return to their organizations with the understanding and skills needed to drive the validation of their firm's computer systems.

When is an introduction to the CGMPs just not enough? Our membership has told us that there is a real need for an "Advanced Topics" course for senior individual contributors who come to a leadership position in our industry for the first time. Participants will come away from this brand new course with an understanding of the issues they need in order to be an effective leader in their organization. They will learn techniques for handling common compliance problems. They will also develop their grasp of current issues in the industry not only in the US, but also in what is rapidly becoming a global set of regulatory requirements. This new course, entitled "Advanced Regulatory Compliance Training for the Supervisor/Manager" is being developed by PDA's VP of Education, Rick Rogers, in conjunction with input from representatives from the Training Interest Group. It will be a two-day course offered for the first time in December at the PDA Annual Conference.

All PDA-TRI courses are designed to provide the participant with lively interaction with the faculty and class. Complete details and registration information for these and all PDA-TRI offerings can be found at www.pda.org. ■

—Rick Rogers & Leslie Zeck

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For registration information on this conference, please visit our Web site at

www.pda.org.

Be sure to advise the reservationist that you are attending PDA's Annual Conference, to ensure the discounted rate.

$185.00 Single
$205.00 Double
Each Additional Person $20

Cut off Date: November 9, 2001
Check in Time: 3:00 pm
Check out Time: 12:00 noon

Make your plans now to attend PDA's largest conference, courses and exhibition on December 3–7, 2001. This meeting will attract nearly 1,000 international scientists for high-level education and networking. The opening plenary session for the conference will feature Michael Beatrice of Abbott Laboratories. Beatrice will discuss real-life compliance challenges faced by his company over the past several years. The closing plenary session will focus on *Compliance Challenges: Real World Experience in Consent Decree Management*, with presentations by Leon Lachman of Lachman Consultant Services, and Claudio Pincus of the Quantic Group, Inc.

Concurrent tracks will allow attendees to focus on papers presented by industry colleagues in specific areas of interest, including biotech issues, computer issues, laboratory issues, manufacturing, sterilization and much more. Interactive breakfast roundtables will facilitate ongoing discussion among conference participants.

A special bonus forum on BSE/TSE issues will also be offered immediately following PDA's annual meeting on Wednesday and Thursday, December 5–6. The industry's leading international scientists have been invited to present a state-of-the-science perspective on BSE and how it has impacted the pharmaceutical industry. FDA representatives have been invited to share the latest information. Industry representatives will share their company's strategies and experiences. Make your plans now to stay for this forum, the first of its kind in our industry!

Don't miss this opportunity to interact with your industry colleagues to discuss compliance strategies for your future.

PDA Technical Reports continued from cover

PDA Technical Report No. 34

Design and Validation of Isolator Systems for the Manufacturing and Testing of Health Care Products

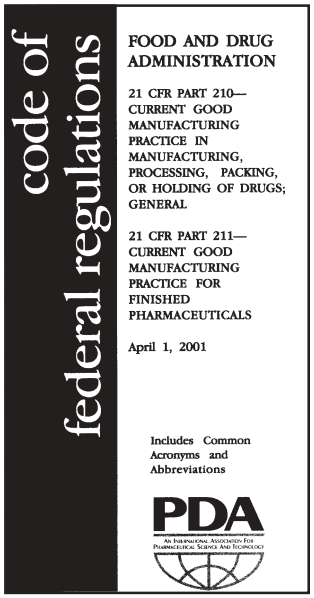
This comprehensive report addresses essential user requirements for the application of isolator technology to a broad range of manufacturing, development and testing applications in the health care product manufacturing industry. It covers not only product sterility assurance, but also the use of isolators for the containment of hazardous materials.

Until now, the health care industry has lacked a uniform set of definitions for isolator technology. The committee recognized this need, so TR 34 provides useful definitions for isolator and barrier systems. The committee also recognized that in some regions of the world, processing environments called "isolators" are widely used in the clinical pharmacy setting. These devices have some general features in common with isolators as defined in this document, however, they are distinctly different from the isolator systems currently in use for sterile product manufacturing and testing in the health care product industry.

Early Availability

As mentioned above, the reports will accompany the September/October issue of the *PDA Journal of Pharmaceutical Science and Technology*. Members who desire to purchase an extra copy of either or both of these technical reports may go to the PDA Web site at www.pda.org. ■

—Russell E. Madsen



To Order, use the form on page 44 or Contact PDA—www.pda.org (301) 986-0293

2001 CGMP Pocket Guide Now Available

The popular ***CGMP Pocket Guide*** that is produced annually by PDA is **NOW AVAILABLE**. This new update contains **21 CFR Part 210**—Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General and **21 CFR Part 211**—Current Good Manufacturing Practice for Finished Pharmaceuticals (updated April 1, 2001). For your reference, a listing of common acronyms and abbreviations is included.

These handy Pocket Guides are a convenient way to keep 21 CFR Parts 210, 211 at your fingertips. Order now for yourself, your staff and your clients. Quantity discounts are available, plus you may order the Pocket Guides with your logo printed on the covers.

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101–1,000 ..... $3 each
1,001+ ..... $2 each

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Item No. 13004

CGMP Pocket Guide to 21 CFR Parts 210, 211 (April 2001)
Single copy price is $4 member/$7 nonmember

To Order your copies use the form on page 44. Contact Janny Chua PDA at (301) 986-0293 ext. 127, chua@pda.org if you have questions.

For Personalized Orders Only, Contact Janet Raysick at PDA, (301-986-0293 ext. 120, raysick@pda.org).

REGISTRATION FORM PDA/FDA Viral Clearance Forum

October 1-3, 2001 ❖ Hyatt Regency ❖ Bethesda, Maryland

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

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

Job Title Membership Number (if known)

Company (indicate full company name)

Business Address

City State/Province Zip + 4/Postal Code Country

Business Phone Fax E-mail

☐ Substituting for

(check here only if you are substituting for a previously enrolled colleague. If you are a nonmember substituting for a member, the additional nonmember fee must be paid.)

2. Fees Individuals registering at the nonmember rate receive one full year of PDA membership. (If you DO NOT want to become a PDA member, please check this box ☐). **Nonmembers registering for multiple events need only pay the nonmember fee once.**

	PDA Member	Nonmember	Government/Academic
Full registration (10/1-3)	☐ $995	☐ $1,145	☐ $275
Monday only (10/1): *includes lunch and reception*	☐ $450	☐ $600	☐ $175
Tuesday only (10/2): *includes lunch and reception*	☐ $450	☐ $600	☐ $175
Wednesday only (10/3): *includes lunch*	☐ $350	☐ $500	☐ $150
TOTAL FEES			$_____

Full Forum Registration Includes: Forum reference materials on site, Lunch each day, Reception and Poster Session on October 1 and October 2.

Government/Academic: You must be an employee of an official government agency or accredited university to quality for this discounted rate.

3. Please check the appropriate box

☐ Check Enclosed ☐ Wire Transfer Charge to: ☐ MasterCard/EuroCard ☐ VISA ☐ AMEX

Account Number_____ Exp. Date_____

Name Exactly as on Card _____

Signature_____ Date _____

4. Return completed form with payment (payment must be included to be considered registered) made to:

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Payments must be made to PDA in US dollars by check drawn on a US bank, by electronic money transfer (SunTrust Bank ABA #051000020, PDA Account #209364254, Swift #UVBIUS33), net of all bank charges; by MasterCard, VISA or American Express.

Confirmation: Written confirmation will be sent to you once payment is received. You must have written confirmation to be considered enrolled in a PDA event. **Substitutions:** If a registrant is unable to attend, substitutions are welcome and can be made at any time. If you are pre-registering as a substitute attendee, indicate this on the registration form. A nonmember substituting for a member must pay the additional fee. **Refunds:** Refund requests must be made in writing. Registrants whose written requests for refunds are received at PDA on or before **September 1, 2001** will receive a full refund less a $35 (US) processing fee. Registrants whose written requests for refunds are received after **September 1** and on or before **September 15** will receive 50% of the registration fee. After that, no refunds can be made.

Please tell us how you learned about this event

- ☐ I'm a PDA member
- ☐ Advertisement
- ☐ Direct Mail
- ☐ Fax
- ☐ Internet
- ☐ Colleague
- ☐ Other_____

Business Environment (check one)

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

Professional Interest (check all that apply)

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

LTR 09/01

PDA Use: Date:_____ Check #:_____ Amount:_____ Account:_____

Upcoming PDA-TRI Education Courses

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

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

To register, call PDA headquarters in Bethesda, Maryland at (301) 986-0293. PDA-TRI Location/Hotel Information follows.

Cleaning Validation (PDA #400), October 22–24, 2001—*taught by Jon Voss, cGMP Systems, and Bob O'Brien, BIOPURE*; $1,900 members/$2,050 nonmembers.

Validating a Steam Sterilizer (PDA #322), *one date remaining:* October 25–26, 2001—*taught by Ronald Kraus, Associate Director of KMI Systems and Christopher Mansur, Sr. Computer Validation Compliance Specialist, Genetics Institute*; $1,500 members/$1,650 nonmembers.

Basic Microbiology: Theory & Practice (PDA #109), November 12–14, 2001—*taught by Leah Autrey, Abbott Laboratories, Hospital Products Division*; $1,850 members/$2,000 nonmembers.

Computer Products Supplier Auditing Process Model: Auditor Training (PDA #474), October 11–12, 2001; November 15–16, 2001 in Baltimore, Maryland; $950 PDA members/$1,100 nonmembers. *For more information, vist our Web site,* www.pda.org.

Introduction to Developing Effective Audit Strategies for CGMP Cleanrooms (PDA #200), November 15–16, 2001—*taught by Strother Dixon, GMP Trainer for PDA-TRI*; $1,150 members/$1,300 nonmembers.

Identification of Microorganisms Using Comparative DNA Sequencing (PDA #232), November 28–29, 2001—*taught by Michael G. Waddington, Accugenix*; $1,500 PDA members/$1,650 nonmembers.

Contamination Control Basics (PDA #213), *One date remaining*: November 30, 2001—*taught by Sandra A. Lowery, President of Quality Systems Consulting*; $750 PDA members/$900 nonmembers. ■

PDA-TRI Location/Lodging Information

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

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

Unless otherwise noted, PDA Institute courses are held at: PDA Training and Research Institute, 1450 South Rolling Road, Baltimore, MD 21227, Tel: (410) 455-5800; Fax: (410) 455-5802. PDA has not secured any specific room blocks for participants attending courses at the Training and Research Institute. There are several hotels in the Inner Harbor (downtown Baltimore) and BWI airport areas. These include, but are not limited to:

- **Baltimore Hilton & Towers Inner Harbor**—Tel: (410) 539-8400; Fax: (410) 625-1060
- **Baltimore Marriott Inner Harbor**—Tel: (410) 962-0202; Fax: (410) 625-7892
- **Embassy Suites-BWI**—Tel: (410) 850-0747; Fax: (410) 859-0816
- **Holiday Inn-BWI**—Tel: (410) 859-8400; Fax: (410) 684-6778
- **Holiday Inn Inner Harbor** —Tel: (410) 685-3500; Fax: (410) 727-6169
- **Homewood Suites BWI****—Tel: (410) 684-6100; Fax: (410) 684-6810
- **Hyatt Regency Baltimore Inner Harbor**—Tel: (410) 528-1234; Fax: (410) 685-3362
- **Sheraton Inner Harbor Hotel**—Tel: (410) 962-8300; Fax: (410) 962-8211.
- **Marriott Residence Inn-BWI****—Tel: (410) 691-0255; Fax: (410) 691-0254. ■

***no on-site restaurant*

Aseptic Processing 2002

January 14–18 & February 11–15, 2002

April 8–12 & May 6–10, 2002

September 9–13 & October 7–11, 2002

October 28–November 1 & November 18–22, 2002

in Baltimore, Maryland

A Comprehensive Program in Manufacturing Sterile Products

For Course Content Information, contact PDA-TRI directly at (410) 455-5800.

For Registration Information, contact PDA at (301) 986-0293 or visit www.pda.org.

Palm Springs Courses

October 16–18, 2001

Miramonte Resort, Indian Wells, CA

Training for Performance (PDA #409) — October 16, 2001

Drug Labeling Regulation (PDA #464) — October 16, 2001

Introduction to Validation (PDA #397) — October 16–17, 2001

Auditing Foreign Active Pharmaceutical Ingredient (API) Manufacturers (PDA #473) — October 16–17, 2001

Knowledge & Skills of the Successful QA/QC Manager in the Pharmaceutical Industry (PDA #410) — October 16–17, 2001

GMP Fundamentals (PDA #493) — October 17, 2001

Computer-Related Systems Validation (PDA #651) — October 17–18, 2001

Root Cause Analysis (PDA #754) — October 18, 2001

Introduction to Writing and Auditing CGMP Documentation (PDA #755) — October 18, 2001

Designing Regulatory Training That Works (PDA #407) — October 18, 2001 ■

This event is being held at:

Miramonte Resort
45-000 Indian Wells Lane
Indian Wells, CA 92210

Toll Free:
1 (800) 237-2926

Tel:
(760) 341-2200

Fax:
(760) 568-0541

Visit www.pda.org to download the Registration Form, or use the form on page 38!

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Technovation

PDA-TRI Education Courses Registration Form

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/Postal Code

Tel 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.)

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)
			TOTAL :	$

3. Please check the appropriate box:

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

Account Number_____ Exp. Date _____

Name _____
(exactly as on card)

Signature_____ Date _____

Payments must be made to PDA in US dollars by check drawn on a US bank, by electronic money transfer **(SunTrust Bank ABA #051000020, PDA Account #209364254, Swift#UVBIUS33), net of all bank charges**; by American Express, MasterCard, or VISA.

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)

Payment must be included to be considered registered.

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.*
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 start of an event (course series, conference, etc.), a full refund, minus a $35.00 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 the event must be canceled, registrants will be notified as soon as possible and will receive a full refund of fees paid. PDA will not be responsible for discount airfare penalties or other costs incurred due to a cancellation.*

LTR 09/01

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

Q7A Training Workshop Registration Form

Chicago, IL – October 22-24, 2001
Princeton, NJ – November 7-9, 2001
Newport Beach, CA – February 25-27, 2002
San Juan, PR – April 8-10, 2002

ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (APIs)

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

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

Job Title

Company (indicate full company name)

Business Address

City State/Province Zip + 4/Postal Code Country

☐ Substituting for

Business Phone Fax E-mail

(check here only if you are substituting for a previously enrolled colleague.

2. Fees. Please plan to attend all three days of this training workshop. One-day registration is not available. **Full Workshop Registration Includes:** Conference reference materials on site, Lunch on each day, Networking Reception on Day 1.

	Industry	Government*
Chicago, IL – October 22-24, 2001	☐ $995	☐ $395
Princeton, NJ – November 7-9, 2001	☐ $995	☐ $395
Newport Beach, CA – February 25-27, 2002	☐ $995	☐ $395
San Juan, PR – April 8-10, 2002	☐ $995	☐ $395
TOTAL FEES		$_____

*Government: You must be an employee of an official government agency to qualify for this discounted rate.

3. Please check the appropriate box

☐ Check Enclosed ☐ Wire Transfer Charge to: ☐ MasterCard/EuroCard ☐ VISA ☐ AMEX

Account Number_____ Exp. Date _____

Name Exactly as on Card _____

Signature _____ Date _____

4. Return completed form with payment (payment must be included to be considered registered) made to:

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Payments must be made to PDA in US dollars by check drawn on a US bank, by electronic money transfer (SunTrust Bank ABA #051000020, PDA Account #209364254, Swift #UVBIUS33), net of all bank charges; by MasterCard, VISA or American Express.

Please tell us how you learned about this event

- ☐ Advertisement
- ☐ Direct Mail
- ☐ Fax
- ☐ Internet
- ☐ Colleague
- ☐ Other_____

Confirmation: Written confirmation will be sent to you once payment is received. You must have written confirmation to be considered enrolled in this event.

Substitutions: If a registrant is unable to attend, substitutions are welcome and can be made at any time. If you are pre-registering as a substitute attendee, indicate this on the registration form. Refund deadlines and amounts are as follows:

Chicago, IL: If request for refund is received at PDA ***on or before September 24*** registrants will receive a full refund less a $35 (US) processing fee. If received ***after September 24 and on or before October 8*** registrants will receive 50% of the registration fee. After ***October 8***, no refunds can be made.

Princeton, NJ: If request for refund is received at PDA ***on or before October 8*** registrants will receive a full refund less a $35 (US) processing fee. If received ***after October 8 and on or before October 22*** registrants will receive 50% of the registration fee. After ***October 22***, no refunds can be made.

Newport Beach, CA: If request for refund is received at PDA ***on or before January 21*** will receive a full refund less a $35 (US) processing fee. If received after ***January 21 and on or before February 4*** registrants will receive 50% of the registration fee. After ***February 4***, no refunds can be made.

San Juan, PR: If request for refund is received at PDA ***on or before March 8*** registrants will receive a full refund less a $35 (US) processing fee. If received ***after March 8 and on or before March 22*** registrants will receive 50% of the registration fee. After that, no refunds can be made.

LTR0901

PDA Use: Date:_____ Check #:_____ Amount:_____ Account:_____

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

Australia Chapter
Contact: **Mary Sontrop**
ZLB Bioplasma AG
Tel: +41-31-344-4305
Fax: +41-31-344-5555
E-mail: *mary.sontrop@zib.com*

Canadian Chapter
Contact: **Grace Chin**
Pellemon, Inc.
Tel: (416) 422-4056 x230
Fax: (416) 422-4638
E-mail: *ching2@snc-lavalincom*
Web site: ***www.pdacanada.org***

Capital Area Chapter
Areas Served: Maryland, District of Columbia, Virginia, West Virginia
Contact: **Allen Burgenson**
DynPort Vaccine Company, LLC
Tel: (301) 607-5046
Fax: (301) 607-5099
E-mail: *BurgensA@dynport.com*
Web site: ***www.pdacapitalchapter.org***

Delaware Valley Chapter
Areas Served: Delaware, New Jersey, Pennsylvania
Contact: **Mark Kaiser**
Lancaster Laboratories
Tel: (717) 656-2300 x1263
Fax: (717) 656-2681
E-mail: *Mwkaiser@lancasterlabs.com*
Web site: ***www.pdadv.org***

Central Europe Chapter
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PDA Europe Office
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Fax: +41-61-703-1689
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Metro Chapter
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Fax: (732) 521-5933
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Midwest Chapter
Areas Served: Illinois, Indiana, Ohio, Wisconsin, Iowa, Minnesota
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Fax: (847) 581-6553
E-mail: *robert.s.murphy@monsanto.com*

Mountain States Chapter
Areas Served: Colorado, Wyoming, Utah, Idaho, Nebraska, Kansas, Oklahoma, Montana
Contact: **John M. Elvig**
Colorado Quality Assoc., Inc.
Tel: (303) 666-0319
Fax: (303) 926-9006
E-mail: *carl10@prodigy.net*

New England Chapter
Areas Served: Massachusetts, Connecticut, Rhode Island, New Hampshire, Vermont, Maine
Contact: **Robert A. Pazzano, P.D.**
Validation and Training Services
Tel: (508) 870-0007 x140
Fax: (508) 870-0224
E-mail: *robert_pazzano@vtsinc.net*

Southeast Chapter
Areas Served: North Carolina, South Carolina, Tennessee, Virginia, Florida, Georgia
Contact: **Mary Carver**
Eisai, Inc.
Tel: (919) 474-2149
Fax: (919) 941-6934
E-mail: *carver@eisai.com*
Web site: ***www.pdase.org***

Southern California Chapter
Areas Served: Southern California
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West Coast Chapter
Areas Served: Northern California
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E-mail: *randallt@filtrex.com*

PDA
An International Association For Pharmaceutical Science And Technology

Calendar begins on back cover

2002

JANUARY

January 14-18, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 1)
PDA-TRI Baltimore, MD

January 16-18, 2002
PDA-TRI Lake Tahoe Course Series
Hyatt Regency Lake Tahoe Resort & Casino
Incline Village, NV
January 16
A Comprehensive Guide to OOS Regulations
A Practical Guide to Change Control
Calibration in the GMP Setting
Cost Effective Validation
Training for Performance
January 16-18
GMP Training Manager Workshop
January 17
GMP Fundamentals
Strategic and Practical Approaches to Part 11 Compliance
January 17-18
Basic Concepts in Cleaning and Cleaning Validation
Validation by Design
January 18
Basic Statistical Tools for Quality Assurance and Manufacturing Personnel
Designing Regulatory Training that Works

FEBRUARY

February 11-15, 2002
Basel 2002: PDA International Congress, Courses and Exhibition
Adding Value to the Pharmaceutical Industry—Leveraging the Future
Basel Convention Center, Basel, Switzerland

February 11-15, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 2)
PDA-TRI Baltimore, MD

February 25-27, 2002
Training Workshop
ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (APIs)
The Sutton Place Hotel, Newport Beach, CA

MARCH

March 11-15, 2002
2002 PDA Spring Conference, Courses and Tabletop Exhibition
Environmental Monitoring and Aseptic Processing: Reaching a Common Understanding of the Regulatory and Technical Requirements
Rosen Hotels and Resorts, Orlando, FL

APRIL

April 8-10, 2002
Training Workshop
ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (APIs)
Caribe Hilton, San Juan, Puerto Rico

April 8-12, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 1)
PDA-TRI Baltimore, MD

April 29-May 1, 2002
PDA Isolation Technology Conference
Hilton East Brunswick, East Brunswick, NJ

MAY

May 6-10, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 2)
PDA-TRI Baltimore, MD

May 19-22, 2002
PDA/USP Joint Conference on Sterile Product Manufacturing
Sanibel Harbour Resort, Fort Myers, Florida

JUNE

June 3-5, 2002
PDA-TRI Florida Course Series
The Diplomat Resort Country Club & Spa
Hollywood, FL

AUGUST

August 27-29, 2002
PDA-TRI Vermont Course Series
Sheraton Burlington Hotel & Conference Center,
Burlington, VT

SEPTEMBER

September 9-13, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 1)
PDA-TRI Baltimore, MD

September 23-26, 2002
2002 PDA/FDA Joint Regulatory Conference, Courses and Tabletop Exhibition
Hyatt Regency on Capitol Hill, Washington, DC

OCTOBER

October 7-11, 2002
PDA 2002 Biennial Training Conference
Charting a Course for Success
Hyatt Regency Tampa, Tampa, FL

October 7-11, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 2)
PDA-TRI Baltimore, MD

October 28-November 1, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 1)
PDA-TRI Baltimore, MD

NOVEMBER

November 18-20, 2002
PDA-TRI Las Vegas Course Series
Alexis Park Resort & Spa, Las Vegas, NV

November 18-22, 2002
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 2)
PDA-TRI Baltimore, MD

DECEMBER

December 10-13, 2002
2002 PDA Annual Meeting, Courses and Exhibition
New Orleans Marriott, New Orleans, LA

PDA
An International Association For Pharmaceutical Science And Technology

PDA Books Available

For a full listing of documents available, please contact PDA or visit our Web site, www.pda.org.

Change Control; *C. Reid*; 2001; 40 pp; $90 members/$109 nonmembers. This manual provides a well-organized, practical process for the management of changes to Information and Control Systems used in GxP-related operations. Contents include process definitions for system changes to databases, operating systems, standard and application software, and recommendations for ways to handle changes in hardware, processes, and the environment. It provides a complete example of the change control process, details about planned and unplanned changes, sample report forms for errors/changes, change requests, a log of change-related actions, a log of maintenance actions, recommended actions in case of changes to the hardware, software, or users, and much more. A very valuable reference. **Item No. 17189**

Cleaning & Cleaning Validation: A Biotechnology Perspective; *R. Brunkow* et al.; 1995; 190 pp; $125 members/$145 nonmembers. **Item No. 13002**

Electronic Records and Electronic Signatures Compliance Assessment; *C. Reid and B. Mullendor*; 2001; 50 pp; $90 members/$109 nonmembers. Electronic Records and Electronic Signatures (ERES) provides practical guidance on the interpretation of 21CFR Part 11 and defines the steps you need to take to address current and future compliance issues. This quick guide is designed to help you identify ERES business benefits, establish policies, procedures, and processes that ensure compliance, and define and evaluate system requirements. This excellent resource and reference also contains invaluable appendices containing examples of warning letters, a valuable list of records specifically identified in predicate rules, numerous examples of electronic records relating to specific system types, and very extensive sets of ERES assessment questionnaires. This guide is a must-have for everyone concerned with any aspect of ERES regulation. **Item No. 17177**

GMP in Practice: Regulatory Expectations for the Pharmaceutical Industry; *J. Vesper*; 2001; 224 pp; $100 members/$124.50 nonmembers. This is a comprehensive, easy-to-use reference, designed to simplify and enhance understanding of most of the current GMP expectations and how they apply to ongoing manufacturing tasks. **Item No. 17191**

Microbiology for Pharmaceutical Manufacturing; *R. Prince, ed.*; 2001; 908 pp; $240 members/$299 nonmembers. This book systematizes and updates the technical discipline of pharmaceutical microbiology. Providing valuable knowledge for the novice and expert alike, it contains the wisdom and guidance of 40 leading pharmaceutical microbiologists, engineers, and other thought leaders. **Item No. 17185**

Pocket Code of Federal Regulations GMP Guide - 2001 Edition; 21 CFR Part 210-CGMP in Manufacturing, Processing, Packing, or Holding of Drugs; general. 21 CFR Part 211; 56 pp; $4 member/$7 nonmember. CGMP for Finished Pharmaceuticals. Reproduced in pocket size by PDA. April 1, 2001. **Item No: 13004**

Quality Control Systems for the Microbiology Laboratory: The Key to Successful Inspections; *L. Clontz*; 2001; 192 pp; $120 members/$149 nonmembers. Written by an experienced microbiologist, this manual contains chapters covering: current inspection trends; chemical and biological reference standards; laboratory equipment and facilities; preparation of media, buffers and reagents; environmental monitoring; water systems for laboratory use; data trending and statistical process control; use of disinfectants and sanitizers; training of laboratory personnel; and the quality assurance program for the laboratory. **Item No. 17176**

The Internal Quality Audit; *M. Grimaldi and J. Gough*; 2001; 100 pp; $120 members/$149 nonmembers. Here is the common-sense guidance you need to perform an effective, systematic internal quality audit. As a quality professional, you are well aware of the repercussions caused by a nonconforming product entering the marketplace; customers may experience adverse effects or worse, and your company will certainly lose credibility and profit. This book helps you identify and prevent systemic weaknesses by providing you with the evaluation tools you need to prevent such occurrences. Contents include: staffing; partnering not policing; setting a company wide schedule; reporting and assessing; establishing scope and depth; determining regulations; reviewing documents, previous reports and records; understanding measurements; creating the audit plan; keeping notebooks; tips on how to audit a system or process, observe activities, and identify nonconformance; auditing batch records, history files, or other documentation; compiling the observations; remaining unbiased; preparing the report; writing report guidelines; and formatting and presenting the audit report. **Item No. 17179**

Understanding GMP: An Expert's View on Merging Global Regulatory and Manufacturing Perspectives; *M. Becker*; 2001; 224 pp; $120 members/$149 nonmembers. Now at Merck, Sharp, and Dohme Ltd., Martyn Becker is an ex-UK MCA Manager and Senior Medicines Inspector. In this book, he shares his expertise and perspectives on GMP regulations, legislation, applications and practical challenges and solutions to applying GMP to the manufacturing environment. Anyone concerned with quality and GMP should have this book on a shelf nearby. **Item No. 17174**

Part 2—Complying with 21 CFR Part 11, Electronic Records and Electronic Signatures; 92 pp; $95 members/$180 nonmembers **Item No. 19001**

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TR 33 Evaluation, Validation and Implementation of New Microbiological Testing Methods; This report is intended to provide a general approach to the introduction of new microbiology methods in a government-regulated environment. It is also intended to provide guidance for the successful evaluation, validation and implementation of new microbiological methods needed by the pharmaceutical, biotechnology and medical device industries to assure product quality. These new methodologies offer significant improvements in terms of the speed, accuracy, precision and specificity with which testing can be performed. 2000; 37 pp; $75 members/$125 nonmembers.

TR 32 Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations; Developed in response to an FDA challenge to develop a standard way to assess the structural integrity of acquired software, TR 32 was written by the PDA Supplier Auditing and Qualification Task Group (SA&Q), which included pharmaceutical companies, suppliers, auditors and FDA members who used their experiences with supplier audits and performed research to draft a common practice to satisfy industry needs. The scope of the project included audits of computer products and services and describes how the SA&Q Task Group, led by George J. Grigonis, Jr., Merck and Co., Inc., developed and tested a Process Model and Data Collection Tool. Use of these tools will provide consistent audit information that can be shared within the industry. December 1999; 277 pp; $90 members/$140 nonmembers (paper copy); **TR 32**. $50 members/$75 nonmembers (CD-ROM format) TR32 CD.

TR 31 Validation and Qualification of Computerized Laboratory Data Acquisition Systems; Prepared by the PhRMA CSVWG and the PDA Computer Related Systems-Laboratory Systems Task Group, TR 31 provides guidance to lab scientists, technicians and managers responsible for the implementation, testing, control and usage of Laboratory Data Acquisition Systems (LDAS) used within a GMP-, GLP- or GCP-regulated environment. Addresses computerized LDAS within a regulated environment; also applicable to systems critical to the operation of a company, department or function, regardless of the system's regulatory impact. 1999; 12 pp; $50 members/$75 nonmembers.

TR 29 Points to Consider for Cleaning Validation; This document provides guidance relative to the validation of cleaning for a broad range of processing systems and product types within the pharmaceutical industry. The report includes perspectives on the application of cleaning validation guidance in the areas of finished pharmaceuticals, bulk pharmaceutical chemicals, biopharmaceuticals and clinical products. It is the pharmaceutical companion to *Cleaning and Cleaning Validation: A Biotechnology Perspective* published by PDA in 1996. 1998; 23 pp; $75 members/$125 nonmembers.

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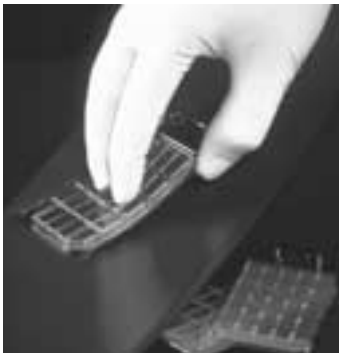

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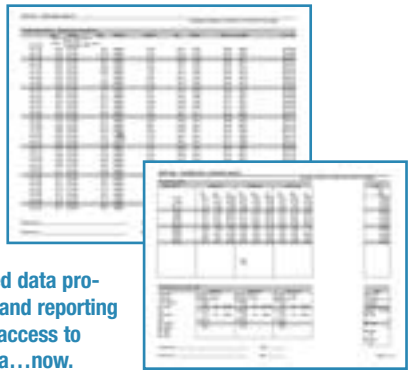

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2001

OCTOBER

October 1-3, 2001
PDA/FDA Viral Clearance Forum
Hyatt Bethesda, Bethesda, Maryland

October 1-5, 2001
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 1)
PDA-TRI Baltimore, MD
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October 11-12, 2001
PDA-TRI Course: Computer Products Supplier Auditing Process Model—Auditor Training
PDA-TRI Baltimore, MD

October 15-17, 2001
PDA Isolator Technology Conference
Hilton East Brunswick, East Brunswick, NJ
Rescheduled: April 2002

October 16-18, 2001
PDA-TRI Palm Springs Course Series
Miramonte Resort, Indian Wells, CA
- October 16
  - **Drug Labeling Regulation**
  - **Training for Performance**
- October 16-17
  - **Auditing Foreign Active Pharmaceutical Ingredient (API) Manufacturers**
  - **Introduction to Validation**
  - **Knowledge & Skills of the Successful QA/QC Manager in the Pharmaceutical Industry**
- October 17
  - **GMP Fundamentals**
- October 17-18
  - **Computer-Related Systems Validation**
- October 18
  - **Designing Regulatory Training That Works**
  - **Root Cause Analysis**
  - **Writing and Auditing CGMP Documentation**

October 22-24, 2001
Training Workshop
ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (APIs)
The Allerton Crowne Plaza, Chicago, IL

October 22-24, 2001
PDA-TRI Laboratory Course:
Cleaning Validation
PDA-TRI Baltimore, MD

October 25-26, 2001
PDA-TRI Laboratory Course:
Validating a Steam Sterilizer
PDA-TRI Baltimore, MD

NOVEMBER

November 5-9, 2001
PDA-TRI Laboratory Course:
Aseptic Processing Training Program (week 2)
PDA-TRI Baltimore, MD
Sold Out

November 7-9, 2001
Training Workshop
ICH Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (APIs)
Hyatt Regency Princeton, Princeton, NJ

November 12-13, 2001
The Extractables Puzzle: Putting the Pieces Together
Resolving Analytical, Material, Regulatory and Toxicology Issues to Find Solutions
Doubletree Hotel, Rockville, MD

November 12-14, 2001
PDA-TRI Laboratory Course:
Basic Microbiology—Theory & Practice
PDA-TRI Baltimore, MD

November 15-16, 2001
PDA-TRI Course: Computer Products Supplier Auditing Process Model—Auditor Training
PDA-TRI Baltimore, MD

November 15-16, 2001
PDA-TRI Laboratory Course: An Introduction to Developing Effective Audit Strategies for CGMP Cleanrooms
PDA-TRI Baltimore, MD

November 28-29, 2001
PDA-TRI Laboratory Course: Identification of Micro-organisms Using Comparative DNA Sequencing
PDA-TRI Baltimore, MD

November 30, 2001
PDA-TRI Laboratory Course:
Contamination Control Basics
PDA-TRI Baltimore, MD

DECEMBER

December 3-7, 2001
2001 PDA Annual Meeting, Courses and Exhibition
Compliance: Challenges and Pragmatic Solutions
Marriott Wardman Park, Washington, DC
- **PDA-TRI Courses:**
  - December 6
  - **Auditing Techniques for CGMP Compliance**
  - December 6-7
  - **Advanced Regulatory Compliance Training for the Supervisor/Manager**
  - **Computer-Related Systems Validation**
  - December 7
  - **Change Control and Documentation**

December 10-11, 2001
PDA-TRI Laboratory Course:
Environmental Mycology—Identification Workshop
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