Volume XL, No. 10

PDA Letter

October 2004

Reminder: Please Return your completed PDA Board of Directors election ballot (mailed with last month's issue) to PDA by October 29.

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.

Next month's issue will feature expanded coverage of this remarkable event, as well as full coverage of the latest news regarding FDA's 21st Century regulatory overhaul.

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

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PDA Letter

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
- **November 17-19—Practical Aspects of Aseptic Processing,** Basel, Switzerland
- **December 6-7—New Sucess Factors for Bio/ Pharmaceuticals Manufacturing in Europe,** Paris, France
- **February 28-March 4, 2005—PDA International Conference,** Rome Italy

IN THIS ISSUE...

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   (Item no. 12001, US$ 45/member, US$ 60/nonmember)

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   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)

10. Fundamentals of an Environmental Monitoring Program, PDA Technical Report No. 13 Revised
    (Item No. 01013, US$ 75/member, US$ 270/nonmember)

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Neal G. Koller
PDA President

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

Vice President's Message

George A. Robertson
VP, Science & Technology

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. ■

Call for Volunteers

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

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✓ **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)455-5981; Fax: +1 (410) 455-5802

Or, visit **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."

"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."

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." A document lacking a clear definition for 'risk' and other key concepts "will be a disservice," he asserts.

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. I think there is another bigger picture which is a little bit more high level: Most companies might have people dedicated to what they call risk management, but they overlook how to apply the total concept of risk management in all the areas of the business. I think maybe that is an area with opportunities for education and development. So risk management as a business strategy. That is much bigger than looking at just product risk management. It is actually looking at the whole spectrum of business. Product risk management is probably one piece of maybe seven pieces."

When asked about the other types of risk management, Prof. Chan explains that everyone from finance to marketing should be operating according to the company's risk management plan. "I think risk management is very beneficial to business, but I do not believe companies are applying it to the whole enterprise. I think there are so many opportunities." As to how to do this, Prof. Chan is working on it: "I've been doing studies to actually translate this risk management into the enterprise."

"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."

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

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.

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.

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

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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.

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.

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.

The HACCP approach for medical products is gaining momentum. Last year, the World Health Organization (WHO) endorsed HACCP as a quality tool for pharmaceuticals in its WHO Technical Report Series, No. 908, 2003.

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."

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 PUBLICATIONS AVAILABLE LATE AUTUMN 2004

4 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

3 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

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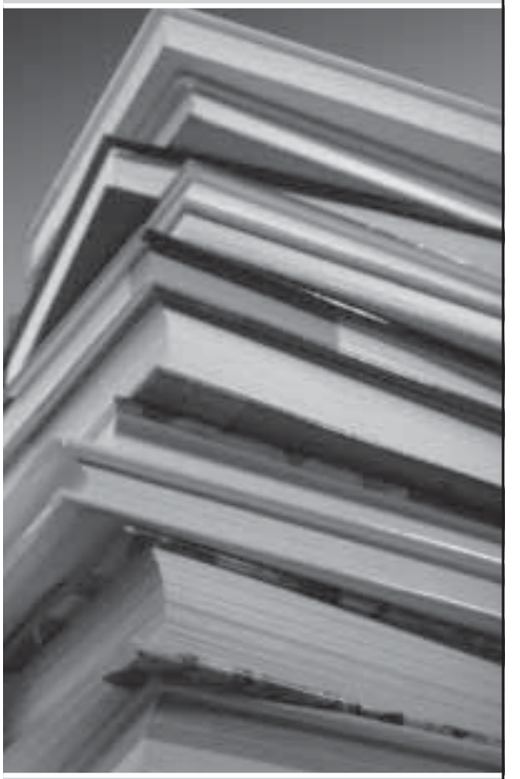

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PROGRAMS AND MEETINGS CALENDAR

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

TRAINING AND RESEARCH INSTITUTE CALENDAR

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

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

27-28 Developing/Validating Cleaning & Disinfection Prgms. for Controlled Envn.

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

On July 22, PDA hosted an audio conference on "Implementing a Global Risk Standard to Assess Risk and Improve Quality Processes." The speaker, Victoria Lander, Application Development Manager, NuGenesis Technologies Corporation, detailed why ISO 14971 is the only standard for devices to meet risk benchmarks in both the European Union and the United States. In fact, ISO 14971 is being integrated into every technical standard for medical devices. Ms. Lander discussed how ISO 14971 blends with the risk management portion of 21 CFR 820.

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 mangement standards. She makes a good case for why pharmaceutical companies should pay attention to these standards, particularly ISO 14971. The second excert jumps ahead to Ms. Lander's conclusion. In between these two segments, Ms. Landards 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 21CFR 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, 21CFR 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....

[JUMP FORWARD]

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—improv-ing quality, using your resources more efficiently, helping your management make more well-informed decisions, especially about risk mitiga-tion, 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. ■

Recent Sci-Tech Discussions

The following, unedited remarks are taken from the Pharmaceutical Sci-Tech Discussion Group, a PDA-sponsored Online Forum at www.pda.org. PDA Online Forums are free of charge and open to the public. They serve as a platform for exchanging practical and sometimes theoretical, ideas within the context of some of the most challenging issues confronting the pharmaceutical industry. If you are not currently a member of a discussion group, we encourage you to visit our Web site and join. Visit **www.pda.org** to sign up via the Web or send an e-mail to **requests@www2.pharmweb.net.**

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 endotoxine 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.

I have numerous articles on lyophilization. If you would like to contact me directly, I would be happy to pass some along.

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?

Call for Posters

2005 PDA Extractables/Leachables Forum

"The Extractables Puzzle: An Integrated Team Approach"

Marriott Bethesda North, Bethesda, Md.

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 CONSIDERATON

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.

PDA Annual Conference 2005: *Pharmaceutical Manufacturing Science in the 21st Century*

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.

PDA Viral & TSE Safety Conference

In Co-sponsorship with EMEA and FDA

Hyatt Regency Bethesda ■ Bethesda, Maryland ■ May 16-18, 2005

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.

PDA
An International Association For Pharmaceutical Science And Technology

presents

Aseptic Processing: The New Guidance

Hear from Industry Experts (FDA invited)!

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

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

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

Two dates and venues are offered for your convenience:

Washington, D.C.
29 October 2004

Frankfurt, Germany
16 November 2004

Venues

Washington, D.C.
Park Hyatt Washington
24th & M St., NW
Washington, DC 20037
(202) 789-1234

Frankfurt, Germany
Sheraton Frankfurt
Hotel and Towers
Rhein-Main Airport
Frankfurt Am Main
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Registration Fees

PDA Member	**US$ 695**
Nonmember	**US$ 890**
Government	**US$ 320**
Student	**US$ 150**

Registration

For more information and to register, visit www.pda.org/asepticforums or complete the attached registration form and fax or mail to:

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

For more information visit www.pda.org/asepticforums

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

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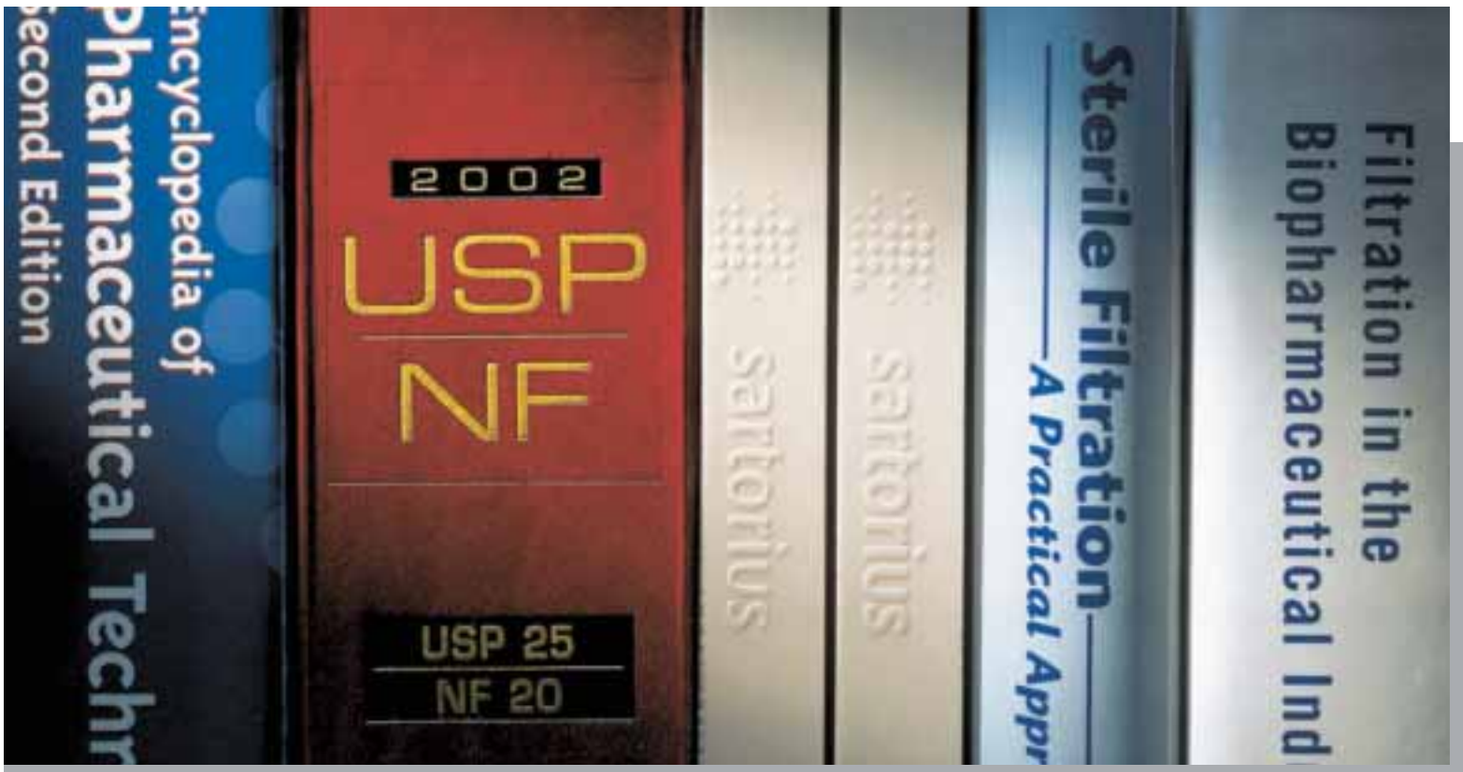

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37075 Goettingen, Germany
Phone +49.551.308.0
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crossflowbook@sartorius.com
www.sartorius.com

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
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Japan Chapter
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STE Compliance Services
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Capital Area Chapter
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Delaware Valley Chapter
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Web site: www.pdadv.org

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

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2004 New Technical Book Releases!

Cleanroom Clothing Systems: People as a Contamination Source
By Bengt Ljungqvist & Berit Reinmueller

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.

Item No. 17206
US$ 135 member/US$ 169 nonmember

Pharmaceutical Quality
Edited by Richard Prince

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.

Item No. 17207
US$ 240 member/US$ 299 nonmember

Quality Assurance: A Practitioner's Guide
Author: U. G. Barad

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.

Item No. 17212
US$ 185 member/US$ 229 nonmember

Filtration handbook: Liquids
Authors: Maik W. Jornitz & Theodore H. Meltzer

This training guide provides both an overview and a comprehensive training course that is invaluable to filtration professionals at all levels.

Item No. 17208
US$ 185 member/US$ 229 nonmember

Good Practice and Compliance for Electronic Records and Signatures, Part 3, Models for Systems Implementation and Evolution

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.

Item No. 13003
US$ 95 member/US$ 190 nonmember

PDA Technical Report No. 32 revised:
Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations

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.

Item No. 01032 Paper version
Price: US$ 100 member/US$ 295 nonmember

Item No. 01132 CD-ROM version
Price: US$ 75 member/US$ 270 nonmember

Document Order Form

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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.

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TOTAL	

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

Job Title Membership Number

Company/Organization

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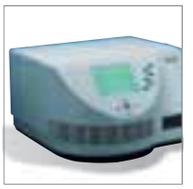

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- Successfully apply risk management tools to your processes

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- The most current experience and tactics on the Directive from Europe's expert leaders

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- 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

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