Science • Technology • Quality • Regulatory • Community

PDA Letter

Volume XLI • Issue #3

March 2005

In This Issue...

A HACCP Framework for Risk Management in Bio/Pharmaceutical Processes

Tony C. Chan, Virginia Polytechnic Institute and State University

As the economy enters the 21st century, pharmaceutical and biopharmaceutical developers and manufacturers, as well as researchers and producers of all medical products, must focus on efficient and effective approaches to managing quality and safety while working towards the harmonization of global regulations. In the face of growing consumer demand for safer, more effective and better quality health products that, at the same time, cost less, government health authorities, like the U.S. FDA, and non-governmental organizations, like the International Conference on Harmonisation for pharmaceutical products and the Global Harmonization Task Force for medical devices, are setting higher standards to meet these expectations. The U.S. FDA's risk-based approach to pharmaceutical cGMPs, for one, is a great example of a governmental health authority rising up to meet the challenge.

Integrated Hazard Analysis and Critical Control Point Risk Management (HACCP RM) represents a paradigm shift in methods for discovery, development, manufacture, submission for approval or certification, and monitoring of product quality and safety issues. HACCP RM also has a significant impact on product transfer and post-production activities including storage, distribution, delivery of service, field use, disposal, and the planning of future generations of products and processes.

HACCP RM is a total-product life-cycle process that integrates the seven principles of Hazard Analysis and Critical Control Point management within the framework of the sound risk management principles encapsulated in the International Organization for Standardization (ISO) 14971 Standard – Application of Risk Management to Medical Devices (henceforth, the Standard). With no equivalent standard yet available for pharmaceutical and biopharmaceutical products, the framework defined by the terminology and stipulated by the requirements in the Standard are suitable surrogates. HACCP's seven principles strengthen the requirements of the ISO Standard (the Standard), particularly clauses: Four – Risk Analysis, Five – Risk Evaluation and Six – Risk Control (see Figure 1).

The foundation of HACCP RM is built upon five pillars (The **5 P's**): 1) a **p**olicy that stipulates principles and guidance on how to manage risk; 2) a **p**lan

(continued on page 14)

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The conference will be truly international in scope by bringing together representatives from both EMEA and FDA with biopharmaceutical manufacturers, manufacturers of enabling technologies and contract testing organizations.

By participating in this conference you will receive the latest information on:

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- Contamination control, **risk assessment and mitigation** including facility-wide decontamination, segregation and inactivation procedures (e.g. resin and membrane cleaning);
- Current issues in **TSE safety**;
- Risk mitigation and control of **animal and human derived raw materials** (e.g. trangenics, plasma products, tissue products); and,
- Current **regulatory perspectives** from EMEA, FDA and industry.

Who Should Attend

This conference will be of value to mid- and senior-level professionals with specific interest in the viral and TSE safety and evaluation of medicinal products, including:

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✓ **Biotechnology**

✓ **Manufacturing Sciences**
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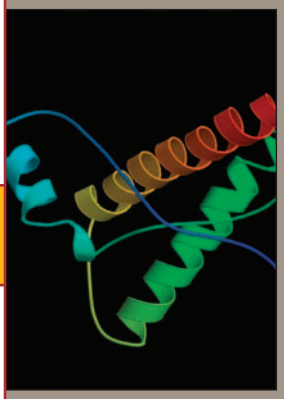

Venue

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Bethesda, MD 20814

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+1 (888) 591-1234

Room rate: $209 + tax

Reservations can be made until Friday, April 22, 2005

Registration Fees

PDA Member	**US$ 1,050**
Nonmember	**US$ 1,245**
Government	**US$ 430**
Student	**US$ 160**

To Register

Online at **www.pda.org/viral2005**

OR: complete the attached registration form and fax or mail to:

PDA
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (301) 986-1093

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Table of Contents

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1) New Vendor Technologies at PDA TRI

2) The 2005 PDA NITE™ Exhibitors Finalists

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A PDA Conference
Regulatory Developments – The Science & Technology to Comply™

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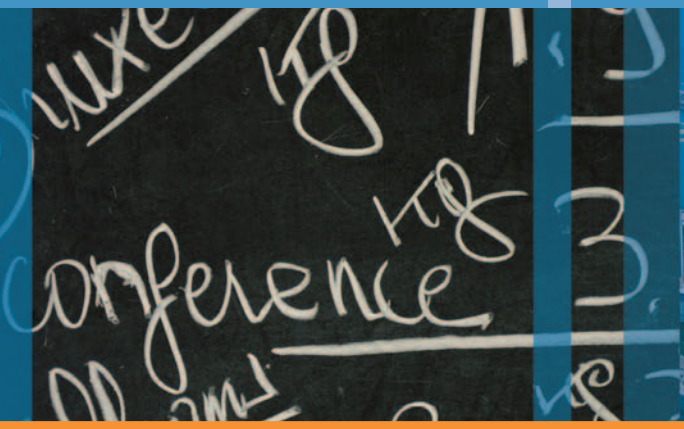

April 4-8, 2005
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  - **Manufacturing & Engineering**
  - **Academic & Research and Development**
- **20 New Case Studies**
- **4 FDA Updates**
  - **Rapid Methods**
  - **Viral Filtration**
  - **PAT**
  - **Combination Products**
- **3 New PDA Technical Reports**
  - **Viral Filtration**
  - **Validation of Protein Manufacturing**
  - **Sterile Filtration of Gasses**
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  - **Refining Risk Management Approaches - The FDA Collaborative Project**
  - **Implementing PAT: Advantages for Industry**
- **10 Interactive Training Courses**
- **PDA *New Innovative Technologies*™ (NIT) in the Exhibition**
- **New PDA Annual Graduate Research Symposium**
- **Career Fair**

www.pda.org/annual2005

Neal G. Koller
PDA President

President's Message

Helping the Community Meet the Risk Management Challenge

The use of Hazard Analysis and Critical Control Point (HACCP) methodology and other risk management/assessment modalities are being accepted worldwide for pharmaceutical and biopharmaceutical products. In 2001, the World Health Organization (WHO) Expert Committee on Specifications for Pharmaceutical Preparations acknowledged HACCP for risk assessment and included references to HACCP in its 2003 Technical Report Series document number 908: *WHO Expert Committee on Specifications for Pharmaceutical Preparations.*

In this issue of the *PDA Letter*, we are publishing a comprehensive article on HACCP Risk Management by risk management specialist **Tony Chan** from the Virginia Polytechnic Institute and State University. This group has substantial experience teaching HACCP and risk management to medical products companies as well as other industries. As part of PDA's commitment to fulfilling its Mission of *promoting scientifically sound and practical technical information and education for industry and regulatory agencies*, we are exploring with Mr. Chan and his colleagues at the University's Center for Applied Sciences in Health Products and Processes how to introduce and teach HACCP for the PDA community.

All the various risk management/assessment modalities are becoming increasingly important as the U.S. FDA, the EMEA and health authorities around the world expect companies to raise the level of manufacturing quality and efficiency. PDA is working in many ways to help the community meet the challenge.

In addition to Mr. Chan's article, PDA VP of Quality and Regulatory Affairs Victoria Dedrick contributed an article to this month's *PDA Letter* on the U.S. FDA's approach to a risk management strategy. Moreover, the January/February *PDA Journal of Pharmaceutical Science and Technology* contains two excellent manuscripts on risk.

Discussions of risk management and quality systems are becoming more frequent at PDA Conferences and Training and Research Institute (TRI) courses. In the first half of 2005 alone, PDA is offering a number of conference sessions and TRI courses on risk management.

At the 2005 PDA International Congress, three presentations and a TRI course addressed various aspects of risk management. TRI is introducing a new course on risk, *Overview of Risk Assessment and Risk Management,* which is being offered during the San Francisco course series in April and at the 2005 PDA Annual Meeting in April in Chicago.

Furthermore, the opening Plenary Session of the 2005 Annual Meeting is dedicated to *The Move to Risk-Based Quality Systems.* PDA is excited that Professor Jeffrey Macher, PhD, Georgetown University, will be delivering the opening keynote presentation on *Refining Risk Management Approaches – The Pharmaceutical Manufacturing Research Project.* Following the plenary session, the Quality and Regulatory Track of the conference includes a number of excellent presentations on risk managment.

PDA's volunteers are showing incredible initiative with respect to risk management. In May, for example, the India Chapter has scheduled a two-day workshop entitled, *Risk-based Validation.* And the UK/Ireland Chapter is holding a one-day workshop on *Risk Analysis* in June.

PDA is here to help the community—industry, government and academic in the pharmaceutical and biopharmaceutical industries—keep up with the latest advances in science, technology and regulatory affairs. We are sure that the articles, programs and courses covering risk management will be a valuable part of the community's *Career-long Learning*™ in 2005.

Member Volunteer Opportunities

Product Quality Research Institute Technical Committees

PDA is looking for two volunteers to represent PDA in the Drug Substance Technical Committee (DSTC) and the Drug Products Technical Committee (DPTC) within PQRI. Committee members meet monthly by teleconference and quarterly in person. The normal commitment time-frame is two years. For more information, click the links below for the committee work plans.

If you are interested in participating in a PQRI Technical Committee representing PDA please contact Vicki Dedrick, Vice President, Quality and Regulatory Affairs, at dedrick@pda.org for more information.

PDA Program Planning Committees

PDA is looking for volunteers to serve on the planning committees for upcoming PDA events. We are currently forming committees for the PDA International Congress, PDA Annual Meeting and PDA/FDA Joint Regulatory Conference through 2007.

If you are interested in participating on a PDA Program Planning Committee, please contact Wanda Neal, Director, Programs and Meetings, at neal@pda.org.

PDA Regulatory Affairs and Quality Committee (RAQC) Task Forces

RAQC is always looking for Task Force Volunteers. We keep an on-going list of volunteers in a variety of expert areas to call upon for assistance. Most commitments are ad hoc of 60 - 180 days to prepare regulatory comments. It is necessary to prepare regulatory comments under time constraints so flexibility is required.

Task Forces are currently forming to comment on:

Step 2 ICH Q8 document

EMEA Guideline on the Requirements to the Chemical and Pharmaceutical Quality Documentation Concerning Investigational Medicinal Products in Clinical Trials (IMPD): Comments are due in June 2005

If you are interested in participating on an RAQC Task Force, please contact Vicki Dedrick, Vice President, Quality and Regulatory Affairs, at dedrick@pda.org for more information.

PDA Letter Editorial Committee (PLEC)

PDA is looking for member volunteers to serve on the new Editorial Committee for the *PDA Letter*. As PDA's primary publication on science, technology, quality, regulatory and our community, the *PDA Letter* requires member input to remain focused on and relevant to their evolving needs.

The PLEC will meet periodically each year via teleconference, and at the PDA Annual Meeting and the PDA/FDA Joint Regulatory Conference. The PLEC will work to develop a 10-month editorial calendar of topics, comment on potential interview and feature story subjects and help PDA staff solicit articles from the membership.

The inaugural PLEC meeting will take place at the PDA Annual Meeting in Chicago, April 4-8, 2005.

If you would like to volunteer, please forward a brief summary of your professional experience and your contact information to PDA Senior Editor Walter Morris at +1 (301) 656-5900, ext. 148 or morris@pda.org by March 15.

PDA Training and Research Institute Advisory Board (TRIAB)

The TRIAB is has been formed to help focus the TRI curriculum to best serve industry, academia and health authority audiences with practical training courses. The TRIAB will establish instructional design criteria; oversee course development; and guide the implementation of comprehensive training curricula and certificate programs as they relate to the needs of the PDA membership and the pharmaceutical and biopharmaceutical communities.

If you would like to volunteer to participate on one of the subcommittees being established to develop training criteria, content and certification programs, e-learning opportunities, and other training and education related programs, please provide a brief summary of your professional experience and your contact information to PDA Training and Research Institute Director Gail Sherman at +1 (410) 455-5981 or sherman@pda.org.

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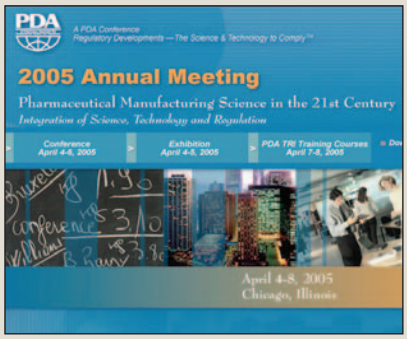

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www.pda.org/careers/fair

For additional information, contact Dorothea McGuire
+1 (301)656-5900 x150 mcguire@pda.org

George A. Robertson
Vice President, Science and Technology

Vice President's Message

The PDA Survey Program

One of the most important ways PDA serves its members is through its scientific survey program. Results of surveys have been included in numerous Technical Reports, most recently TR # 36, *Current Practices in the Validation of Aseptic Processing,* 2001.

There are currently four surveys on the PDA Web site at this time. I would like to describe these projects and invite you to participate in this important PDA program.

Extractables: This survey requests data on the current approaches of the industry in the areas of extractables regulation, toxicology, materials science and chemistry and their potential for materials to migrate into drug products. This survey will form an important part of the discussion during the 2005 PDA Conference: *The Extractables Puzzle: Putting the Pieces Together: Resolving Chemistry, Material, Regulatory, and Toxicology Issues to Find Solutions.*

Pharmaceutical Water: This survey is designed to gather information about the current state of water used by the pharmaceutical industry, the use of different types of water and other water-related issues. The survey should identify those issues of greatest concern.

AQL Glass Defects: The purpose of this survey is to compare what defect levels companies are assigning to various glass defects. There have been numerous regulatory actions on this topic; often the regulators say or imply other companies use tighter criteria. This survey will provide some objective criteria and, in conjunction with the PDA Technical Report in progress, should help promote consistency and facilitate improvement within the industry.

Terminal Sterilization: This survey is designed to gather data on what is being done in regard to terminal sterilization and aseptic processing. The information will be used to better understand these areas and help us with current and future projects.

To participate, go to www.pda.org/science/Survey/surveyintro.htm. We ask that you complete a demographic profile. These profiles are not directly linked with your response, but rather are analyzed in a separate data pool in order to ensure anonymity.

Technical Report No. 40, *Sterilizing Filtration of Gasses,* mailed with the January/February *PDA Journal of Pharmaceutical Science and Technology.* This TR assists those working with gas filtration in the manufacturing, development and regulatory areas in the selection, qualification and validation of appropriate filters. Early and careful screening of potential filter types can result in fewer technical and regulatory problems. This report is intended to complement PDA TR #26, *Sterilizing Filtration of Liquids.*

TR #40 will be discussed in a special session at the April 4-6 2005 PDA Annual Meeting by the authoring Task Force chair, **Frank Bing.** He will describe the report and emphasize the areas that are new and especially useful for managers and directors in technical and regulatory departments. Additionally, a case study, *Sterilizing Filtration of Gaseous Oxygen for Cell Culturing Applications,* presented by **Christian Martin** of Pall Life Sciences, will demonstrate the applicability of TR #40.

THANK YOU to the members of the Task Force

Frank Bing, *Abbott Laboratories,* retired (Co-Chair)

Srikanth Sundaram, PhD, *Schering-Plough Corporation* (Co-Chair)

Barry Bardo, *Meissner Filtration Products, Inc.*

Thomas Britton, *Millipore Corporation*

Robert Conway, PhD, *Cuno Inc.*

Teresa Feeser, PhD, *Eli Lilly & Co.*

Holly Haughney, PhD, *Pall Corporation*

continued on next page

USP UPDATE

Roger Dabbah, PhD, USP

The first Supplement of *USP 28- NF 23* has been published and will be official as of April 1, 2005, unless otherwise indicated. Thirty new USP monographs appear on a variety of product types, including extended release tablets, sublingual tablets, tablets, capsules, injections, topical gels, oral solutions and injectables. It includes 13 new drug substances. Notable are Somatropin and Somatropin for Injection which are the products of recombinant-DNA technology. A monograph, first in its series, Graftskin is a living bilayered skin substitute. In preparation are more than five products monographs in that series. Three new dietary supplements are also included in the *First Supplement,* along with ten new monographs in NF. A new annotated list of General Notices, Monographs, General Chapters, Reagents, and Tables affected by changes included in this Supplement is a new feature for ease if use. A list of USP Reference Standards that were unavailable, but have become available, and the dates of their availability are also shown on p. 3204 and 3205 of the First Supplement.

A new chapter, <730> Plasma Spectrochemistry, is in this Supplement. It introduces new technologies useful for pharmaceutical analyses.. A new general information chapter, <1043> Ancillary Materials for Cell, Gene, and Tissue Engineering Products, discusses the qualification of ancillary materials, which are materials used in the manufacture of these products, that do not remain in the final products. It also discusses the selection and suitability of these materials . Finally, it establishes risk classification categories that will determine the qualification level of each class of materials. Since these materials are not designed to remain in the final product the removal of these products after manufacturing and the testing of residual in the finished product are discussed. Over 100 monographs are revised in this Supplement.

The January-February 2005 *Pharmacopeial Forum* was published and contains the first Interim Revision Announcement (IRA) to USP 28-NF 23. It was released on January 1, 2005 and became official on February 1. It contains changes in the Bisoprolol Fumarate Tablets monograph and the Glucagon monograph. Seven new USP monographs are proposed with as target *USP 29*. Three new NF monographs are proposed with a target *NF 24*. Forty-two revisions of USP, Dietary Supplements, or NF are proposed with target USP 29, NF 24, or via 2nd IRA of USP 29-NF 23. In the Harmonization section, a large number of USP monographs are to be revised by the removal of reference to the general chapter <724> Drug Release and its replacement by reference to the newly harmonized chapter on Dissolution<711>. These revisions will be published in the 2nd IRA of USP 28-NF23 with a delayed implementation date of April 1, 2006. Three general chapters have been harmonized, <701> Disintegration, < 711> Dissolution, and <724> Drug Release, and they are published in this PF for information only. They will be published as IRA in the 2nd IRA of USP28, with a delayed implementation date of April 1, 2006.

Under the Pharmacopeial Previews section of the same PF, a new general information chapter, <1058> Analytical Instrument Qualification, is presented. A new version of chapter <1090> Drug Product Interchangeability is proposed. The text discusses the different approaches used by regulatory agencies. It also discuss the relationship among WHO, ICH, FDA, and USP for specifications, bioavailability, bioequivalence and dissolution. Comments to the proposed chapter are encouraged

Finally, a Stimuli Article, authored by the PQRI Container-Closure Working Group, is featured: "Basis for Using Moisture Vapor Transmission Rate per Unit Product in the Evaluation of Moisture-Barrier Equivalence of Primary Packages for Solid Oral Dosage Form."

USP congratulates Eric Sheinin, PhD, for his election to the board of Directors of PDA. Dr. Sheinin is Vice President, Department of Drug Standards Development at USP.

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Technology Transfer – Getting It Right Every Time!

By Mark Gibson, PhD, AstraZeneca

Technology transfer from R&D to production is a critical process in the development and launch of any new medicinal product. The timely and effective technology transfer between R&D and production sites, including all the associated knowledge, information and skills to be able to manufacture and test at the receiving site, will depend on many factors. These factors are discussed in detail in a new book, ***TECHNOLOGY TRANSFER: An International Good Practice Guide for Pharmaceuticals and Allied Industries,*** now available from PDA (www.pda.org/estore).

As editor of *Technology Transfer*, and author of several chapters, I have chosen informative articles written by contributors who have extensive knowledge and experience in this field. *Technology Transfer* is intended to give a comprehensive overview and guide to the technology transfer process and to provide practical examples to illustrate some of the important factors for achieving timely and successful transfers.

With the knowledge that each technology transfer is unique because it is the nature of pharmaceutical R&D to develop novel drug substances, drug products, analytical test methods and manufacturing processes, a transfer strategy to document the specific requirements, timings and responsibilities is recommended to take into account the nuances of individual projects. Key decisions to support the transfer should be defined early in the development program.

Below are a few other high-level observations that are important for achieving successful technology transfers right the first time and every time:

- Technology transfer is a multidisciplinary, team-based process, requiring input from both the R&D and production site organizations. Good communication, planning and teamwork are essential.
- An agreed-upon technology transfer process within the company should be in place. Different organizational approaches may be acceptable, including the point of handover from R&D to production, providing that the responsibilities and accountabilities have been clearly defined for the process.
- A structured approach to development and technology transfer is more likely to be successful. It is recommended that you follow a logical order such as: product design, product optimization, process design, process optimization, scale-up at R&D, tech-nology transfer and scale-up at the production site, optimization at the production site, and validation of the process.
- The development activities undertaken leading up to the technology transfer are just as important as the actual transfer itself.
- The manufacturing processes and test methods for drug substance and drug product should be based on sound science. Quality needs to be built in during development, and the product and manufacturing process to be transferred needs to be sufficiently robust. It is a mistake to think that suboptimal manufacturing processes or non-robust analytical methods will settle down with time or can be easily fixed after being transferred.

Additional topics discussed are:

- The business, economic and regulatory considerations and how they impact on technology transfer.
- Overcoming cultural and language barriers in global companies where transfers are performed across international boundaries to achieve cohesive teamwork and productive communications.
- The final hurdle to product launch is often passing a preapproval inspection (PAI) if the product is destined for the United States. Recommendations are given in a separate chapter on preparing for a PAI to give the best chance of success.

Finally, it is important that new learning points from transfers be captured and documented within a company, bearing in mind that it is often the case that the current team is disbanded and different personnel may be involved the next time. *Technology Transfer* will lead the reader through all of these issues to help you successfully navigate the waters of technology transfers to mitigate delays in product registration and loss and alleviate the risk of adding to the already huge cost of getting a new product to the market.

Dr. Gibson is responsible for pharmaceutical development of new chemical entities and new product opportunities, including clinical trial manufacture, technology transfer to production and support to marketed products at AstraZeneca R&D Charnwood, a division of AstraZeneca. He has over 20 years of experience of working in R&D both as a bench scientist and a manager. He has worked on various technology transfer operational guidelines and has given many seminars and presentations on product development and technology transfer. He previously edited *Pharmaceutical Preformulation and Formulation,* published in 2001 by Interpharm (now CRC Press). Dr. Gibson belongs to a number of pharmaceutical associations.

PDA Interest Groups & Leaders

The following is a list of PDA Interest Groups (IGs). The list below includes the IG's name and contact information for each IG's leader, including the leader's affiliation and his or her e-mail address. More detailed information on PDA's Interest Groups and contact information is available on the PDA Web site at: www.pda.org/science/IGs.html.

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Pfizer Inc.
E-mail:
john.g.shabushnig@pfizer.com
- European Branch

Markus Lankers, PhD
APSYS GmbH
E-mail: markus.lankers@apsys.de

HACCP Framework, continued from cover

on how to manage risk during the entire product life cycle; 3) a description of **p**eople's roles and responsibilities and their pursuit of competence in managing risk; 4) a **p**rocess describing how, what, and when risk management activities are carried out during all the phases of product life cycle (See Figure 1, and the next section on the HACCP RM Process); 5) a **p**aperwork system that records all the necessary documentation for the facilitated transfer of knowledge to incoming product managers, and provides objective evidence for regulatory compliance, as well as for legal purposes.

The HACCP RM approach is a proactive process that uncovers, identifies and mitigates risks during a product's life cycle, and perpetuates this process through future generations of product and process development. Consequently, this process improves product reliability and safety, reduces product recalls and user complaints, and cuts wastes incurred through poor quality products (scrap, rework, warranty and liability). Companies that take advantage of this process may enhance the efficiency of resource allocation, prevent product liability lawsuits, and negotiate better liability insurance coverage.

In summary, HACCP RM is a disciplined, structured and scientific approach that provides a proactive business strategy to enable a company to manage and prevent potential crises. It creates a sustainable strategic advantage while maximizing shareholder value. Through the HACCP RM process, a company is better able to protect and secure its value, guard its growth potential, and hedge against market, capital, operational and financial volatility.

The Language of HACCP RM

One of the essential elements for a successful HACCP RM program is the establishment of a common lexicon for use throughout the company. It should provide for clear and consistent risk communication throughout the entire product life cycle within the company. This section summarizes the most essential terminology—the basic "risk language" that should be fully understood and used by all employees within a company that practices HACCP RM.

An important aspect of HACCP RM is the strong linkage between the negative impacts generated by the product and the product itself. Thus, the following glossary begins with a set of descriptions as related to the fundamentals of risk, after which successive elements of the HACCP RM process are described.

Fundamentals of Risk

- **Control Point:** Any point, step or procedure at which a variable, parameter or quality factor(s) can be controlled within established specifications. [4, Chapter One-Five]
- **Critical:** Denoting a morbid condition in which death is possible. [3]
- **Critical Control Point (CCP):** A point, step or procedure at which control can be applied and is essential to prevent, eliminate or reduce a risk (modified from hazard to risk) to an acceptable level. [4, Chapter One-Five]
- **Critical Limit:** A maximum and/or minimum value to which a product, process or quality parameter must be controlled at a CCP to prevent, eliminate or reduce to an acceptable level the occurrence of a hazard that would result in harm [4, Chapter One-Five].
- **Harm:** Physical injury and/or damage to the health of people or damage to property or the environment. [2, Definition 3.3]
- **Hazard:** Potential source of harm. [2, Definition 3.5]
- **Hazardous Situation:** Circumstances in which people, property or the environment are exposed to a hazard(s). [2, Definition 3.6]
- **Residual Risk:** Risk remaining after protective measures have been taken. [2, Definition 3.9]
- **Risk:** Combination of the probability of occurrence of harm and the severity of that harm. [2, Definition 3.2]
- **Safety:** Freedom from unacceptable risk. [2, Definition 3.1]
- **Severity:** Measure of the possible consequences of a hazard. [1, Definition 2.21]

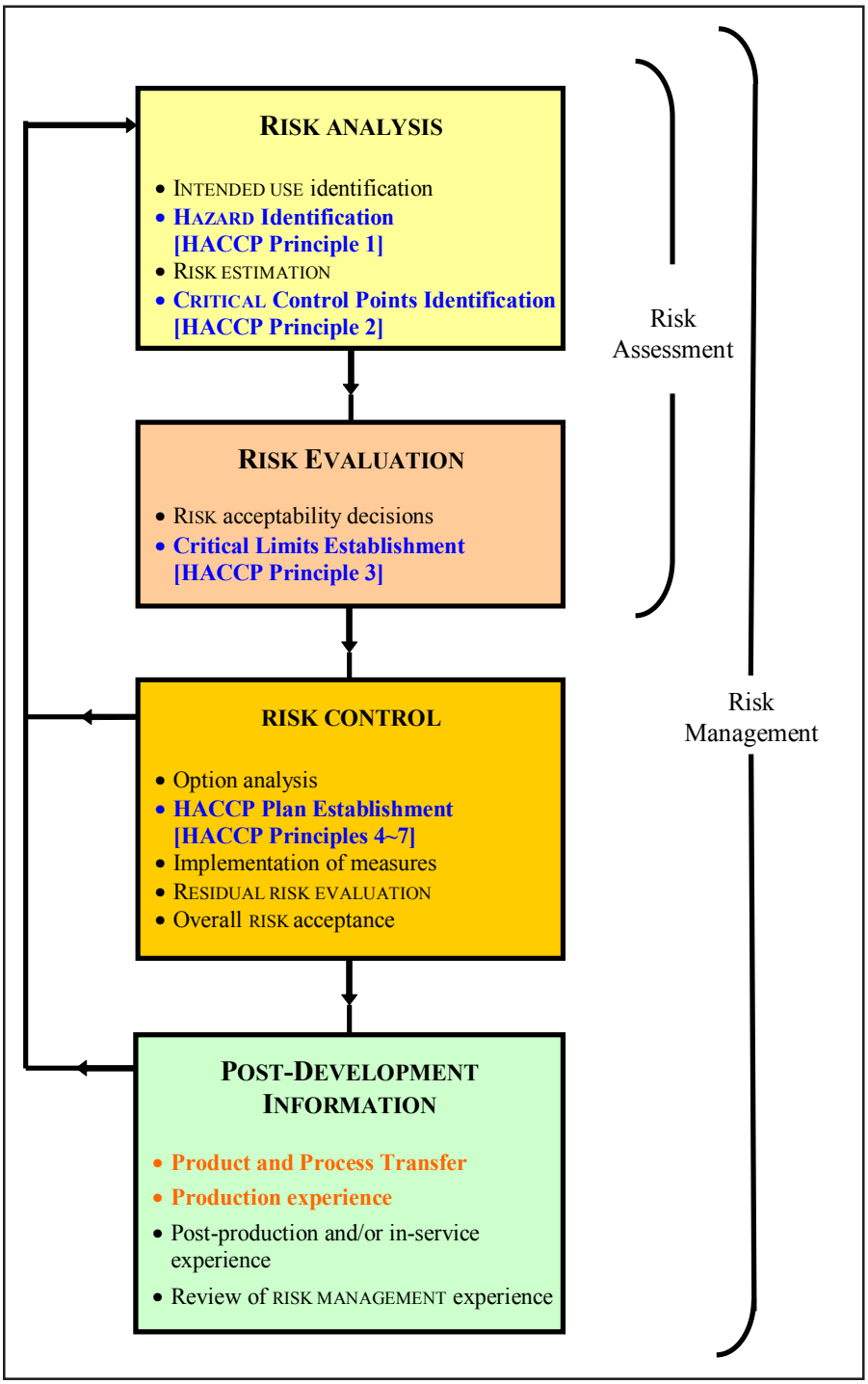
Elements of HACCP RM

- **Establish:** Define, document (in writing or electronically) and implement. [5]
- **Practicability:** Refers to the ability of a manufacturer to reduce risk. It has two components:

  technical practicability refers to the ability to reduce risk regardless of cost, while

  economic practicability refers to the ability to reduce risk without making the provision of the medical device an unsound economic proposition. Cost and availability implications are considered in deciding what is practicable to the extent that these impact upon the preservation, promotion or improvement of human health. [1, Annex E.3.3]
- **Risk Analysis:** Systematic use of available information to identify hazards and eliminate risk. [2, Definition 3.10]
- **Risk Assessment:** Overall process comprising a risk analysis and a risk evaluation. [2, Definition 3.12]

Figure 1: A HACCP RM Process Flow Diagram



- **Risk Control:** Process through which decisions are reached and protective measures are implemented for reducing risks to, or maintaining risks within specified levels. [1, Definition 2.16]
- **Risk Evaluation:** Judgment, on the basis of risk analysis, of whether a risk is acceptable which has been achieved in a given context based on the current values of society. [2, Definitions 3.11 & 3.7]
- **Risk Management:** Systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating and controlling risk. [1, Definition 2.18]
- **Seven Principles of HACCP:** Conduct hazard analysis. Determine the critical control points (CCPs). Establish critical limits. Monitor each CCP. Establish corrective actions. Establish verification procedures. Establish record-keeping and documentation procedures. [4, Chapter One-Three]

The Five P's of HACCP RM

The foundation of a HACCP RM framework consists of five elements:

1) Policy

A risk management policy is essential to a company that utilizes HACCP RM. This policy should take into account all relevant international, national or regional standards and regulations. It should define how to determine acceptable risk during the entire product life cycle. The policy should also stipulate the "who, what and how" of both internal and external risk communication. Risk communication activities may include the review of results of risk management activities at defined intervals. The purpose of the review ensures the continuing suitability and effectiveness of the HACCP RM process. The policy must be established before product-specific HACCP RM processes can be implemented. HACCP RM processes should not be implemented without such policy in place.

2) Plan

The company should prepare a risk management plan for every product in accordance with the established risk management policy. This plan [1] should:

a. Identify and describe the product. Product identification and description should give the

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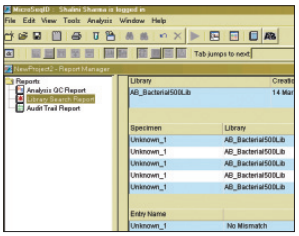

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project team and management the ability to trace risk management activities.

b. Define a scope of the applicable life cycle phases. The scope allows the project team to define its work and the boundaries or the limitations of the project to be managed.

c. State verification activities. Verification activities should be specified as related to both internal and external risk control activities such as design and process validation as well as outsourcing activities.

d. Indicate management roles and responsibilities for the allocated resources. Risk communication, approval process and functional responsibilities should be clarified.

e. Define intervals for review. Project milestones and their subsequent reviews should be defined and stated.

f. Specify criteria for risk acceptability. Risk acceptability criteria should be clear and consistent throughout the product life cycle. They should be derived from top management's risk management policy.

g. Record plan changes and revisions. The plan should bear the initiation date and its current revision for traceability purposes.

3) People

HACCP RM is an integrated total product life cycle approach that requires commitment from top managers as well as total employee involvement to facilitate changes in the culture, organizational structure and the application of scientific approaches. It demands a disciplined and consistent decision-making process that evaluates risks based upon the pre-established RM policy. It also depends on open information sharing by employees who have firsthand experience with the day-to-day operations issues that require immediate attention and response. Top-level managers should ensure the provision of adequate resources and the assignment of trained personnel to perform risk management activities. The breadth and depth of knowledge and experience held by those involved in the RM process provide the foundation for long-term success. Continued success of this approach hinges on a corporate culture that fosters technical competence in risk management when dealing with emerging technologies.

4) Process

The HACCP RM process is an integration of the seven HACCP Principles within the Standard framework as shown in Figure 1. At the broadest level, the HACCP RM process consists of a four-part, continuous management process: 1) to analyze risk, encompassing HACCP Principles One and Two; 2) to evaluate risk to include HACCP Principle Three; 3) to control risk to involve HACCP Principles Four through Seven; and 4) to capture and address feedback from post-development information. The next section (The HACCP RM Process) describes the details of each major activity of the process.

5) Paperwork

Paperwork in this context means recording and documenting the HACCP RM activities, as well as establishing the HACCP RM process. "Paperwork" also refers to electronically-stored records and documents. The purpose of the paperwork system is to record all the necessary information to facilitate the transfer of knowledge to incoming product managers, and to provide objective evidence for regulatory compliance and legal purposes. The paperwork should include policy, procedures, plans and records of all risk management activities during the entire product life cycle.

The HACCP RM Process

At the broadest level, the HACCP RM process consists of a four-part, continuous management process [1]:

1) Analyze Risk

The first two HACCP Principles [4], *conduct hazard analysis* and *determine critical control points*, are integrated into the ISO Standard framework. This involves the following steps:

a. Become familiar with the product.

It is important to thoroughly understand the requirements of developing a product before starting any risk management activities. A basic understanding of the product's requirements in terms of marketing, performance, function, regulations, legal concerns, etc., will provide a firm foundation for persons engaged in RM planning and implementation.

b. Understand intended purpose and use.

In addition to the aforementioned requirements, fully understanding the intended purpose and use of a product will provide an important boundary for subsequent risk management activities. Understanding the medical purpose of the product or process, the anatomy of the organs or systems affected, patient/user profiles, and the application environment for the prod-

uct will form the basis needed to initiate hazard identification and carry out further risk management activities.

c. Identify hazards

In the framework of the Standard, hazard is defined as *the potential source of harm*; and harm is *physical injury or damage to the health of people, or damage to property or the environment*. Thus, one should focus on identifying the potential sources of harm in the product, i.e., the hazard. It is also beneficial to understand that a failure may not always cause harm, either directly or indirectly, and would thus not be classified as hazards. *Hazards* are those product-related incidents or defects that directly cause harm. A full understanding of this concept will help in narrowing down subsequent risk management activities to include only those which could negatively impact health, property or the environment.

d. Estimate risk

Once a hazard is identified, it is necessary to estimate the severity of harm and probability of occurrence of harm that could result. The consequence or severity of harm of a hazard can usually be assessed directly and immediately. However, the probability of occurrence of that harm may be more difficult to assess, since the harm is related to the hazard and the hazard is related to the product. The overall risk level of a hazard would then be estimated based on the probability of occurrence and severity of the harm posed by the hazard.

e. Identify critical control points

Once the risk level of a hazard is estimated, its severity usually will not change. The probability of occurrence of the harm posed by the hazard is more likely to change and needs to be monitored. When hazards pose a risk level that is marginally acceptable or at the edge of going beyond the acceptable level, critical control measures need to be applied. Analysis of such situations will result in the identification of critical control points.

2) Evaluate Risk

The third HACCP Principle [4], *establish critical limits*, is carried out in conjunction with the evaluation of risk. After risk analysis, there is a need to make a decision on the acceptability of that risk. Consequently, there are many actions that need to be taken depending upon the level of risk for each of the identified issues. Generally, there are three kinds of actions. First, the risk could be accepted with no further action required. Secondly, the risk could be deemed so high that control measures must be taken to reduce it to an acceptable level. Lastly, the risk is at a marginally acceptable or rejectable level. It requires further investigation, which might include conducting a risk/benefit analysis, or implementing further risk control measure(s) to reduce the risk to an acceptable level before making a final 'accept or reject' decision. At this juncture it is appropriate to establish critical limits on the identified critical control points to maintain the risk within an acceptable level.

3) Control Risk

After the initial risk analysis and evaluation, risk control measures may be deemed necessary to maintain, reduce or eliminate the risk. In the framework of the Standard, risk has two components: *the probability of occurrence of harm* and the *severity of that harm*. Therefore, a risk control measure(s) could impact either the probability of occurrence of the harm or the severity of that harm. Rarely, a single risk control measure would affect both components of a risk. Generally, it is much easier to work on minimizing the occurrence aspect of the harm. It would take more resources and effort to reduce or eliminate the severity of a harm. In fact, risk control is aimed at controlling the identified hazards that are causing harm.

The Standard is very specific about how risk should be controlled. It stipulates an Option Analysis [1] that requires prioritization when planning risk control measures. Risk control measure(s) should be considered in the following priority order:

a. inherent safety by design (the most preferred risk control measure);

b. protective measures in the product or in the manufacturing process;

c. information for safety (the last resort for risk control measure).

Since HACCP Principles [4] One through Three have already taken into account in the previous risk analysis and evaluation activities, HACCP Plans, in the process of implementing HACCP Principles [4] Four through Seven, should be developed with Option Analysis in mind.

It is crucial to ensure that implementation of these risk control measures has taken place as well as to demonstrate their effectiveness after implementation. Objective evidence of implementation and effectiveness of these measures should be documented.

In practice, risk analysis, risk evaluation and risk control are iterative processes. These activities typically happen at least three times in a product development process. Initially, risk is analyzed and evaluated for acceptability, and then risk-control measures are considered, as necessary, for each hazard. Later, residual risk is analyzed and evaluated for acceptability as related to each individual hazard after control

measures are applied. This process continues until the residual risk of each individual hazard is judged acceptable. Finally, a review of the overall residual risk, i.e., the accumulation of all the residual risks posed by each individual hazard after effective control measure(s) is applied, should take place. It is at this point that a company decides whether a product is safe for use.

If an individual residual risk or the overall residual risk [1] is judged unacceptable using the policy or criteria pre-established by the company, and further risk control is impractical, the company may gather and review data and literature on the medical benefits of the intended purpose and use of the product to determine if those benefits outweigh the residual risk. If the evidence does not support the conclusion that the medical benefits outweigh the residual risk, then the risk remains unacceptable. If the medical benefits are found to outweigh the residual risk, then the company should determine whether other generated hazards have been considered and ascertain the completeness of the risk management evaluation. This iterative process should continue until all individual residual risk and the overall residual risk are judged acceptable before the commercialization of a product.

4) Feedback From Post-Development Information

In this part of the risk management process, the focus is on information received after all risk control measures are deployed. When considering the entire product life cycle, post-development information may be more comprehensive than post-production information, as stated in the Standard. The company should establish and maintain a systematic process for reviewing information gained about the product after development. This information should include information from design and process validation, product transfer, design to production, vendor to company, company to vendor, outsourced activities, production activities, field use, etc. The information should be evaluated for possible relevance to safety [1] especially the following concerns:

a. Are previously unrecognized hazards present?

b. Are the estimated risk(s) arising from a hazard no longer acceptable?

c. Are any portions of the original assessment invalidated by this new information?

If the answer to any of the questions above conditions is 'yes,' the results of the evaluation should be fed back into the risk management process. A review of the appropriate steps of the risk management process for the product should be considered. If there is a potential that the residual risk(s) or its acceptability has changed, the impact on previously implemented risk control measures should be evaluated.

The four risk-management activities listed above are integral elements of continuous process improvement within a management system. Certain activities may be initiated out of the aforementioned order and are still useful if applied appropriately, especially early in the product development process.

Conclusion

HACCP RM is about focusing attention on the few vital hazards that will make a verifiable difference. A comprehensive HACCP RM framework helps a company gain confidence that it understands the risks that really matter, and avoids unexpected crises or surprises. The framework also helps the company know how to avoid, eliminate or contain the causes or drivers of those significant risks that may cripple the business if they were neglected. It also provides a basis for measuring, comparing, controlling, monitoring and preventing those risks that have the potential to have a significant negative impact on the company.

In conclusion, HACCP RM is a disciplined, structured and scientific approach that provides a proactive business strategy to enable a company to manage and prevent potential crisis and create a sustainable strategic advantage while maximizing shareholder value. Through the HACCP RM process, a company is better able to protect and secure its value, guard its growth potential, and hedge against market, capital, operational and financial volatility.

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About the Author

Tony Chan is a Professor at Virginia Tech and Director of Risk Management Programs at the school's Center for Applied Sciences in Health Products & Processes. He holds multiple degrees, including a Master of Science in Quality Assurance and Management (MSQA), a Master of Science in Regulatory Science (MS Reg. Sc.) and a Master of Business Administration (MBA). In addition, is certified in seven Quality Professional categories from the American Society for Quality.

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April 4-8, 2005
2005 PDA Annual Meeting
Chicago, Illinois

May 16-18, 2005
PDA Viral and TSE Safety Conference
Bethesda, Maryland

May 23-25, 2005
PDA Extractables/Leachables Forum
Bethesda, Maryland

September 11-14, 2005
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Washington, DC

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March 7-9, 2005
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March 14-18, 2005
Aseptic Processing Training Program (Week 2)

March 22-23, 2005
Validating a Steam Sterilizer

April 18-22, 2005
Aseptic Processing Training Program (Week 1)
Week 2: May 16-20

May 25-27,2005
Cleaning Validation

June 1-3 , 2005
Practical Aspects of Aseptic Processing
Basel, Switzerland

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May 23-24, 2005
Sterile Pharmaceutical Dosage Forms: Basic Principles

September 26-27, 2005
Computer Products Supplier Auditing Process Model: Auditor Qualification

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March 16, 2005
PDA Metro Chapter
Risk Analysis
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PDA Captial Area Chapter
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April 11, 2005
PDA Canada Chapter
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April 12, 2005
PDA Delaware Valley Chapter
Sterile Components/Containers: New Technologies in the Filling of Pharmaceutical Final Dosage Units
Malvern, Pennsylvania

April 20, 2005
PDA New England Chapter
Genzyme Tour and Networking Dinner
Boston, MA

April 27, 2005
PDA Metro Chapter
Real Quality
Clark, New Jersey

June 1, 2005
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May 9-10, 2005
Similar Biological Medicinal Products
Lyon, France

May 12, 2005
PDA EuroForum
PDA and the and the PDA UK/Ireland Chapter present
Pharmaceutical Packaging
London, England

June 1-3, 2005
PDA Training & Research Institute Laboratory Course
Practical Aspects of Aseptic Processing
Basel, Switzerland

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PDA EuroForum
PDA and the PDA Prague Chapter present
PAT - Industry, Regulator and Academic
Budapest, Hungary

June 2, 2005
PDA and the PDA Prague Chapter present
PDA EuroForum
Technology Transfer and Contract Manufacturing
Prague, Czech Republic

June 6, 2005
PDA EuroForum,
PDA and the PDA Spain Chapter present
IVIVC (In Vivo in Vitro Correlation) and
BPC (Biopharmaceutical Classification System)
Barcelona, Spain

June 13, 2005
PDA EuroForum,
PDA and the and the PDA UK/Ireland Chapter present
Risk Analysis
London, England

June 20, 2005
PDA and the PDA Italy Chapter present
PDA EuroForum
Rapid Micro TM 33
Milan, Italy

INDIA

March 18-19
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PDA and the PDA India Chapter present
IVIVC / BPC
Mumbai, India

May 20-21
PDA IndiaForum
PDA and the PDA India Chapter present
Risk-based Validation
Goa, India

July 19-20, 2005
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PDA and the PDA India Chapter present
Q7A Update
TBD

August 23-24, 2005
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FDA's Progress Toward a Risk-based Quality System Approach Using Risk-Based Management Practices

Vicki Dedrick, PDA

Efficient risk management enables FDA to provide the most public health bang for its regulatory buck. This is particularly true in the area of product manufacturing. It is impossible for FDA to inspect every prescription drug pill, every diagnostic testing kit, every animal vaccine and every food parcel that is manufactured or processed. However, by promoting the best possible manufacturing practices through tested, quality-improvement modalities, FDA hopes to assure high quality products. For this reason, FDA has outlined the latest, scientific practices in manufacturing across the public health spectrum—drawing significantly from successes in other manufacturing industry areas.

Highlights

FDA took the first steps to modernize regulations for the manufacture of medical products and to encourage the use of the latest innovations. These activities include the introduction of quality systems and Pharmaceutical Analytical Technologies (PAT) to the bio/pharmaceutical manufacturing environment, the new aseptic processing guidance and the promise of a new process validation guidance, possibly out in draft form in 2005.

FDA proposed updating manufacturing regulations; this could possibly mean a new GMP which after more than 25 years, may be on the horizon.

FDA designed a risk-based methodology to conduct inspections. This methodology encompasses both an in-house assessment by staff to help them internally target and prioritize, and a large-scale contracted assessment on more than ten years of historic inspection data to help identify inspectional issues that contribute to product failures.

FDA Priorities

FDA's priorities for 2005 include continued work to advance modernization of their cGMP requirements across several regulated product categories and to implement quality systems and risk-based prioritization in their field-work planning. Specific areas of emphasis include:

Pharmaceutical Quality: In the fall of 2004, FDA began to implement a risk model-based approach to target inspections of those facilities manufacturing drugs. FDA intends to refine this model over time to incorporate information about product and process understanding and quality management. At the same time, FDA will begin to apply risk-based principles to the product quality review process.

FDA expects that these changes will not only allow, but also facilitate, continuous improvement in pharmaceutical manufacturing. This builds on work over the past two years that focused on assessing the current quality assurance systems, including some in practice for several decades. FDA has found that in many cases, it is currently possible for manufacturers to develop robust processes that reliably produce high-quality products that will accommodate process changes.

Tissue Safety: FDA will finalize its regulatory framework for tissue safety, continue outreach to the tissue industry, and develop an interdisciplinary tissue safety team.

Quality and Safety of Imports. FDA is in the process of developing a strategic plan for the inspection of imports and will issue this plan within the next 12 months. FDA expects the number of FDA-regulated imports to continue growing rapidly, further outpacing our ability to examine a large fraction of line entries.

Mad Cow Disease: After the discovery of bovine spongiform encephalopathy, also known as BSE or mad cow disease, in a cow in the United States, FDA published an interim final rule banning certain cattle-derived materials from human food and cosmetics. These banned materials are considered to be high risk for transmitting the agent that causes this fatal disease from cows to humans. FDA also proposed recordkeeping requirements that complement the interim final rule. FDA concluded that it would be most protective to remove the "specified risk materials" most likely to contain the infectious agent from all animal feed and requested comment on this proposal. FDA is currently working on a proposal to assure the removal of these specified risk materials from feed. In addition, FDA is evaluating test methods for detecting prohibited protein in animal feed as an additional safeguard against the spread of this disease.

Background

FDA's mission has become more complicated. Public health protection now includes addressing unprecedented challenges and threats—ones that are more sophisticated and complex than those of the last century. The number of medical products—drugs and devices—that FDA regulates now exceeds 150,000, far more than ever before, including more complex products. Almost 3,000 investigational new drugs are under development, with manufacturers seeking the evidence needed to support approval. Access to

this growing range of products offers opportunities for improving health and improving lives, but it creates new kinds of vulnerabilities and risks to public health.

FDA has identified efficient risk management as the primary modality to making the most effective use of resources to address these challenges. This approach incorporates:

- Rigorous analysis to consistently identify the most important risks.
- Use of a quality systems approach to designing and conducting core business processes.

A high-priority application of FDA's principle of efficient risk management is focused on their current standards and guidance to industry on the way medical products are manufactured, known as "current Good Manufacturing Practices." The cGMP regulations for drugs have not been substantially revised in over 25 years. Meanwhile, best practices in manufacturing technologies and methods have undergone significant progress over that time, particularly in other high-tech industries. FDA wants to make sure their regulations are encouraging such progress in the pharmaceutical industry. So, they are working on a broad-based program to develop new guidance based on the latest science of risk management and quality assurance.

Moreover, FDA's capacity to examine imports physically has not kept pace with this growth. To further enhance import security with limited resources, FDA is implementing new regulations to address threats and improve their ability to target their field resources to imports that present the most significant risks.

FDA's approach to risk-based management includes using the best available data and analytic methods to assess risk and to develop the most effective approaches to identify the most significant hazards, plan inspection work and conduct other compliance and enforcement activities.

FDA Progress to Date

During 2004, FDA pursued several key initiatives to achieve the goal of efficient risk-based management. Some efforts addressed the fundamental approach they take to allocating their resources and performing the work. FDA has also undertaken very significant efforts targeted at particular types of product manufacturing and quality assurance.

Over the past year, FDA's Management Council has reviewed and adopted the FDA Quality Systems Framework for application across the full range of their programs and processes. Through application of this framework, they will use quality systems to control, assure and improve the effectiveness of their processes to deliver a quality product or service. The quality system framework, which is now incorporated in the FDA Staff Manual Guide, defines the essential quality elements for management to address in any system that controls an internal regulatory activity and its relevant management, facility, purchasing, and information technology support, referencing key ANSI/ISO and other external quality management and risk management standards.

FDA regulates the manufacture of pharmaceuticals to ensure that the drug supply in the United States is of consistently high quality. In the past, as a result of the many uncertainties in drug manufacturing, FDA exercised extensive control over every aspect of the process. Over the past year, FDA has completed a rigorous assessment of current practices and the available new tools of manufacturing science that would enable a progression to controls based on quality systems and risk management. The assessment adhered to five guiding principles:

1. Risk-based orientation.
2. Science-based policies and standards.
3. Integrated quality systems orientation.
4. International cooperation.
5. Strong public health protection.

FDA has taken a number of steps to move regulatory practices in this direction, including:

Finalize a guidance document on electronic records and signatures to incorporate principles of the cGMP initiative to ensure the latest technological advances are encouraged.

Publish a **draft guidance on process analytical technologies** to facilitate adoption of modern quality management systems.

Complete a memorandum of understanding between the Office of Regulatory Affairs and the Center for Drug Evaluation and Research to establish a **Pharmaceutical Inspectorate** and develop course curricula for inspectors. The Pharmaceutical Inspectorate is a state-of-the art, first-of-its-kind inspection cadre consisting of dedicated, highly trained employees within the field force who will devote the majority of their time to conducting inspections for highly complex or high-risk drugs.

Establish a pilot program that will allow for the rapid, objective resolution of scientific and technical questions or issues **(dispute resolution)** that may arise either during an inspection or as the result of an inspection. This program has been designed to promote integrity, neutrality, consistency, transparency, fairness, and scientific soundness in the dispute resolution process.

The progress being made reflects FDA's commitment to the consistent adoption of risk-management principles. This will result in an inspection and enforcement program that the agency anticipates will be the founda-

tion for a strong, robust Agency centered on protection of the public health.

FDA's work over the past year has involved establishing a process for programs to set compliance priorities by conducting assessments that identify the internal and external hazards a regulated firm faces, address risk estimate and characterization of the hazard, and determine the consequences to the public health as a result of our action or inaction.

FDA made substantial progress in developing appropriate risk criteria and a process for applying the criteria to the inventory of regulated facilities. Risk criteria in development across centers include factors, such as:

- Previous violations,
- Volume of production,
- Product class,
- Manufacturing process characteristics,
- Probability and severity of harm,
- Manufacturing risk control measures,
- Pathogen contamination risk.
- Vulnerability of the product to deliberate tampering or contamination, and
- Health consequences for humans or animals.

Facilities FDA has identified as high priority based on such criteria will be included in their inspection work plan for fiscal year 2005.

During fiscal year 2004, FDA implemented the expansion of Good Clinical Practices in clinical studies funded by the Orphan Products Development grants program. Good Clinical Practices will be used when they evaluate grant funding applications for orphan products and conduct site visits of grantees.

How is PDA Contributing?

During 2004, PDA's Regulatory Affairs and Quality Committee (RAQC) contributed seven sets of scientifically based comments to FDA on an array of topics (Guidances and White Papers) to provide input into the evolving regulatory process. PDA also submitted proactive comments to FDA on Manufacturing Chromatography Systems Post-approval Changes: Chemistry, Manufacturing and Controls. PDA is grateful to the large number of expert volunteers who produced detailed science-based comments on:

1. *Draft Guidance for Industry on Formal Dispute Resolution;*

2. *Scientific and Technical Issues Related to Pharmaceutical Current Good Manufacturing Practice*;

3. Draft Guidance for Industry on *Powder Blends and Finished Dosage Units; Stratified In-Process Dosage Unit Sampling and Assessment;*

4. FDA White Paper: *Defining the Customer in a Regulatory Agency,*

5. FDA White Paper: *Risk-Based Method for Prioritizing CGMP Inspections of Pharmaceutical Manufacturing Sites – A Pilot Risk Ranking Model;*

6. Draft Guidance for Industry on *Good Manufacturing Practices for Combination Products;*

7. Draft Guidance for Industry on *Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations*;

PDA remains actively involved with the Product Quality Research Institute (PQRI) as a founding member and an active participant through volunteers in a number of technical committees working on FDA-agreed projects.

During 2004, PDA administered over 88 scientific and regulatory training and laboratory courses, conducted 21 audio conferences and held 26 meetings, conferences, forum, and workshops to educate industry, health authorities and academia on a broad range of scientific and regulatory topics to advance the bio/pharmaceutical industry. One of these, the PDA/FDA Joint Regulatory Conference, represents a long-term and ongoing collaboration between PDA and FDA. After 16 years, it has become one of the pharmaceutical community's premier events held each September in Washington, D.C. The 2004 PDA/FDA Joint Regulatory Conference provided an unprecedented opportunity for FDA to roll out their phase 2 plans for the 21st Century Risk-Based GMPs initiative. FDA provided 23 senior staff persons from four centers to present the next steps to community. More than 800 industry, authority and academic colleagues attended this landmark meeting.

Throughout 2005, PDA will continue its collaboration with FDA in a number of areas, including aseptic processing, viral safety, PAT, quality and regulatory initiatives and more. PDA member certainly will help shape the future of science-based regulation.

[Author's Note: This article was based on the FDA report Food and Drug Administration Progress and Priorities 2004 Protecting and Advancing America's Health.**]**

Victoria Ann Dedrick
Vice President, Quality and Regulatory Affairs

Vice President's Message

Behind the Scenes at PDA: Event Planning

This month I would like to share with you an important aspect of what goes on behind the scenes at PDA: how our Meetings and Programs department works with member volunteer program committees and the PDA Quality & Regulatory and Science & Technology departments to put together all of the exceptional *Career-long learning*™ opportunities that come your way each year.

Planning for any major conference starts more than a year in advance. Meeting and conference topics do not get picked "out of the sky." Rather, PDA assembles Program Committees of expert volunteers from industry, government and academia, as well as PDA staff. As a team we identify those topics that are "hot" and "necessary" for our members to learn more about to do their jobs. These committees rely heavily on the program evaluation forms received from past meetings (so don't forget to fill out yours next time!) as a launching point. Often, the program committees meet and consult with regulatory bodies to gain an understanding of their annual work plans and what is important to communicate to our community. PDA meetings are good places for health authorities to roll out new initiatives and to seek advice on how to improve compliance initiatives.

I can't say enough about the hard work and dedication that is exemplified by the volunteers who populate our Program Committees. These individuals work tirelessly with staff to evaluate all the input, prioritize it and come up with great science and technology oriented events. They read and review abstracts, suggest tracks and content, they contact speakers, discuss direction for presentations and ensure, along with staff, that the appropriate balance between science, regulatory expertise and academic input is met.

For all major meetings PDA also sends out a *Call for Papers*. These *Call for Papers* are very important as they allow PDA members to bring forward original research and initiatives that are ongoing in their companies. These first-hand presentations of process studies and emerging technologies provide a new look at some of the best practices emerging from industry.

PDA worked hard in 2004 and is working even harder this year to ensure that you, the members, get the most out of your experience at each PDA event. We know that the conferences you choose to attend are largely based on the value of what you can take away and the value of the networking experience you will encounter. To this end, PDA has restructured many of its larger events to provide dedicated tracks to ensure that our meetings offer the depth and breadth you need to meet your career requirements.

I sincerely believe that the PDA 2005 Annual Meeting, to be held in Chicago, Ill., in April, will be one of the best PDA events in years. Not only is the program content excellent—bringing an integration of the latest science, technology and regulation to you—but it will feature the premier of the new PDA Annual Graduate Research Symposium and will host twelve Interest Group meetings for you to network with your industry colleagues on common topics of concern. I look forward to seeing all of you at the Gala PDA Dinner and Educational Event to be held at the Museum of Science and Industry. The exhibition is exciting; I am especially looking forward to *Genetics: Decoding Life*; *Imaging: The Tools of Science* and the new permanent exhibit *Enterprise* where you can explore business innovation through a "virtual company." Maybe some of you would like to join me in becoming a CEO for a few hours?

As you attend PDA events during 2005, please take the opportunity to tell PDA staff and the program committee members (all identified by their badges) what you like—and also what you don't like—so that we can continue to improve your experience with PDA.

I want to wrap up this month by thanking the Program Committees for all of their dedication and hard work. They are wonderful volunteers without whom PDA could not exist. Lastly, everyone in our community should be grateful for the "behind the scenes" effort put forth by Wanda Neal Ballard and her team.

Regulatory Briefs

Europe

EDQM Grants U.S. FDA Observer Status to the European Pharmacopoeia Commission (EPC)

The European Directorate for the Quality of Medicines (EDQM) announced in January that the U.S. FDA has been granted "Observer Status" to the European Pharmacopoeia Commission (EPC). This status will enable FDA to participate in the scientific work of the Commission for the elaboration of quality standards in the field of blood products and to benefit from European experience in this area. This international relationship fits into the context of more cooperation at an international level between Europe and the United States within the global international harmonization process. This request from the FDA firmly establishes the scientific exchanges that have taken place over the last number of years, enhances the partnership for improvement and advances the standardisation of biological methods.

This collaboration includes the exchange of information on pharmaceuticals and the participation of American experts in the meetings of the European Pharmacopoeia's Blood products group of experts. In this specific field, Canadian and Australian experts also participate in these meetings as Observers. The European Pharmacopoeia Commission now has 15 observers including the World Health Organisation (WHO). Contact: Caroline Larsen Le Tarnec, Public Relations Unit, EDQM/European Pharmacopoeia, Tel.: + 33 3 88 41 28 15, E-mail: publicrelations@pheur.org.

United States

FDA Publishes for Comment ICH Q8: Pharmaceutical Development

This guideline describes the suggested contents for the 3.2.P.2 Pharmaceutical Development section of a regulatory submission in the ICH M4 Common Technical Document (CTD) format.

The Pharmaceutical Development section provides an opportunity to present the knowledge gained through the application of scientific approaches and risk management to the development of a product and its manufacturing process. It is first produced for the original marketing application and can be updated to support new knowledge gained over the lifecycle of a product. The guideline also indicates areas where the provision of greater understanding of pharmaceutical and manufacturing sciences can create a basis for flexible regulatory approaches. The Pharmaceutical Development section is intended to provide a more comprehensive understanding of the product and manufacturing process for reviewers and inspectors.

The comment period closes on April 11, 2005. Links to the guidance and the *Federal Register* announcement are available at: www.pda.org/regulatory/RegNewsArchive-2005.html#05-5.

CDER Holding Public Hearing on Color Labeling

FDA's Center for Drug Evaluation and Research (CDER) is announcing a public hearing on the current practice of applying color to pharmaceutical product packaging and labeling to help identify, classify, and differentiate those drug products. The purpose of the hearing is to obtain public input on the benefits and potential drawbacks of applying color to drug packaging and labeling to help identify, classify, or differentiate those products.

The public hearing will be held on March 7, 2005. Written or electronic comments will be accepted after the hearing until April 7, 2005. The administrative record of the hearing will remain open until April 7, 2005. A link to more information is available at: www.pda.org/regulatory/RegNewsArchive-2005.html#05-5.

FDA Publishes Draft Revision to ANDA Impurity Guidance

This draft guidance provides revised recommendations on what chemistry, manufacturing and controls (CMC) information to include regarding the reporting, identification, and qualification of impurities in drug substances produced by chemical synthesis when submitting: Original abbreviated new drug applications (ANDAs), drug master files (DMFs) including type II DMFs, and ANDA supplements for changes in drug substance synthesis or process. The guidance also provides recommendations for establishing acceptance criteria for impurities in drug substances. The guidance, when finalized, will replace a 1999 guidance of the same name: ANDAs: Impurities in Drug Substances.

The revision was initiated to:

1. To update information on listing of impurities, setting acceptance criteria, and qualifying impurities (thresholds and procedures) in ANDAs in conformance with the revision of the guidance for industry (February 2003) on Q3A Impurities in New Drug Substances (Q3A)(R).

2. To remove those sections of the 1999 guidance containing recommendations that are no longer needed because they are addressed in the more recent Q3A(R).

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The public comment period ends May 2, 2005. Links to the guidance and the *Federal Register* announcement are available at: www.pda.org/regulatory/RegNewsArchive-2005.html#05-5.

CBER Extends Comment Period for Critical Path Workshop

The Center for Biologics Evaluation and Research (CBER) is reopening until January 27, 2006 the comment period for its October 2004 workshop entitled, "From Concept to Consumer: Center for Biologics Evaluation and Research Working With Stakeholders on Scientific Opportunities for Facilitating Development of Vaccines, Blood and Blood Products, and Cellular, Tissue, and Gene Therapies." The workshop is part of CBER's effort to fulfill the Critical Path initiative that FDA launched last year. CBER reopened the comment period to allow interested persons additional time to submit comments and to receive any new information. For more information and links, go to: www.pda.org/regulatory/RegNewsArchive-2005.html#05-5.

Update From PIC/S Winter Meeting

Third Czech Health Institute Joins PIC/S

The Committee invited the Czech Institute for State Control of Veterinary Biologicals and Medicaments (ISCVBM) to join PIC/S as a new Participating Authority, starting July 1. The Czech Institute is the first veterinary Agency to join PIC/S. It is the third Czech health institution to enter into PIC/S, joining the Czech Institute for State Control of Veterinary Biologicals and Medicaments and the Czech State Institute for Drug Control (SÚKL), responsible for medicinal products for human use.

Argentina, United States To Join PIC/S

The Committee appointed a Rapporteur (Australia) and a Co-Rapporteur (Italy) to evaluate the membership application received by Argentina's Instituto Nacional de Medicamentos (INAME). Argentina is the first Latin American country to apply for PIC/S membership.

It noted the decision taken by the U.S. FDA to seek PIC/S membership as part of its 21st Century Initiative on the Regulation of Pharmaceutical Manufacturing.

Poland Under Review

The Committee discussed the report made by the PIC/S Delegation, which inspected Poland's Main Pharmaceutical Inspectorate (MPI) in September 2004. It appointed a new Rapporteur (Netherlands), who was invited to evaluate the encouraging replies given by the MPI to the Delegation's main recommendations.

UNICEF Among PIC/S Applicants

The committee decided to invite the United Nations Children's Fund (UNICEF), who has applied to become an Observer to PIC/S, for a hearing at the next Committee meeting and appointed a new Rapporteur (Switzerland). It also briefly reviewed other membership applications: Estonia's State Agency of Medicines, Israel's Ministry of Health, Lithuania's Department of Pharmacy, South Africa's Medicines Control Council and the Ukraine's Ministry of Health.

The Committee took note that the reassessment of Italy's Agenzia Italiana del Farmaco (AIFA) had been successfully completed. It was also informed on the forthcoming follow-up visit to Romania's National Medicines Agency (NMA) following its reassessment in November 2002 and on the on-going reassessment of the Norwegian Medicines Agency (NOMA).

PIC/S Picks New Leaders

The Committee elected Jacques Morénas of France's Health Products Safety Agency (AFSSAPS) as First Deputy Chairman for the year 2005 in replacement of France Dansereau (Canada) who had retired. Johann Kurz (Austria/Federal Ministry for Health and Women) was elected Second Deputy Chairman for the year 2005. Eija Pelkonen (Finland/National Agency for Medicines) and Mr. Michel Keller (Switzerland/Swissmedic) were elected as Members of the Executive Bureau for 2005-2006 in replacement of Dr. Vassiliki Revithi (Greece) and Dr. Martin Valcháø (Czech Republic).

[Editor's Note: These briefs were taken from health authority releases.**]**

PDA Israel Chapter Holds Annual Meeting in Tel Aviv

Karen Ginsbury, PCI-Pharmaceutical Consulting Israel Ltd.

The PDA Israel Chapter PDA held its annual meeting on 29 December 2004, with its usual large number of attendees. At the end of 2004, the Chapter had 650 members, no small achievement for a country of Israel's size. We were honored by the presence of Gautam Maitra, PDA European Director, and **Mrvova Zdenka** *(Zentiva)*, President of the PDA Prague Chapter.

The meeting was opened by **Benny Klener** *(Teva Pharmaceuticals)*, Chapter President, who presented a summary of Chapter activities during the past two years in anticipation of the elections held later that evening. In accordance with its usual format, the evening was divided between updates on past activities, future chapter plans and professional content.

The professional content was on the cutting edge, providing leading speakers from the local industry who addressed topics relating to FDA's risked-based 21st century GMP initiative. The first presentation covered the application of risk management to medical devices and implementation in pharmaceutical manufacturing.

This was followed by an important financial report from Chapter Treasurer **Karin Baer** *(Omrix-Biopharmaceuticals)*. **Sigalit Portnoy** *(Taro)*, Chapter Vice President, presented the Chapter's plans for 2005 which include a wide array of seminars and conferences on "hot" topics. Gautam Maitra raised the possibility of planning an international conference to be held by the Red Sea in Eilat towards the end of 2005 or early 2006, an idea that was warmly welcomed by the Chapter Executive Committee.

During the coffee break, participants had a chance to visit the exhibitors and to vote for the new Executive Committee. The elected committee members are presented at the end of this article.

After the break two more professional presentations were heard. The first was a detailed insight into the performance of Failure Mode & Effect Analysis (FMEA) within a pharmaceutical framework. It provided Chapter members with the opportunity to understand the utility of this tool in our industry to reduce the failure rate for products and to increase quality standards. The second presentation provided an overview of FDA's draft guidance: *A Risk Based Approach to Pharmaceutical CGMPs*. This presentation, entitled: "Risk Based Approaches in the Pharmaceutical Industry – FDA Policy & Requirements," took a look at the use of scientific tools such as risk assessment and FMEA in pharmaceutical quality assurance systems. This lecture rounded off the evening by integrating the two other professional presentations to show participants how they can meet FDA's expectations and how the company is likely to profit from this new guidance with greater knowledge and fewer failures.

As with every Chapter event held to date, Chapter members left feeling that they had enriched their knowledge base while networking with colleagues, experiencing new products presented by vendors and being fully updated on Chapter activities.

2005 Israel Chapter Executive Committee

President: **Sigalit Portnoy,** Taro

Vice President: **Raphy Bar,** Raphael Bar Pharmos

Treasurer: **Karin Baer,** Omrix-Biopharmaceuticals

Im. Past Presiden: **Benny Klener**, Teva

Einat Frydman, Teva

Karen Ginsbury (Chapter Liaison), PCI-Pharmaceutical Consutling Israel

Mordechai Izhar, Ludan

Dudi Meraro, Taro

Capital Area Chapter Institutes First Scholarship Program

Barry Friedman, PhD, Cambrex Bio Science Baltimore, Inc.

PDA's Capital Area Chapter recently inaugurated its first joint scholarship program with the University of Maryland Baltimore County (UMBC). This scholarship program represents the first-ever joint program offered by one of PDA's worldwide Chapters. The two scholarships, which are for the 2004-05 academic year, were designed to assist individuals who would be considering biotechnology or pharmaceuticals as a career. This joint program, wherein UMBC matched the US$ 5000 scholarship offered by the Capital Area Chapter, is the first of several that the Capital Area Chapter hopes to establish with area universities.

Applicants for these awards were initially screened by UMBC, and a final selection was made by the executive board of the Capital Area Chapter. The awardees this year include **Jaime Miller** and **Erin Voss**. Jaime is a junior majoring in biochemistry. Upon completion of this degree, Jaime is considering a MD/PhD program at a local university. Erin is a senior majoring in biochemical engineering and is contemplating graduate school following completion of her undergraduate studies. Both awardees will be the Capital Area Chapter's guests at our dinner meeting on Wednesday, March 23, at the Holiday Inn in Gaithersburg, Md. and will receive their awards at that time.

Monies for these scholarships are derived from vendors that support each of our dinner meetings. These vendors participate with tabletop exhibits during our "Meet 'n Greet" hour that precedes dinner. The Capital Area Chapter would like to recognize the following vendors as contributors to these scholarships: **Accugenix**, **BD, Doe & Ingalls**, **Lancaster Labs**, **Millipore**, **PML Microbiologicals**, **Pall**, **Veltek** and **VWR**.

To learn more about the Capital Area Chapter, visit their Web site at www.pdacapitalchapter.org or contact Barry Friedman, Chapter President, at +1 (410) 563-9200, ext. 285, or, barry.friedman@cambrex.com.

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Quality Assurance: A Practitioner's Guide
Author: U. G. Barad
(2004) Hardcover. 298 pages. ISBN: 1-930114-66-4. Member: $185, Nonmember $229 – Item 17212

Pharmaceutical Quality
Editor: Richard Prince
(2004) 758 pages. ISBN: 1-930114-61-3. Member $240, Nonmember $299 – Item 17207

Quality Control Systems for the Microbiology Laboratory: The Key to Successful Inspections
Author: Lucia Clontz
(2001) Hardcover, 175 pages. ISBN: 1-930114-28-1. Member $170 Nonmember $209 – Item 17176

Cleanroom Microbiology for the Non-Microbiologist, Second Edition
Author: David M. Carlberg
(2004) Hardcover, 216 pages. ISBN: 084931996X. Member $120 Nonmember $139.95 – Item 06056

Training CD:
Quality Assurance Standards for the Manufacture and Control of Injectable Products
30 minutes presentation with 36 slides.
Member: $300, Nonmember $495 – Item 11007

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Filtration Handbook: Liquids
Author: Maik W. Jornitz and Theodore H. Meltzer
(2004) Hardcover, 298 pages. ISBN: 1-930114-62-1. Member $185 Nonmember $229 – Item 17208

Filtration Handbook: Integrity Testing
Author: Maik W. Jornitz and Theodore H. Meltzer
(2003) Hardcover, 150 pages. ISBN: 1-930114-50-8. Member $185 Nonmember $229 – Item 17197

Sterilizing Filtration of Liquids, Technical Report No. 26
(1998) 31 pages. Member: $75, Nonmember $270 – Item 01026

***NEW!* Sterilizing Filtration of Gases, Technical Report No. 40 Volume no. 58 Issue No. S-1**
(2005) 42 pages. ISBN: 0-939459-08-6 Member: $75, Nonmember $270 – Item 01040

Technology Transfer

Technology Transfer
Editor: Mark Gibson
(2004) Hardcover. Member $200 Nonmember $249 – Item 17218

Training CD:
Technology Transfer Process for Pharmaceuticals and Bio-Pharmaceuticals
50 minutes presentation with 56 slides.
Member: $300, Nonmember $495 – Item 11011

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Chapter Contacts

The following is a list of the PDA Chapters, organized by the area of the world they are located. Included are the Chapter name, the area(s) served, the Chapter contact person and their e-mail address. Where applicable, the Chapter's Web site is listed. More information on PDA Chapters is available at www.pda.org/chapters/index.html.

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3. Laboratory Validation: A Practitioner's Guide
   Edited by Jeanne Moldenhauer - Item No. 17201, PDA member: US$ 250, PDA nonmember: US$ 309
4. Microbiology in Pharmaceutical Manufacturing
   Edited by Richard Prince - Item No. 17185, PDA member: US$ 240, PDA nonmember: US$ 299
5. Good Practice and Compliance for Electronic Records and Signatures - Part 3: Models for Systems Implementation and Evolution
   Item No. 13003, PDA member: US$ 95, PDA nonmember: US$ 190
6. GMP in Practice: Regulatory Expectations for the Pharmaceutical Industry, Third Edition
   By James Vesper - Item No. 17199, PDA member: US$ 105, PDA nonmember: US$ 129
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8. Pharmaceutical Quality
   Edited by Richard Prince - Item No. 17207, PDA member: US$ 240, PDA nonmember: US$ 299
9. Introduction to Microbiology & GMP Video CD module
   Item No. 15253, PDA member: US$ 390, PDA nonmember: US$ 485. Video module - Item No. 15254, PDA member: US$ 390, PDA nonmember: US$ 485
10. Steam Sterilization: A Practitioner's Guide
    Edited by Jeanne Moldenhauer - Item No. 17183 PDA member: US$ 215, PDA nonmember: US$ 269

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2005 PDA Annual Meeting

Pharmaceutical Manufacturing Science in the 21st Century: *Integration of Science, Technology and Regulation*

This year, PDA's Annual Meeting has been organized into three specialized learning tracks that, together, address *Pharmaceutical Manufacturing Science in the 21st Century: Integration of Science, Technology and Regulation.* The tracks cover quality and regulatory issues, manufacturing science – research and development, and manufacturing science – engineering.

Special focused was placed on ensuring that each track offered distinctive presentations, avoiding overlap and helping participants maximize the quality of their experience. Combined with PDA's new low price of US$ 895, the 2005 PDA Annual Meeting is truly a remarkable value.

The discussion of science, technology and regulation kicks off with **keynote speaker Jeffrey Macher,** PhD, Georgetown University, who will present publicly for the first time the preliminary results of his two-tiered Pharmaceutical Manufacturing Research Project. Macher launched the project in 2001 with his colleague, Jackson Nickerson, PhD, Washington University in St. Luis. Macher's keynote address provides an initial look at their results, which are expected to help the pharmaceutical industry in the same way they improved the semiconductor business.

The first tier of the study examines the model used by FDA to inspect pharmaceutical manufacturers. FDA has been collaborating with the researchers as part of its strategic initiative to modernize the regulation of pharmaceutical manufacturing and product quality. The goals of the FDA inspection portion of the study are to: develop a risk based assessment of GMP outcomes (try to understand why and when we see various outcomes); identify those attributes that are correlated with those inspection outcomes; and implement solutions at FDA.

The other tier of the Macher-Nickerson study explores unrealized efficiencies in pharmaceutical manufacturing. The researchers report strong participation from the industry. The manufacturing study aims to identify the managerial, organizational and technical practices that underlie good and poor manufacturing and regulatory performance, and then provide a confidential score card to specific manufacturing facilities on how they perform against other, anonymous manufacturers. Through this exercise, a standard set of benchmarks for measuring manufacturing and regulatory performance can be created.

Following Macher's keynote address, the opening plenary session continues with three timely presentations on the industry and regulatory "Move to Risk-Based Quality Systems."

Industry consultant **Michael Van Der Werf** will discuss FDA's draft guidance, *Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations,* released in September 2004. Van Der Werf co-chaired the PDA Regulatory Affairs and Quality Committee (RAQC) Task Force that authored comments on this important FDA guidance (see the *PDA Letter,* January 2005, p. 22). This presentation will help the community identify specific changes to the roles and responsibilities of management and customers.

FDA's White Paper on the new risk-based inspection criteria will be discussed next by **Marie Breen,** Senior Compliance Manager, Schering-Plough. Breen chaired the PDA RAQC Task Force that authored comments on this document.

The session concludes with a discussion of FDA's White Paper: *Defining the Customer in a Regulatory Agency,* by **Cindy Rockel,** Regulatory Affairs, Millipore Corporation. Rockel chaired the PDA RAQC Task Force that authored PDA's comments on this document.

The closing plenary session of the 2005 PDA Annual Meeting features FDA's **Ajaz Hussain,** PhD, CDER Office of Pharmaceutical Science, who will provide an up-to-date report on the status of FDA's Process Analytical Technology initiative and the latest developments in industry. Already, a number of firms have moved forward with the on-/at-/near-line sensor technologies and have experienced significant gains in efficiency and cost reductions.

In between the opening and closing plenary sessions, the 2005 PDA Annual Meeting offers three specialized learning tracks on quality and regulatory, manufacturing science – research and development, and manufacturing science – engineering.

PDA is proud to introduce the **PDA Annual Graduate Research Symposium.** This session features three top fellows speaking on their original research in the area of pharmaceutical science. Also, PDA will introduce new **Technical Report #40** (see page 8 for more information on TR #40) at the this year's Annual Meeting.

Go to www.pda.org/annual2005 for more information on speakers, exhibits, networking and PDA TRI courses at this year's Annual Meeting in Chicago.

2005 PDA Extractables/Leachables Forum

Raymond Colton, Chemistry Subcommittee Chair, (Validation Resources, LLC)
Michael Gross, Material Subcommittee Chair, (QLT Inc.)

Extractables are the broad set of compounds that can be extracted from a product-contact material. Leachables are the subset of extractables that actually can migrate into a pharmaceutical formulation. Testing conditions for extractables are extreme with regard to temperature and time since the objective is to find the extractables. The challenges of effective extractables tests include choosing solvents and conditions that will be best at extracting. When testing for leachables, the actual pharmaceutical formulation is used at actual "worst-case" conditions. The level of leachables can be much less then than the level of extractables, making detection even more difficult. In addition, the leached compounds can co-elute with components of the pharmaceutical formulation and therefore be difficult to detect.

It would be nice if all detected leachables had been previously identified when looking for extractables. It does not always work that way, however. What happens when a new compound is detected? Was it present in the material but not extracted? Or was it an extractable that degraded or reacted with the pharmaceutical formulation?

Learn how industry addresses these complications at the upcoming 2005 PDA Extractables/Leachables Forum in Bethesda, Md., May 23-25. The forum will present a unique opportunity to learn about and share experiences and viewpoints from industry experts and regulatory authorities from the United States, Canada and Europe about the current regulatory expectations and industry practices regarding the potential for drug product/material interactions.

A full morning of the forum will be dedicated to the methods and techniques for detecting, identifying and quantifying leachables and extractables. While the primary focus of the conference is to address final container closures, the techniques discussed in this session will also be applied to the evaluation of processing materials that have product contact. The presentations and discussions give recent practices that are meant to comply with current regulatory requirements and expectations.

The "materials" session of the meeting will stress the importance of using a team approach when addressing extractables/leachables issues and having as much information as possible from suppliers of materials used in pharmaceutical manufacture and storage. The session on materials will cover three case studies emphasizing the importance of gaining information from vendors about the materials used. This will be followed by perspectives from the manufacture and vendor side on the mechanics and problems of sharing of proprietary information about packaging and manufacturing materials. The advice of a legal expert also will be provided on this subject. The session will close with a discussion of special situations, including drug contact with multicomponent systems and multilayered materials. The session will include panel discussions and a summary of lessons learned.

While the "chemistry" session will address the analytical instruments and appropriate protocols as they are applied to extractables and leachables testing. Some of the instruments used to analyze extractables and leachables are High Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), Mass Spectroscopy (MS) and Fourier Transform Infrared (FTIR). Each has its preferred applications and distinct limitations. Rarely is any one method used exclusively; often rather these methods are combined frequently. The best practices currently used for extractables and leachables analysis will be presented by one of the industry's leading experts.

Additionally, there were be plenty of opportunity for Q&A and over twenty posters, many of which give the results of pertinent case studies on testing techniques and instrumentation applications. On the final day of the Forum, breakfast roundtables will provide attendees an opportunity to discuss the issues addressed at the Forum with the presenters as well as their colleagues. For more information and to register for the 2005 PDA Extractables and Leachables Forum please visit www.pda.org.

Raymond Colton is the President of Validation Resources, LLC. He Chairs the Chemistry Subcommittee of the Program Committee for the 2005 PDA Extractables/Leachables Forum. Michael Gross, PhD, is the Vice President of Regulatory Affairs for QLT Inc. He Chairs the Material Subcommittee of the Program Committee.

Vice President's Message

Gail Sherman

"DID YOU KNOW……"

As I sat watching the Super Bowl a few weeks ago – hoping that my home town Philadelphia Eagles would have soared and I could have used that theme for this month's message – I was trying to think of some creative and fun stuff that I could tell you about TRI, that maybe you didn't already know – or became lost in the recesses of your very busy minds!

You all know the general things that you hear and see about us every day – our one of a kind Aseptic Processing Training (10 days worth – and many more than 80 hours!) – multiple laboratory courses, including our newly launched and extremely popular Pharmaceutical and Biopharmaceutical Microbiology 101 and our Lecture Course Series around the globe (well almost around the globe, but at least in the US and Europe for now). And then there are those few dedicated lecture training sessions that have been held at TRI in the last year - like Computer Supplier Auditor Qualification.

And did you know that our labs are also used by companies to fill product during the research and development phase? And did you know that we are able to go into companies and work with staffs on-site, which need training in some very specific areas. And did you know that we trained the Italian Inspectorate in 2003, and some unnamed other sources are asking what could become some very provocative questions in the future? Am I piquing your interest?

So, in this world of changing paradigms, we are also changing our paradigms. TRI is moving its Computer Supplier Auditor Qualification into a lecture course series (Princeton, NJ, in May) for the first time ever. And we are scheduling dedicated lecture training at TRI throughout the year, on various topics such as biotechnology and train the trainers courses.

And did you know that we held the first ever Open House at TRI last month, and entertained our neighbors and colleagues in the industry? And did you know that we are repeating our "Aseptic Processing Europe" course in Basel in June and December? And that we are going to hold a lecture course series in Basel, Switzerland, for the first time ever? And that we want to move this activity around the "continent" to locations that would love to entertain TRI in Europe? And that we really want to work with you to facilitate your training needs.

Just recently, PDA TRI participated in a site visit with the State of Maryland Department of Economic Development. There is great potential for TRI to train many staff in biopharmaceutical manufacturing processes. Participation in this site visit has put PDA and TRI on the map of possible educators in the State of Maryland – right along side of the phenomenal and diverse university system already in place. It also gives PDA TRI the opportunity to reach out and join cooperative education efforts with these potential partners.

I would be remiss if I didn't mention that the Training and Research Institute Advisory Board (TRIAB) has been appointed and has met, with a face-to-face scheduled for the Annual Meeting in Chicago in April. Its objectives will be closely aligned to the initiatives in the PDA Strategic Plan and include such initiatives as e-learning., curriculum development and standards setting. I will keep you informed of our progress in future issues, and I will tell you that this is a group of dedicaed professionals who are excited about all that PDA TRI can do for you!

TRI's Chicago and Princeton Course Series

Strother Dixon, PDA TRI

PDA TRI is offering ten courses at the 2005 PDA Annual Meeting in Chicago, Ill., April 7-8, and ten courses at the Pharmaceutical Course Series in Princeton, N.J., May 2-4.

With the theme of the 2005 PDA Annual Meeting on *Pharmaceutical Manufacturing Science in the 21st Century: Integration of Science, Technology and Regulation,* PDA TRI selected the following nine courses to complement the *Career-long Learning*™ experience:

- Cleanroom Management; Faculty: Anne Marie Dixon
- Preparing for FDA PreApproval Inspections, cGMP & Post Market Inspections; Faculty: Jeff Yuen
- DoE Basics for PAT Application; Faculty: Lynn Torbeck
- Q7A: Understanding the History, Intent and Application of ICH Q7A; Faculty: Max S. Lazar
- Root Cause Investigation for CAPA; Faculty: Tom Weaver
- Basic Concepts of Cleaning and Cleaning Validation; Faculty: Destin A. LeBlanc
- Change Control: A Practical Workshop; Faculty: Peter D. Smith
- Overview of Risk Assessment and Risk Management; Faculty: James Vesper
- Visual SOPs; Faculty: David Gallup, EdD and Scott Knutson
- GMP Quality Auditing for the Pharmaceutical Industry; Faculty: James Vesper

The courses offered in Princeton later will provide training on emerging manufacturing, validation, laboratory and compliance trends paramount to the pharmaceutical industry:

- Cleanroom Microbiology Workshop; Faculty: David Matsuhiro
- API Manufacture and Validation; Faculty: Daniel H. Gold, PhD
- Computer Products Supplier Auditing Process Model: Auditor Qualification; Faculty: Charles Waite
- Antimicrobial Preservative System Design and Evaluation; Faculty: J. Kirby Farrington, PhD
- Meeting the New Compliance Requirement; Faculty: Elaine Lehecka Pratt
- How to Develop Validation Protocols; Faculty: Harold Baseman, PhD
- Introduction to Writing and Auditing cGMP Documentation; Faculty: Elaine Lehecka Pratt
- Managing the Analytical Chemistry Lab; Faculty: Clifford Nilsen, PhD
- Design, Monitoring and Validation of Pharmaceutical HVAC Systems; Faculty: Daniel H. Gold, PhD
- Sterile Manufacturing with Blow/Fill/Seal Technology; Faculty: Harold Baseman, PhD

Look for these future PDA TRI course series to be offered later in the year: 2005 PDA/FDA in Washington, D.C., September 15-16, the Medical Device Series in Denver, Colo., October 24 – 26, and the *Career-long Learning*™ Series in New Orleans, Louisiana on November 29 – December 1.

Go to www.pda.org/TRI to learn more.

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