ISO 14971––A Standard Good For All Health Care Products, page 20

Over 800 Participants at the 2004 PDA/FDA Conference Learn Details of FDA’s 21st Century “Actualization” Plan

Host of New Documents Pending, Says FDA’s Horowitz

The 2004 PDA/FDA Joint Regulatory Conference (September 20-22) has just concluded and it was a resounding success! More than 800 professionals representing the pharmaceutical/biopharmaceutical industries, health authorities and academia participated in this two-and-a-half day event in Washington, D.C.

On Monday morning, FDA’s David Horowitz, JD, Director, Office of Compliance, Center for Drug Evaluation and Research (CDER), outlined the agency’s plan to release approximately 17 documents to the public. Among these will be a comprehensive report, five guidances and four white papers—all scheduled for publication in early October.

The report will summarize the 21st Century initiative assessment period, which took place over the last two years, and will describe the implementation period which is now underway.

Of the five guidances, three will be final: aseptic processing, dispute resolution and process analytical technology. Two draft guidances will be published as well, covering computer systems for clinical trials and quality systems.

The white papers will cover manufacturing science, risk-based inspection site selection and the evolving paradigm at FDA for chemistry, manufacturing and controls review.

Other documents scheduled for release in the near future will address combination products, risk assessment and global harmonization.

FDA has put forth much effort on what has become a truly remarkable initiative. As usual, the PDA/FDA Joint Regulatory Conference served as the perfect forum for agency representatives to discuss their latest work with stakeholders.

Risk Management and Opportunity: “Two Sides of the Same Coin”

PDA Speaks with Tony Chan About Risk Management—a “Top” Area of Concern for PDA Members

Risk management is quickly becoming the central focus of pharmaceutical and biopharmaceutical manufacturing and quality assurance.

It is a concept PDA members have identified as a top area of interest. For this reason, PDA is exploring many options and opportunities to bring educational tools to its members and is opening new dialogues to facilitate this process.

On August 4, 2004, PDA met with Tony Chan, Professor at Virginia Polytechnic Institute and State University (Virginia Tech) and Director of Risk Management Programs at the school’s newly formed Center for Applied Sciences in Health Products & Processes, to discuss the work he is doing to help health science companies institute risk management concepts to improve their products, procedures and businesses. Professor Chan 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, he holds a certification in seven Quality Professional categories from the American Society for Quality. Joining our discussion was George J. Flick, Jr., PhD, University Distinguished Professor in Virginia Tech’s Food Science and Technology Department, who brought Prof. Chan to the university.

continues on page 10

Reminder: Please Return your completed PDA Board of Directors election ballot (mailed with last month’s issue) to PDA by October 29.
If you created a company with unparalleled expertise in ..... 

....a solutions company that could keep pace with problems of your pharmaceutical, medical device, biotech, biologics or generic drug company - 

PSI would be that company.

Pharmaceutical Systems, Inc.
909 Orchard Street • Mundelein IL 60060
Tel: 847.566.9229 • Fax: 847.566.4960
www.pharmaysystems.com
THE HOTTEST JOBS SERVED UP JUST FOR YOU

www.pda.org/careers

THE HOTTEST JOBS, THE TOP EMPLOYERS ARE WAITING FOR YOU ON:
www.pda.org/careers

LOG ON TO:

> Create, edit, and store your resume and cover letter for employers to see
> Control the information displayed through our confidentiality feature which lets you omit your personally identifiable information
> Search and apply to a variety of careers—ranging from entry level to executive level positions
> Receive email notifications when new jobs are available (Available to PDA Members only)
> Schedule in-person interviews at PDA Career Fairs

PDA HEADQUARTERS
3 Bethesda Metro Center
Suite 1500
Bethesda, MD 20814 USA
TEL: +1(301)656-5900
FAX: +1(301)986-0296
The PDA Letter is published monthly by PDA, exclusively for PDA members. Subscriptions are not available. Articles in the PDA Letter may be reproduced with permission—contact the Senior Editor for details. © PDA 2004

**Production Staff**
Walter Morris, Senior Editor
Peter Marinovich, Manager, Web and Production
Matt Clark, Director, Marketing, Membership & Chapters

**Executive Staff**
Neal G. Koller, President
Vice Presidents
Vicki Dedrick, Quality and Regulatory Affairs
Lance Hoboy, Finance and Strategic Planning
Gail H. Sherman, Education and
Director of PDA Training and Research Institute
George A. Robertson, Ph.D., Science and Technology

**Directors**
Gautam Maitra, *Europe*
Wanda Neal-Ballard, Programs and Meetings

**PDA Global Headquarters**
3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900  Fax: +1 (301) 986-0296
E-mail: info@pda.org
Web site: www.pda.org

**PDA European Headquarters**
287 Avenue Louise
BE-1050 Brussels
Belgium
Tel: +32-2-643-2045  Fax: +32-2-645-2671

**PDA Office of European Director**
R-1059, Postfach
Schwarzwaldalle 215
CH-4002 Basel
Switzerland
Tel: +41 61 321 56 30  Fax: +41 61 321 83 48
E-mail: maitra@pda.org

**PDA Training and Research Institute**
c/o UMBC Technology Center
1450 S. Rolling Road
Baltimore, MD 21227 USA
Tel: +1 (410) 455-5800  Fax: +1 (410) 455-5802
E-mail: info-tri@pda.org

**PDA Board of Directors**
Chair
Nikki V. Mehrringer,
Eli Lilly and Company
Chair-elect
Richard V. Levy, Ph.D.,
PAREXEL Consulting
Secretary
Stephanie R. Gray
Treasurer
Georg L. Roessling, Ph.D.,
Schering AG
Immediate Past Chair
Floyd Benjamin,
Keystone Pharmaceuticals, Inc.
Directors
Jennie K. H. Allewell,
Wyeth Research
Vince R. Anicetti,
Genentech, Inc.

**Important Dates...**
- **November 1—** Papers Due for PDA Viral & TSE Safety Conference
- **November 1—** Papers Due for PDA Extractables/Leachables Forum
- **November 16—** Aseptic Processing: The New Reality, Frankfurt, Germany
- **December 6-7—** Practical Aspects of Aseptic Processing, Basel, Switzerland
- **February 28-March 4, 2005—** PDA International Conference, Rome Italy

**In This Issue...**
Over 800 Participants at the 2004 PDA/FDA Conference Learn Details of FDA’s 21st Century “Actualization” Plan
Risk Management and Opportunity: “Two Sides of the Same Coin”

**Science and Technology**
VP’s Message: Dispatch From The PDA/R3 Nordic Conference
Risk Management and Opportunity (cont.)
ISO 14971—A Standard Good for All Health Care Products
Recent Sci-Tech Discussions

**PDA Calendars of Events**
Programs and Meetings Calendar
Chapter Events Calendar
Training and Research Institute Calendar

**Programs and Meetings**
Call for Papers: PDA Extractables/Leachables Forum
PDA Annual Conference 2005: A Return to PDA Tradition
Call for Papers: PDA Viral and TSE Safety Conference

**PDA Contacts and Forms**
PDA Chapter Contacts
PDA Interest Groups & Leaders

**Advertising Deadline:** 1st of each month prior to issue date. Contact Nahid Kiani at kiani@pda.org or +1 (301) 656-5900 ext. 128.
Top 10 BESTSELLERS
From The PDA Bookstore

1. PDA CD Archive Set
   The PDA Archive gives you easy access to more than 55 years of research papers written by highly qualified research scientists in the pharmaceutical/biopharmaceutical industry. (Item No. 01101 US$ 395/member, US$ 590/nonmember)

2. Pharmaceutical Quality
   Edited by Richard Prince (Item No. 17207, US$ 240/member, US$ 299/nonmember)

   By U. G. Barad (Item No. 17212, US$ 185/member, US$ 229/nonmember)

4. Microbiology in Pharmaceutical Manufacturing
   Edited by Richard Prince (Item No. 17185, US$ 240/member, US$ 299/nonmember)

5. Rules and Guidance for Pharmaceutical Manufacturers and Distributors

6. Cleanroom Clothing Systems: People as a Contamination Source
   By Bengt Ljungqvist and Berit Reinmuller (Item No. 17206, US$ 135/member, US$ 169/nonmember)

7. Steam Sterilization: A Practitioner’s Guide
   By Jeanne Moldenhauer (Item No. 17183, US$ 215/member, US$ 269/nonmember)

8. Laboratory Validation: A Practitioner’s Guide
   By Jeanne Moldenhauer (Item No. 17201, US$ 250/member, US$ 309/nonmember)

9. Commercial Off-The-Shelf Software Validation For 21 CFR Part 11 Compliance
   By David Nettleton and Janet Gough (Item No. 17200, US$ 185/member, US$ 229/member)

    (Item No. 01013, US$ 75/member, US$ 270/nonmember)

To order your copy of these or any other PDA book, please visit the E-Store on our Web site at www.pda.org/estore.
President’s Message

2004 PDA/FDA Joint Regulatory Conference: Terrific!

Terrific! There is no other way to describe the 2004 PDA/FDA Joint Regulatory Conference, Exhibition and Training and Research Institute Courses. Over 900 professionals from industry, government and academia—representing 22 countries from around the world—converged on Washington, D.C., for several days of education, training, industry-specific presentations, exhibits and meetings with colleagues.

Our expert speakers from industry and the U.S. FDA spoke to packed rooms and fielded numerous, challenging questions. The conference provided attendees and speakers with new and concrete information to take back to their jobs. The 23 FDA speakers were forthcoming in both their presentations and answers to participant questions, leaving all who attended well-prepared for the regulatory changes about to unfold. The Nov./Dec. issue of the PDA Letter will provide expanded coverage on these announcements and changes, along with full coverage of the 2004 PDA/FDA Joint Regulatory Conference.

In the exhibition hall, which was full of visitors, meeting participants learned all about exciting new technologies. In fact, several new products were introduced at this conference. PDA introduced new learning tools, including PDA Personal Learning Maps that provided each user with a tool to plot a personalized conference agenda, maximizing the value of their experience.

In my August column, I thanked the FDA for being a strong supporter of this annual event—now in its 15th year. This month, I want to thank all of the volunteers on the program planning committee who helped make this year’s conference the great success that it was, starting with Allen Burgenson (Cambrex Bio Science), the committee chair, and moving on to:

- Rafik Bishara, PhD (Eli Lilly),
- Brent Conatser (Eli Lilly),
- Victoria Dedrick (PDA),
- John Friel (CDER, FDA),
- John Gigert, PhD (BioPharmaceutical Quality Solutions),
- Kathleen Greene (Novartis Pharmaceuticals),
- Maria Guazzaroni, PhD (Pfizer),
- Erik Henrikson (CDER, FDA),
- Louise Henry (Vertex Pharmaceuticals),
- Florence Kaltovich (Science Applications International Corporation),
- Elizabeth Leininger (Biologics Consulting Group),
- Mark Lynch (PAREXEL Consulting),
- Vince Mathews (Eli Lilly),
- Wanda Neal (PDA),
- Seamus O’Boyle (CBER, FDA),
- Deborah Ralston (ORA, FDA),
- Cindy Rockel (Millipore),
- Georg Roessling, PhD (Schering AG),
- Susan Schniepp (Hospira),
- Amy Scott-Billman (GlaxoSmithKline),
- Frank Settineri (Chiron), and
- Kathy Zink (Office of the Commissioner, FDA).

PDA thanks all of you for planning and executing such an exciting and productive conference.

Contributing to the success of the 2004 PDA/FDA Joint Regulatory Conference were the PDA committees, task forces and interest group meetings held throughout the conference, including: the Regulatory Affairs and Quality Committee (RAQC), the Science Advisory Board (SAB), the Chapter Council, the program planning committees for the 2005 PDA Annual Meeting and 2005 PDA/FDA Joint Regulatory Conference, the Viral Filtration Task Force, the QA/QC Interest Group (IG), the Visual Inspection IG, the Biotechnology IG, the Strategic Planning Committee, the Executive Committee, and the Board of Directors. Of particular note is that over 50 conference attendees extended their stays and participated in the Biotech IG that met following the close of the conference.

The PDA Training and Research Institute (TRI) lecture series followed the conference and drew twice the number of attendees as anticipated. I want to express PDA’s gratitude to the distinguished faculty who made these courses such a success:

- Renee Galkin (R.B. Galkin and Associates),
- Anne Marie Dixon (Cleanroom Management and Associates),
- Daniel Gold, PhD (D.H. Gold Associates),
- Richard Wood, PhD, (Pfizer, ret.) and
- Destin LeBlanc (Cleaning Validation Technologies).

I also want to recognize PDA’s newest staff addition, Gail Sherman, VP of Education and Director of TRI and all of the TRI staff for doing an outstanding job.

The 2004 PDA/FDA Joint Regulatory Conference was a terrific meeting for which all PDA members should be proud! Thank you for all your support.
Coming Soon: New And Improved PDA Letter

A few months ago, PDA Senior Editor Walter Morris promised there would be design and format improvements “coming soon” for the PDA Letter. We’re excited to announce that four of those enhancements will be unveiled in the November/December issue.

First, we will transition away from the old 2-color newsletter format and toward a top-shelf, 4-color magazine. While we would never compromise the personal touch our members have come to expect from the PDA Letter, we know this image overhaul will provide greater value for both our members and advertisers.

Second, we will combine the November/December and July/August publications into expanded single issues with greater topic-specific coverage. This transition from 12 to 10 publications per year allows us to increase both the depth and breadth of our features in these two expanded issues.

Third, each issue of the PDA Letter will be topic-specific. Features, stories, interviews and reports will be woven together through the common thread of thematic congruity. In this way we hope the PDA Letter will find extended shelf-life and become an integral part of your personal and corporate reference libraries.

And finally, these improvements mean that we can slate an entire year’s worth of PDA Letter publications in advance. The substantial increase in topic lead time allows us to ensure that subject matter experts are prepared and committed for articles, interviews and reports. Our readers can plan for, anticipate, and even contribute to, topic-specific issues long before they are even delivered. Advertisers can hone in and fine tune their messages so that their products and services blend together seamlessly inside the new and improved PDA Letter.

We’re excited that these enhancements are finally being rolled out and look forward to your feedback with the delivery of the November/December expanded issue of the PDA Letter.

—Matthew Clark, Director, Marketing Services, Director, Membership and Chapters

End the destruction.

Until now, you had no choice. Now you do, with advanced headspace analysis technology only from Lighthouse Instruments. Imagine being able to measure pressure, oxygen or moisture levels in seconds without destroying your samples. Join some of the world’s largest pharmaceutical and biotechnology companies and discover the benefits of Lighthouse Instruments’ technology. Headspace analysis has never been faster, easier or less wasteful!


Call us today.

2030 Avon Court • Charlottesville, Virginia 22902 • (434) 293-3081 ext. 235 • Fax (434) 293-7773
headspace@lighthouseinstruments.com • www.lighthouseinstruments.com
Vice President’s Message

Dispatch From The PDA/R³ Nordic Conference

The purpose of my article this month is to discuss some of the “hot” science and technology topics presented at the joint PDA and R³ Nordic Association conference, which took place in collaboration with the Royal Institute of Technology KTH in Stockholm Sweden, June 7-8. From my point of view, two of the most exciting topics discussed at this meeting were Process Analytical Technology (PAT) and the issues around cleanroom contamination and monitoring.

PAT was covered in three presentations: an overview by Christopher Watts, Office of Pharmaceutical Science, Center for Drug Evaluation and Research, U.S. FDA; case studies/examples of Pfizer’s success with PAT presented by Norman Winskill, PhD, Vice President, Manufacturing; and a detailed look at a PAT technology, rapid microbial methods, by yours truly.

Norman presented a fascinating look at how Pfizer has been using PAT successfully in manufacturing operations. The use of PAT requires process understanding. He demonstrated with examples how the use of near-infrared spectroscopy was used in incoming inspection, API blending and tablet core potency measurements. Near-IR has been used in our industry for many years and is a standard for chemical identification. Now, with the spectrometer located “at line” as an integral part of the blending equipment, the results can be translated into immediately usable data. In processes that were time defined, the actual physico-chemical state of the product can be monitored in real time.

This technology fits nicely in the context of Chris’ talk from FDA’s point of view, relating to “risk-based” enforcement. Increased process knowledge from the intelligent use of PAT would result in reduced risk, and such a reduction in risk should result in reduced regulatory scrutiny.

My talk centered on a specialized series of technologies related to PAT, rapid microbiological methods (RMM). I discussed how much of microbiological methods were “a hundred years of tradition unimpeded by progress,” principally because they all depended on the growth of the organism to either become visible or for specific chemical activity to become detectable. Two of the most interesting detection technologies are the chemo-luminescent detection of ATP metabolism and the use of epi-fluorescent dyes. These are not “real time” in the sense Near-IR can provide data as the process happens, but I can trim days, if not weeks from the testing cycle. The other advance in RMM is in identification. Here, without the need for microbes to grow, recombinant DNA techniques have led the way in precise and accurate identity determinations based upon genomic sequences. Rather than relying on the actual growth of the organism, one can use the biochemical technique of polymerase chain reaction. Here, locus-specific sequences can be amplified and analyzed. Genes coding to the 16S ribosomal RNA have been mapped extensively, and are available for identification of a wide variety of environmental (and clinical) organisms. It should be mentioned that a major comparability guideline used throughout the industry is PDA Technical Report 33: Evaluation and Validation of New Microbiological Testing Methods.

Not surprisingly, the two driving forces behind this PDA/R³-Nordic Meeting also presented some of the most interesting papers in the area of environmental science. Berit Reinmuller, PhD, and Bengt Ljungqvist, PhD, (both with KTH) presented a series of papers on the nature of human (operator) contamination and on cleanroom risk management. What is remarkable is the mathematical rigor with which the subjects were described. Many “good practices” have been based on empirical “seems right” observations. In the analyses presented here, concepts as overgarment maintenance, proper use of undergarments and the effects of repeated washing/sterilization cycles all contributed to particle shedding. Another study assessed the contamination risks of a cleanroom-dressed operator from both a mathematical and an experimental point of view. Not only do the data show that the particles shed in a vertical unidirectional airflow and follow mathematical predictions, but the air speed and distance from the top of the head are major factors in the magnitude of contamination risk. The other series of papers included a discussion of the method for estimation of potential microbiological risks of airborne contamination in clean zones in a systematic way. The procedure follows this logical sequence:

- Visualize the airflows and identify turbulence zones, where contaminants could be accumulated or dispersed in an unpredictable way.
- Perform an actual challenge test with particle counters to ascertain actual risk zones.
- Evaluate the risk situation by calculating the risk factor.

Due to space limitations, I have not been able to present all of the excellent scientific papers presented at the conference. However, the slides are available for viewing in the “members’” section of the PDA Web site.
Science, technology and training are the hallmarks of PDA. Volunteers, through PDA Boards, Committees, Task Forces and Interest Groups, make it all happen. They are the heart and soul of PDA, providing value and service to the PDA membership and the global pharmaceutical and biopharmaceutical communities.

PDA is forming three new Advisory Boards to further the PDA Mission and Strategic Plan, and provide the membership with new opportunities to participate in a shared commitment to the advancement of science, technology and training.

Three New PDA Advisory Boards

**PDA Biopharmaceutical Advisory Board (BioAB)**

The BioAB is being formed to establish the strategic perspective and provide oversight for PDA's scientific, technical and regulatory activities in the biopharmaceutical community through the development of guidances, technical monographs, and interaction with regulatory authorities.

**PDA Program Advisory Board (PAB)**

The PAB is being formed to provide oversight and support for all domestic and international conferences. The PAB will focus on such areas as conference purpose, theme, topic selection, Program Committee chair and chair elect, communication and coordination with other PDA Committees and activities.

**PDA Training and Research Institute Advisory Board (TRIAB)**

The TRIAB is being 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.

Like other PDA Boards, Committees, Task Forces and Interest Groups, these new advisory boards will be very much a part of the significant work PDA performs for the membership and the community, providing global value and impact.

Get the most out of your PDA membership. Grow professionally, enhance your skills and network. Make a difference!

**How to Get Involved**

By October 31, 2004, provide to the appropriate Advisory Board liaison listed below...

1. A brief summary of your professional experience and interest
2. Your contact information

- **Biopharmaceutical Advisory Board**
  - George Robertson, PhD: E-mail: robertson@pda.org; Tel: +1 (301) 656-5900, ext. 139; Fax: +1 (301) 986-1093

- **Program Advisory Board**
  - Wanda Neal: E-mail: neal@pda.org; Tel: +1 (301) 656-5900, ext. 111; Fax: +1 (301) 986-1093

- **TRI Advisory Board**
  - Gail Sherman: E-mail: sherman@pda.org; Tel: +1 (410) 455-5802

Or, visit [www.pda.org/volunteer](http://www.pda.org/volunteer) to learn more about these three new Advisory Boards and to respond to this call for volunteers online.
Risk Management and Opportunity, from cover

Having served in the medical device industry during its transition from traditional GMP regulations and quality assurance methodology into the risk management paradigm, Professor Chan is encouraged by recent developments in the pharmaceutical and biopharmaceutical (pharma/biopharma) industries.

With industry at the threshold of this process, Prof. Chan believes “there are going to be a lot of opportunities.” The hard work of defining, identifying, evaluating and controlling risk will open doors to manufacturers, he says, because “to me, managing risk is managing your opportunities, too. Risk and opportunities are always two sides of the same coin. That is why companies also need to look at the opportunities sides.”

Authorities Drive Risk Initiatives

As was the case with medical devices, the impetus for risk management in the pharma/biopharma industries comes from the health authorities and is global in nature.

Back in the early 1990’s, health authorities and medical device companies began looking to upgrade manufacturing and QA practices. Based on the experience of other industries, risk management principles were identified as an ideal and optimal solution. The U.S. FDA incorporated risk management concepts into its 1996 Quality Systems Regulations (QSRs) for medical devices. The preamble to the QSRs referenced the European risk-based policy, “European Norm” (EN) 1441, for medical devices.

Both FDA and the EU health authorities identified the desirability of a harmonized approach to risk-based regulation, each citing the work of the International Organization for Standardization (ISO) in this area (see story, “ISO 14971: A Worldwide Risk Management Standard,” page 20). Earlier this year, the ISO risk management standard was adopted in the EU, replacing EN 1441.

The regulatory harmonization body for medical devices, the Global Harmonization Task Force—the equivalent of the pharma/biopharma industries’ International Conference on Harmonisation (ICH)—has taken up risk management. Prof. Chan is heavily involved in that working group.

On the drug side, the uptake of risk management has lagged behind. While risk concepts underpinned evolving post-approval changes requirements in both the U.S. and the EU in the 1990’s, it wasn’t until 2002 before a major health authority—the FDA—endeavored to orient its drug cGMPs to risk management concepts. In 2002, FDA launched an initiative to reform the cGMPs and many of its Chemistry, Manufacturing and Controls requirements, a project dubbed the “Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach.”

In the two years since, health authorities in the EU, Japan and other countries have taken a keen interest in risk management concepts. To ensure harmony in approaches, ICH formed a working group on risk management, quality topic “Q9.” Industry has become a strong advocate for risk management approaches and the harmonized approach. The major pharmaceutical trade associations in the U.S., Europe and Japan have all endorsed ICH’s effort in this area.

Define Risk Management First

When asked about ICH Q9, Prof. Chan believes the project could be very successful. He cautions, however, that there needs to be agreement up front on the definition of risk management. The definition, so far, “may not be totally accurate,” he says. “I see the approach—at least the document that has come across my desk—is not consistent” with respect to terminology.

“Everybody talks about risk management,” comments Prof. Chan, but “what is it? That is a fundamental terminology. It is very important because when you define ‘risk,’ everybody will follow your definition. But if you don’t define it, everybody will define it themselves.”

Prof. Chan’s concern with the final definition of risk in the ICH Q9 document grows out of his experiences with the industry via public conferences and the Orange County Regulatory Affairs’ (OCRA) Medical Product Risk Management Discussion Group of Southern California—a group he founded to prompt a discussion about risk management among the region’s many health products manufacturers.

“I have a feeling nobody has a clue which definition to adopt. Even the OCRA Group—when I talk to the executives who attend the discussions, when they mention risk, they talk about everything. But is that the intention of Q9 and
FDA? Professor Chan believes that, without good definitions, “there will be chaos.”

Right now, the health authorities and industry are grappling with the concept of ‘risk to patient.’ Prof. Chan, however, believes ‘risk to patient’ is just one of the risks—albeit a very important one—that needs consideration. Manufacturers, however, need to look at the big picture, which Prof. Chan defines as ‘enterprise risk.’

“If I’m working for a company,” he explains, “I would say the ‘enterprise risk management’ needs to be defined, and ‘patient risk’ is one of the risks. For compliance purposes, focus on patient risk, because FDA is not going to care too much about how much you spend to make it safe for the patient. It needs to be safe, period. That is the requirement. How much you spend on it, that is the company’s business.

“On the other hand, from the company’s perspective, it is not only the patient risk, it is also a business risk. So that is why the enterprise risk approach needs to be applied, otherwise your risk management system starts to focus on patient risk, which may not be optimal for the business in terms of cost-effectiveness. That is why you need an enterprise risk management system.”

Prof. Chan states that the compliance portion of an enterprise risk management system opens up tangible business opportunities to a firm—the two sides of the same coin argument.

“Compliance is an advantage to the business instead of a burden to the business,” asserts Prof. Chan. “I think risk management can actually play a part in both of these issues, both the quality and compliance issues.

Prof. Chan is working on it: “I’ve been doing studies to actually translate this risk management into the enterprise.”

A Desire To Teach

And that is what drives Prof. Chan today, his ability to educate.

After earning an electronics and computer engineering degree, Prof. Chan was drawn to a career in reliability engineering. At that time,” he notes, “they didn’t call it ‘reliability engineering,’ they called it ‘assurance.’” Soon, he found himself looking to improve his skills, but in the early 1980’s, quality assurance and reliability engineering weren’t big concerns for many U.S. industries. Back then, he explains, “there was not a degree or advanced degree or graduate degree in reliability engineering or quality or things like that. Around the whole country there

NOT ENOUGH HOURS IN THE DAY?
We do ID’s all day, everyday. Like clockwork. 150,000 FAME ID’s since 1988.
Experts in pharma microbiological QC.
FDA registered, GMP laboratory.
ISO 17025 quality system.
Rapid, reliable, accurate results.
Specialists in environmental organisms. Aerobes, anaerobes, molds.
www.microcheck.com 877 WE ID BUGS
was only one school that offered a Master of Science degree in reliability engineering and that was the University of Arizona." As such, he took it upon himself to learn about reliability methodologies. He found that his attraction to the field was so strong, it seemed as if he was "born with it in my blood."

By the late 1980’s, quality was becoming a key concern in various industries, Professor Chan relates, "because the whole United States, the car industry and electronics industry seemed to be taken over by the Japanese. And a few schools actually started to put together a curriculum on quality engineering or quality assurance. It happens that a Cal-State consortium put together a Master of Science program in Quality Assurance and Management.” Prof. Chan signed up immediately and received an MSQA in the consortium’s first class.

Prof. Chan took his skills and degree to the medical device industry. "I joined a company working on medical devices. They hired me as their first reliability engineer to develop their reliability engineering function." After working for a few other medical device companies, Prof. Chan landed a position in Guidant’s reliability engineering department. “Eventually I became the section head of the department.”

It was while with Guidant that Prof. Chan managed the challenges posed by the new risk management paradigm for the medical device industry. Crediting the company as being “maybe the best I have ever worked for at the time,” Prof. Chan explains that Guidant had the right kind of management system to adapt to the new realities. “Guidant was pretty progressive company in terms of the regulation.” The new quality systems regulations were not a “shock” to the large company, which quickly understood and implemented them.

Smaller competitors, however, struggled to adjust. From what Prof. Chan saw, many small companies had difficulty “even understanding the implication of the regulation. I would say that the smaller the company and depending on what stage they were at, they had a much harder time. They focus more on the performance attributes of the product, how to develop it. But in terms of getting the regulatory compliance side, I would say no, their focus is not on the compliance piece.”

Prof. Chan believes most medical device companies can “improve on how to use quality reliability and apply the concepts of risk management to leverage their business. There are a lot of things that I still see as opportunities, and a lot of these opportunities are being overlooked—really overlooked, maybe even neglected.”

Being in a position to help a broader segment of the industry was a big factor in Prof. Chan’s decision to leave industry for an academic career at Virginia Tech.

“There are so many misconceptions out there,” Prof. Chan declares. “I have more than 20 years of experience going through various industries and, with my background, I do think that my observations and my insights are beneficial.” On top of this, he explains, “Teaching has always been a goal to me. Even in a company, I teach as an advisor.” His position at Virginia Tech gives him access to a larger student body, which he is grateful to have.

Medical HACCP

The university, on the other hand, is grateful to have someone with Prof. Chan’s knowledge, skills and demonstrated ability. Its new Center for Applied Sciences in Health Products & Processes grew out of an older program to teach Hazard Control and Critical Points (HACCP) to the seafood industry. After running a series of HACCP lecture conferences for seafood producers for a few years, the faculty noticed that representatives from medical device companies were attending. After numerous requests from the FDA and companies, Dr. George Flick organized a course on medical device HACCP, including a comprehensive program manual, and arranged a certification through the Association of Food and Drug Officials (AFDO).

Dr. Flick outlined the evolution of the program for PDA during our conversation in August: “We opened it up because we had requests. The initial stimulus came from companies saying, ‘some of the things you are doing in the seafood area really have application to our industries.’ The medical device people actually came to some of the seafood conferences. We had big companies come in and participate. We decided, based on the feedback, there was a golden opportunity in the medical device industry, and we started offering courses….We wrote the manual and got a certification with AFDO so that it would have some meaning, and participants could also get some credit for use at Virginia Tech.”

The AFDO accreditation is important, Dr. Flick maintains, because it provides “some regulatory
Manic about microbes?

Picky about particulates?

Count on Biotest

APC Airborne Particle Counters and RCS Microbial Air Samplers combine to give you a clear picture of airborne contamination. Biotest Diagnostics Corporation offers a full line of reliably accurate, technically-advanced, hand-held, air monitoring devices. When you’re picky about maintaining air quality standards, count on Biotest. Call today or visit our website at www.BiotestUSA.com.
DECON-SPORE 200^Plus^™
For the Sterilization of Manufacturing, Packaging and Filling Equipment in Aseptic Processes

Available in Unit Dose Containers:
- 2 oz. (makes 4 gallons of disinfectant)
- 13 oz. (makes 2 gallons of sterilant)
- 1 Gallon

✓ Unit dose reduces errors in measuring
✓ Unit dose reduces handling of material
✓ Assures sterility each time
✓ Also available in 1-gallon containers
✓ Excellent Antimicrobial Effectiveness Data
✓ 50% Less expensive than ready to use products
✓ Completely validated for sterility and expiration
✓ Aseptically filtered at 0.2 microns
✓ Less expensive than other concentrates
✓ Reduced odor from ready to use
✓ 80% Less required storage space
✓ USP 25 sterility tested per lot

Call today for your Free Sample and/or our PDF Technical product file!
(888) 478-3745

sterile.com

Veltak Associates, Inc.
15 Lee Boulevard • Malvern, PA 19355-1234
(610)-644-8335 • Fax (610)-644-8336

Innovative Clean Room Products
oversight, you might say, since this is a professional organization of the inspectors.”

An early instructor of the course, Professor Chan was targeted by Dr. Flick as a person who belonged on staff. “We were being overwhelmed, so we hired Tony Chan.” The move brought to the program the required expertise for success. “One of the problems is, as we talk about risk management, people ask questions, and you must be able to answer those questions. We had a lot of people in here who could say, ‘yes I can talk about risk management,’ but when they are asked specifically about a product and they cannot answer it, then you start to lose credibility.” Prof. Chan can answer questions specific to medical devices and health care products.

The program has been largely successful, comments Dr. Flick. “There was really no one school that really was addressing these issues.” To date, Dr. Flick and his team have taught over 50 courses on medical HACCP. Now the program is getting calls from the pharmaceuticals and blood operations, who see applications in their fields.


Prof. Chan views Dr. Flick as the “father of medical HACCP” because it was he whom FDA approached to “translate HACCP from the food industry to medical devices.” Both men share the belief that tools like HACCP can and should be transferred from one industry to the next easily.

**To date, Dr. Flick and his team have taught over 50 courses on medical HACCP. Now the program is getting calls from the pharmaceuticals and blood operations, who see applications in their fields.**

**RACCE To Compliance**

An important concept Prof. Chan wants to teach industry is the “four key principles for risk management.” These principles are captured in “RACCE”: risk acceptability, risk communication, risk control and effectiveness of risk control.

Good international risk management standards incorporate RACCE, says Prof. Chan. “I look at ISO 14971, the whole model of risk management for medical device, you look at the essence of the whole standard—the most important ones I pull out are these four things. If I look at the other system by somebody else, I can see the commonality. These four things are still there. So you cannot avoid these four elements.”

Commenting on the first principle, risk acceptability, Prof. Chan explains that it is “how a company or institution is going to accept risk. It needs to be defined. It is a policy issue. It is high up, almost like the CEO or the Board of Directors—they have to determine what kind of risk they are willing to accept because down the line it is going to be translated into a business metric.” The termination of risk acceptability, according to Prof. Chan, cannot be left to “the engineers.” Rather, “it has to be defined as a policy from the top, the very, very top.” Ultimately, the top executives are responsible for its consequence.

Risk communication is both internal and external. “A more important issue is how to communicate risk within the organization as well as outside the organization,” Prof. Chan maintains. Internal communication involves defining risk, hazards and other key concepts. As a reliability engineer, Prof. Chan states, “the first thing I do in putting together a risk management system is to harmonize the terminology within the company. What is a hazard? How to identify it? That is the first step. You don’t know how much time I spent—I spent two years to get a company to talk about hazard consistently….That is really the first step.”

Prof. Chan looks upon ISO 14971 very favorably because it standardizes the terminology. “You talk about risk in medical device, there is a standard. The standard means they have a terminology [and it] is defined. In the medical device industry we talk about risk as the combination of two elements: One is the probability of occurrence of harm, and the [other is the] severity of that harm. It is very specific. And then it has a definition of harm.”

External risk communication is more difficult, Prof. Chan maintains, because “there are stakeholders such as the regulatory agency, such as the patient groups, such as the physician using the product.” Communication to the stakeholders represents “another big challenge, in particular, for the pharmaceutical industry,” says Prof. Chan. When contacting the regulators, the stakes are extremely high: “Now it is not just the company; now it is almost like the validation of the company’s policy on risk acceptability, because now you have to communicate what I call the residual risk to your stakeholders.” The part of the challenge lies in demonstrating and documenting evidence “to show that your accepted product risk is acceptable to the agency from a public health perspective.” Even more complicated is communicating to the physicians and patients.

Regarding the second “C” in RACCE, risk control, Professor Chan states that responsibility now lies lower down in the company. “Risk control—I think this is definitely something that
the engineers in the companies have to deal with.” Various tools exist for risk control and are being discussed publicly by FDA and industry representatives, including PAT, Six Sigma and HACCP. “These are all control issues. It depends on the culture, the environment and the technical capability of the company, of the institution, how they control risk. Most technical people would jump into risk control immediately,” says Prof. Chan.

Likewise, the effectiveness of risk control resides in the domains of the engineers, although companies should have a policy for determining and demonstrating the effectiveness of individual risk control measure as well as the entire risk management process.

Referring back to ISO 14971, Prof. Chan strongly recommends that the pharmaceutical and biopharmaceutical industries adapt the medical device standard and adopt its terminology. Otherwise, he cautions, the three industries will continue to operate in parallel universes with different standards and different approaches. “That is insane,” he asserts.

To build his case for the ISO risk management standard, Prof. Chan always engages manufacturers of combination products when speaking in public. “I wanted to use combination products because that is the connection. Medical device industry already has a set of terminology for risk management. If the pharmaceuticals and biologics have their own definitions for combination products, which do you follow?”

When the combination products representatives start talking about ISO 14971, it is difficult “to argue with.”

Prof. Chan spoke during the closing plenary session of the 2004 PDA/FDA Joint Regulatory Conference. A report on his remarks will appear in the November/December issue of the PDA Letter, along with comprehensive coverage of the overall conference.

By meeting with experts like Prof. Chan and inviting them to speak at our events, PDA continues to fulfill its mission of promoting scientifically sound and practical technical information and education for industry and regulatory agencies.

— Walter Morris, PDA Senior Editor
New PDA/DHI Technical Books

✓ Technology Transfer .................................................. Item no. 17218
  Author: Mark Gibson
✓ Environmental Monitoring .............................................. Item no. 17211
  Editor: Jeanne Moldenhauer
✓ Pharmaceutical Excipients ..................................... Item no. 17217
  Author: Brian Matthews
Valuable research and a searchable CD Archive included
✓ Risk Analysis ............................................................... Item no. 17219
  Author: James Vesper

New PDA Technical Reports

✓ Industrial Moist Heat Sterilization In Autoclaves,
  Technical Monograph No. 1, revised ....................... Item no. 01001
  Price: paper version - US$ 100 member/US$ 295 nonmember/US$ 40 government
  CD-Rom version - US$ 75 member/US$ 270 nonmember/US$ 30 government
✓ ChromPac Manufacturing Chromatography
  Systems Postapproval Changes; Chemistry,
  Manufacturing and Controls Documentation,
  Technical Report No. 38 ............................................. Item no. 01038
  Price: US$ 75 member/US$ 270 nonmember/US$ 30 government
✓ Cold Chain Management,
  Technical Report No. 39 ............................................. Item no. 01039
  Price: US$ 75 member/US$ 270 nonmember/US$ 30 government

New PDA Pocket Guide

PDA Pocket Guide on Troubleshooting the Top
GMP Issues from FDA 483’s and Warning Letters

Edited by: Vicki Dedrick and Walter Morris;
Contributions by: PDA Regulatory Affairs and Quality Committee (RAQC)

Easily train your employees in the Top Ten 483 and Warning Letter issues. This pocket guide identifies the issues, provides examples from 483’s and Warning Letters, gives the text of the applicable regulation and provides useful tips and advice that you can put to work to ensure your company avoids these problems.

Contact PDA for information on having your company logo imprinted on the back cover and for information on volume discounts.

Item no. 13006
Price: US$ 7 member/US$ 10 nonmember/US$ 5 government
**PDA Calendar of Events**

**PROGRAMS AND MEETINGS CALENDAR**

Please visit www.pda.org/courses/index.html for lodging, registration, and event description information.

### 2004

**October**
- **14** Audio Conference: Minimizing the Legal, Quality and Compliance Pitfalls of Contract Mfr.
- **29** Aseptic Processing: *The New Guidance*  
  Park Hyatt Washington  
  Washington, D.C.

**November**
- **16** Aseptic Processing: *The New Guidance*  
  Sheraton Frankfurt Hotel and Towers  
  Frankfurt, Germany

### 2005

**February/March**
- **28-2** PDA International Congress, Courses & Exhibitions  
  Rome Cavalieri Hilton  
  Rome, Italy

**April**
- **4-8** PDA Annual Meeting, Courses and Exhibitions  
  Hyatt Regency  
  Chicago, Illinois

**May**
- **16-18** PDA Viral & TSE Safety Conference  
  Hyatt Regency  
  Bethesda, Maryland

- **23-25** Extractables/Leachables Forum  
  Bethesda North Marriott  
  Bethesda, Maryland

**September**
- **12-16** 2005 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits  
  Washington, D.C.

**October**
- **10-11** Taormina Conference  
  Taormina, Italy

**CHAPTER EVENTS CALENDAR**

Please visit www.pda.org/courses/index.html for lodging, registration, and event description information.

### October
- **1** New England  
  Workshop on Combination Product Development  
  Cambridge, Massachusetts

- **6** Southern California  
  Management Controls/FDA Inspection Planning  
  Huntington Beach, Calif.

- **6-7** Central Europe  
  “Hands On” Visual Inspection Problem Solving  
  Berlin, Germany

- **18-19** Italy  
  TSE & Viral Safety: Regulatory Expectations & Industry Practices  
  Rome, Italy

- **18-19** Central Europe  
  The Universe of Pre-filled Syringes  
  Hanover, Germany

- **19** Israel  
  Seminar: Process Validation  
  Tel Aviv, Israel

- **20** Southeast  
  Annual Fall Meeting  
  Research Triangle Park, North Carolina

- **25** Spain  
  Complying with FDA’s New cGMPs of the 21st Century Using Risk/Science-Based Validation  
  Barcelona, Spain

- **27** UK & Ireland  
  Biotechnology Conference  
  OSI Pharmaceuticals  
  Oxford, England

### November
- **9-10** Japan  
  Japan Chapter Annual Meeting  
  Tokyo, Japan

- **17-19** Central Europe  
  Aseptic Processing Course  
  Basel, Switzerland

- **17** Delaware Valley  
  Environmental Monitoring  
  Malvern, PA

- **19** Metro  
  Current Compliance Trends  
  Clark, NJ

- **19** Midwest  
  Rapid Microbiology Techniques and PAT  
  Northbrook, IL

### December
- **6-7** France  
  Bio/Pharmaceuticals Manufacturing in Europe  
  Paris, France

- **8** New England  
  Dinner Seminar on PAT  
  Cambridge, MA

- **27** Israel  
  Annual Meeting  
  Tel Aviv, Israel
### Laboratory Courses -- 2004

**October**
- 4-8  Aseptic Processing Training Prgm.: Week 1
- 14-15  Fundamentals of D, F, and z Value Analysis
- 18-22  Rapid Microbiological Methods
- 25-27  Designing, Operating, and Controlling High Purity Water Sys. for Regulatory Compliance

**November**
- 1-5  Aseptic Processing Training Prgm.: Week 2
- 11-12  Developing/Validating Cleaning & Disinfection Prgms. for Controlled Envn.
- 15-17  Cleaning Validation
- 17-19  Practical Aspects of Aseptic Processing
  - University of Basel
  - Basel, Switzerland
- 18-19  Remediation of Existing Computer Systems

**December**
- 2-3  Environmental Mycology I.D. Workshop
- 6-7  What You Need to Know to Select Adequate Thermal Validation Equipment

### Laboratory Courses -- 2005

**February**
- 7-11  Aseptic Processing Training Prgm.: Week 1
- 17-18  Computer Prod. Supplier Auditing Process Model: Auditor Training
- 24-25  Environmental Mycology I.D. Workshop

**March**
- 3-4  Developing/Validating Cleaning & Disinfection Prgms. for Controlled Envn.
- 7-9  Cleaning Validation
- 14-18  Aseptic Processing Training Prgm.: Week 2
- 22-23  Validating a Steam Sterilizer

**April**
- 18-22  Aseptic Processing Training Prgm.: Week 1

**May**
- 16-20  Aseptic Processing Training Prgm.: Week 2
- 25-27  Cleaning Validation

**June**
- 2-3  Environmental Mycology I.D. Workshop

### August
- 10-12  Developing a Moist Heat Sterilization Prgm. w/n FDA Requirements
- 22-26  Aseptic Processing Training Prgm.: Week 1

### September
- 7-9  Adv. Environmental Mycology I.D. Workshop
- 19-23  Aseptic Processing Training Prgm.: Week 2

### October
- 6-7  Fundamentals of D, F, and z Value Analysis
- 17-21  Aseptic Processing Training Prgm.: Week 1
- 25-26  Validating a Steam Sterilizer

### November
- 7-9  Cleaning Validation
- 14-18  Aseptic Processing Training Prgm.: Week 2

### December
- 1-2  Environmental Mycology I.D. Workshop

### Lecture Courses -- 2004

**October**
- 26-27  21st Century cGMPs: A Risk/Science-Based Approach to Validation
  - PDA-TRI, Baltimore, Maryland

**December**
- 6-7  Computer Products Supplier Auditing Process Model: Auditor Training

### Course Series -- 2004

**October**
- 18-20  Boston, Massachusetts
  - Analytical Problem Solving for CAPA Sys.
  - Design and Validation of a Cleaning & Disinfection Prgm
  - Intro. to Writing and Auditing CGMP Doc.
  - CGMPs for Bioprocesses
  - Pharmaceutical Water Sys. Design & Validation
  - Maximizing SOPs - An Untapped Resource of Trng. Solutions
  - Everything You Wanted to Know About Environmental Monitoring but Were Afraid to Ask
  - Qualification and Validation of API Manufacturing Ops.
  - Achieving CGMP Compliance During Development of a Biotechnology Product
  - Annual Product Reviews: How to Comply with FDA & ICH Req.
ISO 14971—A Standard Good for All Health Care Products


ISO 14971 distinguishes itself from previous standards and guidance as being the best path toward global compliance available to date. It is one of the only standards that addresses both risk assessment methodology and risk management concepts.

For pharmaceutical and biopharmaceutical manufacturers, Ms. Lander focused on 21 CFR Part 11 because the 2003 draft guidance on the rule employed risk management strategies. She indicates that when no risk management plan is in place, the FDA assumes—by default—the product or process involved is high risk, which in turn, triggers all technical controls as outlined in Part 11.

The following excerpts are from the July 22 audio conference. In the first excerpt, Ms. Lander has just concluded outlining a number of the international risk management standards. She makes a good case for why pharmaceutical companies should pay attention to these standards, particularly ISO 14971. The second excerpt jumps ahead to Ms. Lander’s conclusion. In between these two segments, Ms. Lander gives a comprehensive overview of ISO 14971.

... The bottom line is that there are a lot of standards and guidances out there that focus on how to do risk assessment and risk management coming out of these harmonization committees. Now you’ve heard me say the word “medical device” a number of times—and I’m on the next slide—so you might be asking yourself, well, why are medical device people coming out with all these great risk assessment and risk management standards? I’m in the drug business. I’m regulated by the center for drugs, or perhaps I’m in the blood product business and I’m regulated by the center for biologics. I’m not interested in medical devices. But that’s really a two-fold question. Question one is why medical device standards and why should I care about them if I’m not in medical devices?

Well, medical device folks have always had to focus on risk. As you know, before you put a medical device out in the market you’ve got to classify that device as either a Class I, Class II or a Class III medical device and when you do that you take into account risk to the public safety, Class III being the highest risk, Class I being lowest. A Class III medical device could be a pacemaker. Class I could be a tongue depressor, for example. So you’ve got to think about risk even before your product is on the market.

The medical device people have been thinking about risk and assessing risk in the process of making their products for a long time. They’re on the cutting edge of risk management. They’ve been out there doing it for a long time and we on the drug side are just really getting involved with risk analysis and risk management, primarily because of the new guidance document – we’ll it’s not really new any more – that the FDA came out with last September third on the new scope and application of 21 CFR Part 11.

But now, to answer the second part of that question, which is, should you care about this when you’re not a medical device company, the answer is yes. Because these are some excellent standards.

Very briefly, what is ISO? ISO is a collaborative body, a harmonization effort that works very closely with other harmonization efforts. Their job, or a part of their job, is to come out with some standards or how-tos for us.

The how-tos are drafted and then sent out to all the member bodies within ISO for editing and approval. Once at least 75% of the members have approved the standards they are published.

On the next slide we talk about what ISO 14971 is. It is a worldwide risk management standard coming from ISO but reviewed internationally. It truly is an international effort and it’s today, in my opinion, the best path towards global compliance using risk management methodology to help meet those requirements.

If you’re in the U.S. it dovetails very well with our QSR, 21 CFR Part 820 and the risk management portion therein. It’s being integrated into every technical standard for medical devices, and some people think it will be the only standard for devices in the future, but it’s by no means only for the medical device folks. It’s a very good standard and methodology for putting together a risk management plan, and so people who are in the drug world and in the biologics world are looking at ISO 14971 as being a paramount risk management standard, very applicable to all types of products....
So in conclusion, I just wanted to summarize a few things. This standard for risk analysis, ISO 14971, is one of the best ones out there because it is so thorough and so comprehensive and I really just wanted to give you a flavor for what was in it. You can purchase it from iso.org or from Thomson or you can purchase it from techstreet.com, but it is by no means the only one out there. We’ve talked about several others, HACCP, HAZOP, FMEA, and FMECA. There are plenty of them out there.

The FDA would like you, especially if you’re interested in 21 CFR Part 11 compliance, to have a risk management plan in place. They have said on a number of occasions, representatives from the Agency have, that if you have no risk assessment plan in place they’ll consider everything high risk, which means you have to have a certain level of Part 11 technical controls on those systems that are high risk to control record integrity and record trustworthiness. A risk assessment will ultimately eliminate the amount of work you have to do for Part 11 compliance. People also use risk assessments to reduce the amount of validation or the extent of validation on regulated systems.

The point is that a risk assessment or risk management plan is a good thing to have. You can use one of these protocols whole-heartedly. You can accept maybe a couple of sections from each protocol or from one protocol and then develop the rest of the plan yourself or you can come up with your own risk management plan on your own. There is no right or wrong. The FDA doesn’t tell you which ones to use.

There are other reasons why you do want to do risk management other than compliance—improving quality, using your resources more efficiently, helping your management make more well-informed decisions, especially about risk mitigation, putting together a thorough assessment of your process and having the documentation available for understanding your process. That obviously can’t hurt anybody.

Ms. Lander will once again deliver her presentation via audio conference for PDA on October 13, 2004. Transcripts and CD audio of all PDA audio conferences can be purchased; contact Nancy Berlin, PDA Audio and Web Conferencing Manager, at berlin@pda.org or +1 (301) 656-5900, ext. 158.
Question 1: Biological Indicators
I have a query related to Biological Indicators: If accidentally some indicator ampoules breaks and solution spreads on the floor or any other material, what treatment should be done to destroy the spores spread on the material or floor? What should be the transportation conditions for Biological Indicators?

Response 1
Our SOP is to flood area with spray of sporocidal solution. We have one that we let sit for 30 minutes and then wipe up and throw wipe into BioBag.

Response 2
I would recommend wetting the spill site with a 500 PPM sodium hypochlorite solution, allowing it to sit for a minimum of 10 minutes before wiping up.

Response 3
Right now I am reading a book related with BFS technology, regarding your questions:

How are the plastic bottles depyrogenated in Blow-Fill-Seal technology? BFS technology melt plastics around 170-230 °C and 350 Bar, this conditions assure sterility of the melted plastic and there are challenge tests with resin contaminated with endotoxines and no endotoxin was proven to be in the filled containers, foreign substances are surrounded by the melted plastic and can not migrate form the plastic to the product.

Is the filled and sealed bottle terminally sterilized? How? Yes, containers are sterilized in sterilization chambers, the parameters used depends on the container plastic (polyethylene, polypropylene).

Question 2: Hydrophobic Filters
It is said that in hydrophobic filters which is .22 microns is considered as .01 micron, is it true? Can you please clarify?

Response 1
Since the separation mechanism acting in air and gas filtration is not the simple sieving effect but rather a combination of other complicated mechanisms such as:
- Diffusion effect
- Blocking effect
- Inertial impaction effect
- Electrostatic effect
- Thermal effect
- Sedimentation effect

The above mentioned factors will enhance both effectiveness of filtration and pore size rating and 0.22 micrometer for liquid filtration is rated as 0.01 micrometer for gas or air filtration.

Response 2
0.2 micron air filters certainly retain particles or contaminants which are smaller than the quoted pore size. This is due to different separation mechanisms in air than in liquid. Due to these retention mechanisms one commonly defines a Most Particle Penetrating Point, instead of the pore size. This MPPP has been found to be 10 times lower than the rated pore size. Nevertheless, this depends very much on the process parameters and environmental conditions. Therefore one cannot make the definitive statement, that a 0.2 micron rated filter will have an MPPP of 0.02 micron.

The MPPP might shift due to humidity or velocity shift and conditions.

Commonly the filter manufacturer has specific test results of aerosol challenges, which he will share with you. This might help especially when you are after a specific airborne contaminant.

Question 3: Shelf-Condenser Temperature Differences
I am being told by production personnel that as long as there is a 20° difference between the condensers and the temperature of the shelves during the primary drying cycle that the final
product will not be affected, even though the product TCs tell me that the difference is much smaller. Where does this 20° difference originate? Is this true? Is there an article that can help me under the lyo cycle? Please help.

Response 1
It has been my understanding that a specific difference between shelf temperature and condenser temperature is not extremely critical. During primary drying the shelf temperature is mainly an energy source for the sublimation process. The condenser’s main role is to condense vapors and help maintain proper chamber pressure, i.e., a rise in condenser temperature is usually associated with an increase in chamber pressure and subsequently a rise in product temperature. The extent of a temperature increase is affected by the duration of the excursion. Condenser’s can be utilized to maintain shelf temperature, depending on your particular setup.

Response 2
The parenteral society in the UK do some useful booklets on Lyophilization The web address is www.parenteral.org.uk.

Response 3
This is an interesting rule. It may have substance. Given that the product is loaded at RT (20°C) and the condenser has only 0°C (what clearly would be a defect) the product will still dry at 0°C. It would not be lyophilized anymore, but it could be dry at reasonable low temperature. On the other hand will 20°C differences at, e.g. -40°C, provide sufficient partial water vapor pressure difference to dry the product with reasonable speed?

I have numerous articles on lyophilization. If you would like to contact me directly, I would be happy to pass some along.
PDA is seeking scientific abstracts for a poster session on extractables and leachables from packaging and production systems in pharmaceutical products. The forum will be held May 23-25, 2005, at the Bethesda North Marriott and Conference Center in Bethesda, Maryland.

In conjunction with PDA’s extensive and intensive 2 ½ day symposium on extractables and leachables, the Planning Committee is soliciting abstracts for a poster session designed to augment the symposium’s high level, comprehensive and insightful presentations on the materials, chemistry, regulatory, and toxicological aspects of extractables/leachables studies. As an adjunct to an extensive schedule of podium presentations on relevant subjects such as:

- Packaging and Processing Materials
- Principles of Conducting Extractables and Leachable Studies
- Key Analytical Techniques for Performing an Extractables/Leachables Study
- Extractables/Leachables from Processing Equipment
- Correlating Extractables and Leachables
- Risk Assessment and Acceptance Criteria

The Planning Committee seeks to provide analytical scientists and their associates with a uniquely focused opportunity to share their best demonstrated practices, strategies, tactics, case studies and lessons learned.

Posters related to all types of pharmaceutical products, including metered dose inhalers, dry powder inhalers, nasal sprays, injectables, otics, ophthalmics, oral dosage forms, topical, parenterals, biopharmaceuticals and drug/device combination products, are welcome.

ABSTRACTS MUST BE RECEIVED BY NOVEMBER 1, 2004 FOR CONSIDERATION

COMMERCIAL ABSTRACTS FOR PROMOTING OF PRODUCTS AND/OR SERVICES WILL NOT BE CONSIDERED

Send via e-mail a copy of the abstract and the presenter’s biography (approximately 100 words in length) by November 1, 2004 to: Jason Brown at jbrown@pda.org

Please include the following information. Submissions received without full information will not be considered:

- Title
- Full mailing address
- E-mail address of the presenter
- Key objectives of your poster and the benefits of someone hearing what you have to present
- Presenter’s biography
- Phone number
- 2-3 paragraph abstract, summarizing your poster
- Explanation of specific take-home benefits to target audience for reviewing presentation
- Additional authors
- Fax number
- Target audience

Upon review by the program committee, submitters will be advised in writing of the status of their abstracts after January 1, 2005.
The world we live in is a continuous evolution of old processes. Change is made recognizing the immediate impact but the long-term effect is not always fully known. The idea is to make better our environment and how we fit into it, and sometimes the result is positive and a new path is created to explore and develop. At other times the new path may not encourage exploration, and the end realization is that the best place to be is where you came from.

The latter is where PDA finds itself. With a renewed sense of purpose and dedication to the organization’s mission, the 2005 PDA Annual Meeting will return to providing access to information, education and training in pharmaceutical and biopharmaceutical technology, both domestically and internationally. Chicago, Illinois, an important “hub” of the pharmaceutical industry and home to a growing biotech community, is where PDA will reestablish this position, April 4-8, 2005 at the Hyatt Regency Chicago.

Relying exclusively on PDA resources and membership support, the 2005 PDA Annual Meeting will reintroduce to the membership PDA core meeting values, tailored educational sessions addressing current and pending regulatory processes backed with scientifically sound information, and abundant networking opportunities.

PDA’s guarantee is that the 2005 PDA Annual Meeting will return to the membership a spirit of tradition that has sustained the organization for more than 58 years.

Continue to check www.pda.org for updates on program information. PDA is considering papers for the Annual Meeting until September 30, 2004.

By Deborah Stokes, Programs & Meetings Manager

PDA’s “New Innovative Technologies” Exhibition™ Program

PDA is looking for new, innovative technologies to launch at the 2005 PDA International Congress in Rome, Italy (February) and 2005 PDA Annual Meeting in Chicago, Ill. (April)

Does your company have new products or services to showcase? If so, you may be eligible to receive:

- A discounted or free booth
- Free advertising in the show directory
- Free advertising in PDA Letter
- Promotion on PDA’s Web site for six month after the show
- A special announcement in opening plenary session at the above meeting

Please contact Nahid Kiani at Kiani@pda.org for more details.
CALL FOR PAPERS

The PDA Viral & TSE Safety Conference, in co-sponsorship with EMEA and FDA, is a three-day workshop to discuss current guidance, critical issues and approaches to viral clearance & TSE issues for biologics.

Abstracts and outlines for 20-25 minute presentations or poster displays are sought on the following topics:

- Virus and TSE reference materials and standardization: virus and TSE challenge preparations and assays
- Advances in technology and engineering: clearance processes, virus and TSE assays and safety strategies
- Robustness: evaluation of robustness of clearance processes, critical process parameters and generic approaches
- Contamination control: decontamination strategies, inactivation procedures, facility segregation, resin and membrane cleaning
- Cell substrates: origin, testing history and species specific testing
- Contamination risk assessment and mitigation: response plans, bench marking, and product protection strategies
- TSE safety: evolution and harmonization of safety approaches
- Risks mitigation and control of animal and human-derived raw materials, transgenics, plasma products, tissue products and vaccine substrates

- Case histories are encouraged

Abstracts and Outlines Must be Received by November 1, 2004

Send via e-mail an electronic copy of the abstract and the presenter’s biography (approximately 200 words in length) by November 1, 2004 to: Jason Brown at jbrown@pda.org. Please include the following information:

- Title;
- General category of presentation (see proposed topics above);
- Presenter’s biography;
- Additional authors;
- Full mailing address, phone number, fax number and e-mail address of the presenter;
- Summary of the presentation;
- Target audience (by job title and department); and
- Explanation of specific benefits to target audience for attending this presentation.

Presentations Should be Designed for a Delivery Time of 20 to 25 Minutes.

Presenters whose abstracts are accepted will receive full complimentary conference registration and will be advised in writing of the acceptance of their abstract by December 1, 2004.
Who Should Attend

This new guidance has direct impact on your job responsibilities if you work in:

✓ Manufacturing
✓ Quality Assurance/Quality Control
✓ Regulatory Affairs
✓ Validation
✓ Engineering
✓ Facilities

Overview

FDA published the final guidance on Sterile Drug Products Produced by Aseptic Processing on September 29, 2004.

This much anticipated guidance represents a significant change from the 1987 guidance, and will impact all sterile manufacturing processors.

PDA’s Aseptic Processing: The New Guidance is an up-to-the-minute responsive forum featuring the working group experts who helped develop the new FDA final aseptic processing guidance. This forum spotlights detailed analysis from the working group experts (FDA invited) who contributed to the final document. These experts will help you navigate the guidance while identifying specific implementation strategies. The forum will help you take the new steps now necessary toward aseptic processing compliance.

Learn practical applications of the new guidance, including how to:

✓ Apply environmental monitoring rationales to ensure appropriate control of viable and non-viable particles in critical areas
✓ Interpret FDA’s new position on process simulation and its impact on current industry practice
✓ Understand how updated media fill requirements impact process simulation results
✓ Design, use and validate isolators to give appropriate assurance of environmental control

Who Should Attend

For more information visit
www.pda.org/asepticforums

To learn more about other PDA Career-long Learning opportunities, please visit www.pda.org.
Sartorius crossflow systems ensure the highest cost efficiency in downstream processing – entirely automated. An incomparable membrane design and an efficient cassette geometry minimize processing time. Our filter units Sartocon and Sartocon Slice are more than just an enhancement to your collection.

Sartorius crossflow – from the people who wrote the book.

Yes, we can.
PDA Chapter Contacts

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

**Asia Pacific**

**Australia Chapter**  
Contact: Ken Dibble  
Millipore Australia  
E-mail: ken_dibble@millipore.com

**India Chapter**  
Contact: Darshan Makhey, Ph.D.  
Nicholas Piramal India Limited  
E-mail: dmakhey@nicholaspiramal.com

**Japan Chapter**  
Contact: Yoshiaki Hara  
E-mail: yoshiaki.hara@sartorius.com  

**Korea Chapter**  
Contact: Jun Yeon Park  
E-mail: jun_yeon_park@pall.com

**Southeast Asia Chapter**  
Contact: K. P. P. Prasad, Ph.D.  
Pfizer Asia Pacific Pte Ltd  
E-mail: prasad.kpp@pfizer.com

**Taiwan Chapter**  
Contact: Tuan-Tuan Su  
E-mail: pdatc@ms17.hinet.net

**Europe**

**Central Europe Chapter**  
Contact: Erich Sturzenegger, Ph.D.  
Novartis Pharma AG  
E-mail: erich.sturzenegger@pharma.novartis.com

**France Chapter**  
Contact: Philippe Gomez  
Sartorius Corporation  
E-mail: philippe.gomez@sartorius.com

**Italy Chapter**  
Contact: Vincenzo Baselli  
Pall Italia  
E-mail: vincenzo.baselli@europe.pall.com  
Web site: http://www.pda-it.org

**Prague Chapter**  
Contact: Zdenka Mrvova  
Léčiva A.S.  
E-mail: zdenka.mrvova@zentiva.cz

**Spain Chapter**  
Contact: Jordi Botet, Ph.D.  
STE Compliance Services  
E-mail: jbotet@stegroup.com

**United Kingdom and Ireland Chapter**  
Contact: John Moys  
Sartorius  
E-mail: john.moys@sartorius.com

**Middle East**

**Israel Chapter**  
Contact: Karen S. Ginsbury  
PCI-Pharmaceutical Consulting Israel Ltd.  
E-mail: kstaylor@netvision.net.il

**North America**

**Canada Chapter**  
Contact: Hein Wick  
HVMR, Ltd.  
E-mail: hwick@hvmr.ca

**Capital Area Chapter**  
Areas Served: MD, DC, VA, WV  
Contact: Barry A. Friedman, Ph.D.  
Cambrex Bio Science Baltimore, Inc.  
E-mail: bary.friedman@Cambrex.com  
Web site: www.p dacapitalchapter.org

**Delaware Valley Chapter**  
Areas Served: DE, NJ, PA  
Contact: Art Vellutato, Jr.  
Veltek Associates, Inc.  
E-mail: art@sterile.com  
Web site: www.padv.org

**Metro Chapter**  
Areas Served: NJ, NY  
Contact: Nate Manco  
Sandoz  
E-mail: nate.manco@gx.novartis.com

**Midwest Chapter**  
Areas Served: IL, IN, OH, WI, IA, MN  
Contact: Amy Gotham  
Northview Labs  
E-mail: PDAMidwest@comcast.net

**Mountain States Chapter**  
Areas Served: CO, WY, UT, ID, NE, KS, OK, MT  
Contact: Jeff Beste  
Pendleton Resources  
E-mail: cmdjeff@aol.com  
Web site: www.mspda.org

**New England Chapter**  
Areas Served: MA, CT, RI, NH, VT, ME  
Contact: Mark A. Staples, Ph.D.  
MicroCHIPS  
E-mail: mstaples@microchips.com

**Puerto Rico Chapter**  
Contact: Silma Bladuell  
Wyeth Lederle, Inc.  
E-mail: bladues@wyeth.com

**Southeast Chapter**  
Areas Served: NC, SC, TN, VA, FL, GA  
Contact: Lisa Eklund  
Hospira, Inc.  
E-mail: lisa.eklund@fresenius-kabi.com  
Web site: www.pdas.org

**Southern California Chapter**  
Areas Served: Southern California  
Contact: John Spoden  
Allergan  
E-mail: spoden_john@allergan.com  
Web site: http://www.pda.org/chapters/Website-SoCal/SoCal-index.html

**West Coast Chapter**  
Areas Served: Northern California  
Contact: Randall Tedder  
IconNova  
E-mail: randall@iconnova.com
PDA Interest Groups & Leaders

The following is a list of PDA Interest Groups (IGs). Starting in 2004, PDA began establishing “Branches” of each IG in the various regions of the world served by PDA. 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. Contact information for a “Branch” leader is included where applicable. 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.

Biotechnology
Frank Matarrese
GxP Consulting
E-mail: frank_matarrese@alamedanet.net

European Branch
Roland Günther
Novartis
E-mail: roland.guenther@pharma.novartis.com

Computer Systems
Barbara L. Meserve
Acculogix, Inc.
E-mail: bmeserve@acculogix-usa.com

Drug-Device
Delivery Systems
Raymond A. Fritchard
Consultant
E-mail: raypri@comcast.net

European Branch
Alexander Schlicker, Ph.D.
Hoffmann La Roche Ltd;
E-mail: Alexandra.schlicker@roche.com

Georgios Imanidis, Ph.D.
Pharmaceutical Technology
E-mail: georgios.imanidis@unibas.ch

Filtration
Jack Cole
Jack Cole Associates
E-mail: jcole@aol.com

European Branch
Roger Seiler
Sartorius
E-mail: roger.seiler@sartorius.ch

GMP Purchasing
Nancy M. Kochevar
Amgen, Inc.
E-mail: nancyk@amgen.com

Inspection Trends/
Regulatory Affairs
Robert L. Dana
Elkhorn Associates Inc.
E-mail: elkhemassoc1@aol.com

Isolation Technology
Dimitri P. Worchansky
Jacobs Engineering Group, Inc.
E-mail: dimitri.worchansky@jacobs.com

Lyophilization
Edward H. Trappler
Lyophilization Technology
E-mail: etrappler@lyo-t.com

Microbiology/
Environmental Monitoring
Jeanne E. Moldenhauer, Ph.D.
Vectech Pharmaceutical Consulting, Inc.
E-mail: jeannemoldenhauer@yahoo.com

Nanotechnology
D. F. Chowdhury
Aption Corporation
E-mail: fazc@aol.com

Ophthalmics
Chris Danford
Alcon Laboratories Inc.
E-mail: chris.danford@alconlabs.com

Packaging Science
Edward J. Smith, Ph.D.
Wyeth Pharmaceuticals
E-mail: smithje@wyeth.com

Pharmaceutical Water
Theodore H. Meltzer, Ph.D.
Capitola Consulting Co.
E-mail: theodorehmeltzer@hotmail.com

Production and
Engineering
Frank Bing
Consultant
E-mail: frankbingjr@aol.com

Quality Assurance/
Quality Control
Don E. Elinski
Eli Lilly & Company
E-mail: elinski@aol.com

Stability
Rafik H. Bishara, Ph.D.
Eli Lilly & Company
E-mail: rbi@lilly.com

Technology Transfer
Volker Eck, Ph.D.
Nerviano Medical Science S.r.l.
E-mail: volker.eck@nervianoms.com

Zdenka Mrvova
Zentiva
E-mail: mrvova@leciva.cz

Training
Thomas W. Wilkin, Ed.D.
University of New York
E-mail: twilkin@citytech.cuny.edu

Vaccines
Frank S. Kohn, Ph.D.
FSK Associate
E-mail: fsk@lowatelecom.net

Validation
Bohdan M. Ferenc
Qualification Services
E-mail: bferenc@aol.com

Visual Inspection
of Parenterals
John G. Shabushnig, Ph.D.
Pfizer Inc.
E-mail: john.g.shabushnig@pfizer.com

European Branch
Markus Lankers, Ph.D.
APSYS GmbH
E-mail: markus.lankers@apsys.de

The following is a list of PDA Interest Groups (IGs). Starting in 2004, PDA began establishing “Branches” of each IG in the various regions of the world served by PDA. 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. Contact information for a “Branch” leader is included where applicable. 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.
# 2004 New Technical Book Releases!

<table>
<thead>
<tr>
<th>Title</th>
<th>Author(s)</th>
<th>Description</th>
<th>Item No.</th>
<th>Price (member)</th>
<th>Price (nonmember)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cleanroom Clothing Systems: People as a Contamination Source</strong></td>
<td>Bengt Ljungvist &amp; Bent Reinmueller</td>
<td>If you have responsibilities for maintaining a cleanroom environment, this book is a must-read guide that provides comprehensive observations from case studies performed in a dispersal chamber.</td>
<td>17206</td>
<td>US$ 135</td>
<td>US$ 169</td>
</tr>
<tr>
<td><strong>Pharmaceutical Quality</strong></td>
<td>Edited by Richard Prince</td>
<td>This book offers examinations of quality from international, government, industry, and individual perspectives. It is a must-have reference guide for both pharmaceutical and biopharmaceutical professionals.</td>
<td>17207</td>
<td>US$ 240</td>
<td>US$ 299</td>
</tr>
<tr>
<td><strong>Quality Assurance: A Practitioner’s Guide</strong></td>
<td>U. G. Barad</td>
<td>This is an indispensable tool for students, beginners and experienced professionals working in pharmaceutical companies – large and small. It covers most of the prevailing regulatory requirements and expectations worldwide.</td>
<td>17212</td>
<td>US$ 185</td>
<td>US$ 229</td>
</tr>
<tr>
<td><strong>Filtration Handbook: Liquids</strong></td>
<td>Maik W. Jornitz &amp; Theodore H. Meltzer</td>
<td>This training guide provides both an overview and a comprehensive training course that is invaluable to filtration professionals at all levels.</td>
<td>17208</td>
<td>US$ 185</td>
<td>US$ 229</td>
</tr>
<tr>
<td><strong>Good Practice and Compliance for Electronic Records and Signatures, Part 3, Models for Systems Implementation and Evolution</strong></td>
<td></td>
<td>Part three of the series Good Electronic Records Management, this document, produced by the PDA Part 11 Task Group, provides further discussion for enhancing information technology practices used in the engineering of new computing environments, the remediation of already-installed computing bases, and the subsequent maintenance of both types of computer systems.</td>
<td>13003</td>
<td>US$ 95</td>
<td>US$ 190</td>
</tr>
<tr>
<td><strong>PDA Technical Report No. 32 revised:</strong></td>
<td></td>
<td>This current revision to the technical report by the PDA Industry Advisory Board (IAB) reflects the lessons learned in four years of successful implementation. Also described is how the original Supplier Auditing and Qualification Task Group developed and tested a Process Model and Data Collection Tool. Use of these tools will provide consistent audit information that can be shared within the industry. The audit information, presented as an audit report, is useful in supporting procurement activities and in inferring structural integrity of supplier products when engineering and validating computer systems, helping to meet the FDA challenge.</td>
<td>01032 Paper version</td>
<td>US$ 100</td>
<td>US$ 295</td>
</tr>
<tr>
<td><strong>PDA Technical Report No. 32 revised:</strong></td>
<td></td>
<td>This current revision to the technical report by the PDA Industry Advisory Board (IAB) reflects the lessons learned in four years of successful implementation. Also described is how the original Supplier Auditing and Qualification Task Group developed and tested a Process Model and Data Collection Tool. Use of these tools will provide consistent audit information that can be shared within the industry. The audit information, presented as an audit report, is useful in supporting procurement activities and in inferring structural integrity of supplier products when engineering and validating computer systems, helping to meet the FDA challenge.</td>
<td>01132 CD-ROM version</td>
<td>US$ 75</td>
<td>US$ 270</td>
</tr>
</tbody>
</table>
Use this form to order PDA Technical Resources. If ordering by mail, include a check payable to PDA to the address below. Be sure to include shipping and handling charges in the total. If ordering by fax, please include all credit card information. All orders must include payment. Prices are subject to change at any time.

- Mr.  
- Ms.  
- Dr.  

Name ___________________________ Member No. __________

Company ____________________________

Address ____________________________

City __________________ State ______ Country ______ Zip+4/Postal Code __________

Tel: __________________ Fax: __________ E-mail: __________________________

Not a current PDA member? Join today and save up to 50% on training courses!

✓ Save on PDA meetings, conferences and publications
✓ Gain access to expert, peer-reviewed information relevant to your career
✓ Connect to global and regional science and regulatory expertise
✓ Become a part of the world’s leading international network of pharmaceutical and biopharmaceutical professionals.

Check below to become a PDA member:

- Individual membership fee: US$ 195 (one year)
- Special discounted government/health authority fee: US$ 80 (one year)*

* Must be an employee of an official government agency or health authority

For more details on PDA and the benefits of becoming a member, visit www.pda.org today.

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Title</th>
<th>Qty.</th>
<th>Price</th>
<th>Total</th>
</tr>
</thead>
</table>

Shipping & Handling Rates—Domestic U.S. orders are shipped via UPS Ground. Second-day and next-day air service is available. Call or e-mail for prices.

### International Orders

<table>
<thead>
<tr>
<th>If your order totals:</th>
<th>Add:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to US$ 199.99</td>
<td>20% (minimum US$ 20)</td>
</tr>
<tr>
<td>US$ 200.00 or more</td>
<td>30% (maximum US$ 300)</td>
</tr>
</tbody>
</table>

All orders amount below US$ 200.00 will be shipped by priority air and are not traceable, delivery in 3-8 weeks.

### U.S., Puerto Rico & Canada

<table>
<thead>
<tr>
<th>If your order totals:</th>
<th>Add:</th>
</tr>
</thead>
<tbody>
<tr>
<td>US$ 15.00 and under</td>
<td>US$ 6.95</td>
</tr>
<tr>
<td>US$ 15.01–75.00</td>
<td>US$ 8.95</td>
</tr>
<tr>
<td>US$ 75.01–150.00</td>
<td>US$ 10.95</td>
</tr>
<tr>
<td>US$ 150.01–250.00</td>
<td>US$ 12.95</td>
</tr>
<tr>
<td>US$ 250.01–500.00</td>
<td>US$ 14.95</td>
</tr>
<tr>
<td>US$ 500.01 or more</td>
<td>US$ 17.95</td>
</tr>
</tbody>
</table>

5. RETURN COMPLETED FORM WITH CHECK OR BANK DRAFT MADE TO: PDA, P.O. Box 79465, Baltimore, MD 21279-0465 USA  
   FAX CREDIT CARD PAYMENTS TO: +1 (301) 986-1093 (credit cards only)
### PDA Training and Research Institute Registration Form

**PDA Training and Research Institute**

**PDA, 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814 USA**

**Deadline:** Enrollment is limited for the benefit of all attendees; this necessitates early registration. Paid registrations must be received one week prior to the event. 

**Confirmation:** Written confirmation will be sent to you once payment is received. You must have this written confirmation to be considered enrolled in a PDA event. Please allow one week for receipt of confirmation letter. 

**Refunds:** Refund requests must be in writing. If received one month prior to the start of the event (course series, conference, etc.), a full refund, minus a US$ 55 handling fee, will be made. If received two weeks prior to the event, one-half of the registration fee will be refunded. After that time, no refunds will be made.

**Event Cancellation:** PDA reserves the right to modify the material or instructors without notice or to cancel an event. If an event must be canceled, registrants will be notified as soon as possible and will receive a full refund of fees paid. PDA will not be responsible for discount airfare penalties or other costs incurred due to a cancellation.

**Course Title/Course No.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Current Member</th>
<th>Join PDA and Attend Course</th>
<th>Attend Course Only; Do Not Join PDA</th>
<th>Government/Health Authority Employee *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*You must be an employee of an official government agency or health authority to qualify for this rate.

**Bank Address:**

UBS AG Basel

Postfach

Aeschenplatz 6

4002 Basel, Switzerland

**Wire Transfer Payments:**

Wire transfer payments must be made in US dollars only to:

PDA, 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814 USA

Net proceeds will be paid directly to UBS AG Basel, Postfach, Aeschenplatz 6, 4002 Basel, Switzerland.

**Bank Address:**

UBS AG Basel

Postfach

Aeschenplatz 6

4002 Basel, Switzerland

**Wire Transfer Confirmation:**

(insert your confirmation of receipt by UBS Bank here.)

**Currency conversions available at:**

www.forex.com/

www.forex_market_commentary.html

**Refund Requests:**

Refund requests must be in writing. If received one month prior to the start of an event (course series, conference, etc.,), a full refund, minus a US$ 55 handling fee, will be made. If received two weeks prior to the event, one-half of the registration fee will be refunded. After that time, no refunds will be made.

**Substitutions:** If a registrant is unable to attend, substitutions are welcome and can be made at any time, even on-site up to the time of the course. If you are pre-registering as a substitute attendee, indicate this on the registration form.

---

**Plus…**

You are not considered registered for a PDA course until payment is received and a confirmation letter is issued by PDA. Should you attend a course without a formal confirmation or receipt of payment you will be required to provide a credit card as guarantee of payment at the time of the course.

**Not a current PDA member? Join today and save up to 50% on training courses!**

- Save on PDA meetings, conferences and publications
- Connect to global and regional science and regulatory expertise
- Gain access to expert, peer-reviewed information relevant to your career
- Become a part of the world’s leading international network of pharmaceutical and biopharmaceutical professionals.

**Check below to become a PDA member:**

- Individual membership fee: $195 U.S. (one year)
- Special discounted government/health authority fee: $80 U.S. (one year)*

* Must be an employee of an official government agency or health authority

**Special discounted government/health authority fee: $80 U.S. (one year)**

**Plus…**

- Gain access to expert, peer-reviewed information relevant to your career
- Become a part of the world’s leading international network of pharmaceutical and biopharmaceutical professionals.

---

**4. Please check the appropriate box:**

- Charge: □ MasterCard/EuroCard □ VISA □ AmEx □ Dinners Club
- Payment Options:
  - A. By Credit Card (VISA, MasterCard/EuroCard, American Express, Dinners Club), clearly indicating account number and expiration date and billing address. Proceed to Item 6 below.
  - B. By Bankers’ Draft/Check forwarded together with the registration form PAYABLE IN US DOLLARS ONLY to:
    - PDA, 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814 USA
    - Please mark here to request a PROFORMA INVOICE from PDA to process your company payment.

**Wire Transfer Payments:**

Wire transfer payments must be made in US dollars only to:

PDA, 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814 USA

Net proceeds will be paid directly to UBS AG Basel, Postfach, Aeschenplatz 6, 4002 Basel, Switzerland.

**Wire Transfer Confirmation:**

(insert your confirmation of receipt by UBS Bank here.)

---

**5. RETURN COMPLETED FORM WITH CHECK OR BANK DRAFT MADE TO:**

PDA, 3 Bethesda Metro Center, Suite 1500, Bethesda, MD 20814 USA

**FAX CREDIT CARD REGISTRATIONS TO:**

+(301) 986-1093 (credit cards only)

---

**Please reference code:**

2-2-2000

---

**Currency conversions available at:**

www.forex.com/

www.forex_market_commentary.html

---

**Note:**

- You are not considered registered for a PDA course until payment is received and a confirmation letter is issued by PDA. Should you attend a course without a formal confirmation or receipt of payment you will be required to provide a credit card as guarantee of payment at the time of the course.
The TexShield product line was developed to address the contamination control concerns of sterile product manufacturers. We realize you need products that offer assured sterility and uncompromised quality. We understand the importance of the documentation you receive with every sterile product you buy. We know you are looking to improve safety and reduce waste when using sterile alcohol products.

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

The TexShield product line includes Sterile 70% Isopropyl Alcohol, Sterile 70% Isopropyl Alcohol with WFI, Isolator Cleaning Tools and Sterile Pens.
For over forty years the Kaye name has been recognized for uncompromising accuracy and reliability in thermal process measurement. We’ve always been very good at what we do, and we’re about to get even better.

With GE’s technical expertise, global reach and financial strength we now have the horsepower to take on even greater challenges. In the months and years ahead look for new and exciting solutions from the people you’ve trusted for decades, but look for us under a new name.

GE Infrastructure Sensing

Sensing change for the better.
together with
PDA France Chapter presents

New Success Factors for Bio/Pharmaceutical Manufacturing in Europe
Insights, Tips and Tactics from European Leaders After the First Six Months of EU Enlargement

6-7 December 2004
Paris, France

A Valuable 2 Days for:

- **Manufacturing**
  Middle Managers
  Senior Managers
  Hear straight from the source about the benefits of a risk management approach in manufacturing for the 21st Century
  New Information You Can Use Immediately:
  - Clear knowledge about what are the risks and how to manage them in pharmaceutical manufacturing
  - Successfully apply risk management tools to your processes
  Get first-hand information from a representative of the EU Commission on the impact of the EU enlargement

- **Quality**
  Middle Managers
  Senior Managers
  Learn the rationale behind the revision of the Directive for GMP of Active Substances and Excipients (Directive 2003-84)
  New Information You Can Use Immediately:
  - Understand why the Directive was necessary and how it will affect you and your organisation
  - The most current experience and tactics on the Directive from Europe’s expert leaders

- **Regulatory**
  Middle Managers
  Senior Managers
  Understand how to evaluate and assess the critical factors to consider when making a strategic decision on where to conduct clinical trials
  New Information You Can Use Immediately:
  - Choose the correct region in Europe to submit your clinical trials application
  - Shortened decision making processes through a full understanding of up-to-date requirements
  Gain a first-hand practical understanding of country-specific requirements for a clinical trial application

New Information You Can Use Immediately:
- Better planning tools for future resource allocation and emphasis in your departments
- Immediate tips from the personal experiences of a senior EU commission representative after 6 months of the EU enlargement

In-depth discussions and practical insights on regulatory compliance and implementation challenges for European manufacturers.

Venue
InterContinental
Legrand-Paris
2 Rue Scribe
Paris, 75009
Tel: 33 (0) 140 07 3232
FAX: 33 (0) 142 66 1251

Register Today!
Visit www.pda.org/paris2004 for the full programme and to register.

Exhibition opportunities available!
For more information, contact:
Robert Jenks
European Business Development Coordinator
Tel: +32 2 643 2045
E-mail: jenks@pda.org

To learn more about other PDA Career-long Learning opportunities, please visit www.pda.org.