Science • Technology • Quality • Regulatory • Community

PDA Letter

Volume XLI • Issue #1

January 2005

In This Issue...

PDA Launches Training Program On FDA Aseptic Processing Guidance

PDA Project Management Tool Introduced at Forums; Audience Survey Sheds Light on Cross-Continental Aseptic Practices

Within one month of the publication of the U.S. FDA's final guidance on aseptic processing cGMPs, PDA sponsored a one-day forum on implementation of the document in Washington, D.C. Two weeks later, the forum was repeated in Frankfurt, Germany.

The forum, called *Aseptic Processing: The New Guidance,* was well received by the PDA community, with the Washington event drawing over 200 participants and Frankfurt nearly 100. Participants deemed the conference highly relevant to their careers and the job functions they perform.

The focus of the forum was on three areas of the guidance: process simulation, environmental monitoring and isolators. (*See page 14 for a list of the speakers.*)

The FDA Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) supported the conference with presentations by **Richard Friedman,** Team Leader, Guidance & Policy, and **Robert Sausville,** Supervisory Consumer Safety Officer, respectively.

A project management tool developed by a member of the program committee was distributed to delegates at both the Washington and Frankfurt events. Another highlight was a survey on aseptic processing practices which was conducted at both locations.

Martin Van Trieste
Bayer Healthcare

What PDA Is About!

PDA President **Neal Koller** opened the Washington meeting by crediting the Program Committee for their hard

continued on page 14

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2005 PDA International Congress

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Neal G. Koller
PDA President

President's Message

You Spoke. We Listened.

The new year promises to be an exciting one for the PDA community, as we introduce several membership enhancements in response to the 2004 Membership Survey.

First, on behalf of the PDA staff and Board of Directors, I want to acknowledge and thank all those who took the time to participate in the survey. Participation was excellent, both in the number and quality of responses.

PDA relies on such data to better tailor our technical resources, events and courses to the ever-evolving professional needs of our membership. In fact, we received great feedback regarding our conferences; and we have made several enhancements to our 2005 event planning strategy in response.

Most of the survey responses related to PDA events focused on the pricing and content of PDA conferences.

With regard to pricing, the membership indicated that price increases implemented over the last four to five years have become an issue. So, we began revamping the conference fees with the 2004 PDA/FDA Joint Regulatory Conference last September, and the policy will carry into 2005.

Specifically, for PDA's 2½-day key conferences, the price has been reduced, per the member survey, to US$ 895 or EU€ 895. For 2½-day focus meetings, the price has been reduced to US$ 1,050 or EU€ 1,050. Single-day events held in conjunction with PDA Chapters have been reduced to US$ 200-300 or EU€ 200-300. We hope this pricing increases the value of PDA *Career-long Learning*™ conferences and significantly increases your opportunity to attend.

The changes we have implemented in the way of conference content are based on member input, and are also aimed at increasing your value and your opportunity to attend. The overriding message in the data was that PDA needs to provide more focused meetings.

In 2005, we are already heading this advice. For instance, we have scheduled a focus meeting on Viral and TSE Safety for May in Washington, D.C., and a focus meeting on Extractables/Leachables for May in Washington, and we are planning a focus meeting on Visual Inspections in October. Moreover, we have scheduled four focus workshops on implementation strategies for the new aseptic guidance from FDA—part of PDA's training program for the aseptic guidance which we launched in 2004 with two focus workshops (*see cover).*

With regard to PDA's key conferences, specifically the International Congress (in March in Rome) and the Annual Meeting (in April in Chicago), each features very focused learning tracks. Every track is very specific to department and job title. So your learning experience will be very close to your job. In fact, for each event, PDA will also provide specialized Learning Maps, to help you target those sessions of the conference that best matches your job and area(s) of interest.

In the coming months, I will discuss additional membership enhancements PDA is enacting in response to the 2004 Membership Survey. The feedback covered a wide range of PDA benefits and services, and the enhancements will greatly increase the value of membership in our community.

Again, thank you for your participation. Together we will continue to make PDA your Association for the latest in science and technology.

PDA
An International Association For Pharmaceutical Science And Technology

presents

PDA Viral & TSE Safety Conference

Updating the Strategy for the 21st Century

In Co-Sponsorship with EMEA and FDA

Overview

This three-day international conference, **co-sponsored for the first time by both EMEA and FDA,** will provide opportunities for dialog on current guidance, critical issues, and new technology and approaches to viral and and TSE safety.

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

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

- Current and future **viral clearance technologies**;
- Current opinions on the need for **standardization** in viral clearance studies;
- Evaluating and understanding of the **robustness** of common clearance steps;
- Contamination control, **risk assessment and mitigation** including facility-wide decontamination, segregation and inactivation procedures (e.g. resin and membrane cleaning);
- Current issues in **TSE safety**;
- Risk mitigation and control of **animal and human derived raw materials** (e.g. trangenics, plasma products, tissue products); and,
- Current **regulatory perspectives** from EMEA, FDA and industry.

Who Should Attend

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

- ✓ **Pharmaceutical**
- ✓ **Biotechnology**
- ✓ **Manufacturing Sciences**
- ✓ **Pathogen Safety Groups**
- ✓ **Quality Assurance**
- ✓ **Quality Control**
- ✓ **Process Development**
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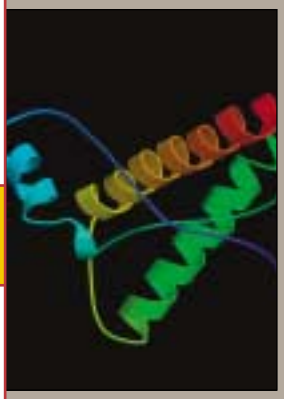
Washington, D.C.

May 16-18, 2005



Venue

Washington, D.C.
Hyatt Regency Bethesda
One Bethesda Metro Center
Bethesda, MD 20814

+1 (301) 657-1234 or
+1 (888) 591-1234

Room rate: $209 + tax

Reservations can be made until Friday, April 22, 2005

Registration Fees

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

To Register

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

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

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

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

2005 PDA Board of Directors

PDA is proud to announce the 2005 Board of Directors. PDA members recently elected two new Directors and reelected two Directors. We congratulate all of them! The election of **Eric Sheinin,** PhD, Vice President of Standards Development, USP, reflects the importance of pharmacopeial matters to the PDA community and the involvement of many members in USP activities. The election of **Laura Thoma,** PharmD, Associate Professor and Director of Parenteral Medications Laboratory, University of Tennessee, reflects the strong ties between PDA and the academic community. By reelecting **Kathleen Greene,** Novartis, and **Tim Marten,** DPhil, AstraZeneca, the PDA community signalled their appreciation for the hard work and many contributions of these two outstanding PDA members.

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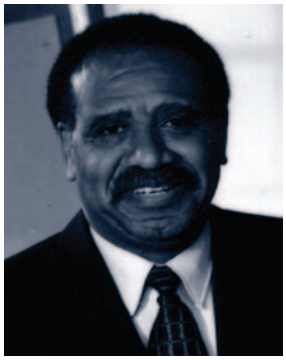

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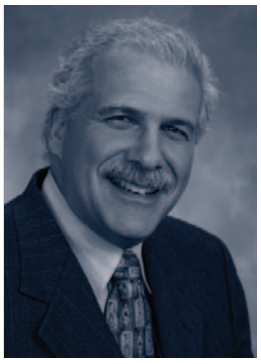

Eric Sheinin, PhD
USP

Lisa M. Skeens, PhD
Baxter Healthcare Corporation

Laura Thoma, PharmD
University of Tennessee

Anders Vinther, PhD
CMC Biopharmaceuticals A/S

George A. Robertson
Vice President, Science and Technology

Vice President's Message

PDA's Pharmaceutical Sci-Tech Discussion Group: A Resource Not To Be Forgotten

I am devoting my Science and Technology column this month to one of the resources that PDA has provided its members and the pharmaceutical scientific community at large for almost ten years.

The discussion group was created by PDA to provide a vehicle for the free exchange of information in the areas of international pharmaceutical manufacturing, quality control, process validation and regulatory affairs, emphasizing but not limited to, sterile products technology. It is open to anybody with an interest in pharmaceutical science and technology.

The moderators are either a member of the S&T headquarters staff or a volunteer. Currently, my assistant, Christopher Flores, has the task.

As you know, selected topics are presented in the *PDA Letter* and comprise some very useful and interesting subjects. This year alone, 20 discussions were published in the *PDA Letter*. Among the topics covered were:

- Rationale and methods for the detection of head space vacuum in lyophilized vials
- What constitutes an acceptable "low" bioburden?
- How are plastic bottles depyrogenated during the blow-fill-seal process?
- Significance of the difference between the condenser temperature and the shelf temperature in a lyophilization apparatus
- Validation of the dye-leak test for sealed ampoules
- Explanation of the "micron" cut-off rating for hydrophobic (and hydrophilic) filters
- Biosafety/contamination concerns with biological indicators
- Effectiveness of washing incoming vials/bottles in lieu of a depyrogenation tunnel
- Discussion of the (non) use of gamma irradiation with sterile injectables
- Are there established limits when setting acceptance criteria for assay parameters such as variance, standard deviation or coefficient variation

As you can see, the scope of the topics spans most of the landscape of interest to PDA members. It should be mentioned that the respondents to these questions are not speaking for any regulatory authority or PDA, and are their own opinions.

One thing I've learned during my first year at PDA is that there is an amazing spirit of camaraderie and cooperation among the members. There's very little "I've got a secret" when it comes to tackling the numerous challenges that we all face in our profession. The comments, freely given, are more examples of how PDA continues to pay dividends to its members.

The Sci-Tech Discussion Group can be accessed through the PDA Science and technology homepage or directly at **www.pharmweb.net/pwmirror/pwq/pharmwebq2.html.**

PDA Web Surveys

PDA has recently created Web-based surveys used by its Task Forces to track the latest developments and recent trends in the industry. Please take the time to fill out one or more surveys on the following topics: Extractables • Pharmaceutical Water • AQL Glass Defects • Terminal Sterilization.

To participate please visit www.pda.org/science/surveys/surveyintro.html

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: www.pharmweb.net/pwmirror/pwq/pharmwebq2.html.

Insecticide fumigation in clean rooms

We have the following questions about the insecticide fumigation in clean rooms for manufacturing injections. Your prompt answers or comments will be greatly appreciated.

Question 1: Is insecticide fumigation for clean rooms a common practice in US or EU?

Question 2: When do you conduct fumigation, after the completion of the clean room construction and before its use, periodically, or both occasions?

Question 3: Are there any other points to consider when selecting an insecticide in addition to the efficacy and the easiness of removing after fumigation?

Question 4: Which insecticide do you recommend, phenothrin, phosphoric compounds or any other insecticide?

Respondent 1

In response to your questions:

Question 1: NO - there is something very wrong with your facility's design, and with your insect control program if insects ever get into your cleanroom. Concentrate your efforts on keeping the insects out of the building, or restrict them to the perimeter areas, do not wait for them to get into the clean room.

Question 2: In the EU, it is common to use formaldehyde as an antibacterial fumigant (typically monthly, or quarterly). It is very uncommon to use such fumigation in the USA.

Question 3: DO NOT USE INSECTICIDES IN A CLEAN ROOM - END OF DICUSSION!

Question 4: NONE

Respondent 2

What are the reasons that your clean rooms need insecticide fumigation? How do insects get in there? The principles of clean room design and construction are preventing contaminants (insect included) from getting IN to begin with.

Fumigation contact time

Please let me know about the minimum contact time for fumigation using formaldehyde. Also please tell a reference.

Respondent 1

There are other methods as effective as formaldehyde. One is using the Core2Clean systems with Peracetic Acid and H202 or just H202. These are portable fogging units. You can see them at www.sterile.com. There are also many other methods that include fixed systems like the Bioquelle.

Formaldehyde may take up to a week of down time before you can release the area. And, you need a medical staff available during the gas time. It is very dangerous and has been basically removed from most operations. And then the issue arises of does such gas residue make it to product bottles. The gas time may be 5-7 hours but the release time is very large. And then, you have to wipe down all critical surfaces. With VHP (H202) you do not need to wipe down and release time may be a day. With PA and H202 the time for release may be a day and you'll have limited wipe down.

But then again, why do we need to fog? Can we not clean the surfaces manually using a multistep cleaning regime? While we search for ways to fog large scale production areas we forget one thing. IT DOES NOT CLEAN THE SURFACES. And thus, we are forced to clean the surfaces BEFORE we fog. Normality is people do this after a shut down. Why? Because they want a quick fix. But during shut down things like wall patching, filter removal/replacement, and stripping and subsequent sealing of floors occurs. This represents a huge level of particulates that if not removed will soak up the active ingredients in our disinfectants and sporicides. That means we have dirtied surfaces that will cause future problems and contamination. Simply, we can't just fog and then be done with it. We need to clean first and then either fog or spray a sporicidal agent to the surfaces for a reasonable wetted time (5 minutes).

I hate to see firms forget the importance of cleaning and assume fogging to kill live cells is the only concern we have.

Respondent 2

I think there are details in the Pharmweb archive for formaldehyde gassing dating from 4-5 years ago (if still available). However, in a few words, as I remember, the conditions are something like this, a minimum exposure time of 4 to 6 h at a concentration between 2g/m^3 and 4 g/m^3 formaldehyde gas. Keep at a temperature between 20°C and 25°C and relative humidity between 60% and 80%.

Somebody please correct me if I remembered incorrectly.

All the companies I worked with (in the EU) have used or do use formaldehyde gassing (or equivalent). I have rarely, if ever heard of it being used in the US. Art is quite right about alternatives and they may certainly be easier and safer though not necessarily cheaper.

Why fog ? That's a bit subjective perhaps. Is it comfort factor ? I've used it as a preventative decontamination step at end campaign for live biologicals, particularly for virus manufacture. Doing it at the start will leave undesirable residues that you may not find. I would never use it as a substitute for cleaning. Art is correct, you always need to follow up with a full clean down since depending on the zone temperature at the end of the gassing you may get significant deposits to clean up. The other point to bear in mind is than formaldehyde is a small molecule and can easily diffuse everywhere. So even if you tape up your clean room you can't assume its airtight. Both the tape seals and silicone joints may leak or you may get induction through your HVAC ducting and AHU system. Formaldehyde gas could end up in lethal concentrations elsewhere !

Respondent 3

This is consistent with the literature on the subject. There are debates about the exact concentration and humidity range as one would expect. See J. Toxicol. Environ. Health 1997 Feb 21: 50(3) 217-63 for this quote "the panel agreed with pother scientific groups who have concluded that cancer risk of formaldehyde is negligible at airborne concentrations that do not produce chronic irritation". The article is a bit old but so is all the data. As I recall the alarming tox studies were done at too high a concentration to be useful.

Why fog ?In this context it's important to remember that fogging works wherever the droplets land but formaldehyde treatment is not by fogging but by vapor!

Area recovery test of clean rooms

Can somebody suggest regarding the type/ amount of particulate contamination we need to generate and the time period of recovery of area . Does this have a correlation with the room air changes of room.

We used to generate DOP/Edina oil smoke in the room and test the recovery every 10 minutes afterwards and have a validated time period of 20 minutes max.

But we have class B clean rooms with both 40 & 60 air changes /hour, sometimes more than 100 air changes in some rooms like gowning etc. But we have observed not so significant difference in the recovery period.

Do the members agree with the procedure we are following in our facility?Of course we do not have any specifications on the amount of contaminants. This we do with our experience.

Respondent 1

I have never encountered "Recovery Test" in qualifying a clean room. I can see the COMPLEXITY of setting a meaningful test involving room size, quantitative distribution of particles inside the room, and the dynamic of clearing the particles, but I cannot see the UTILITY of such a test, since clean rooms do not involve in issues of generating large amount of particles to be effectively cleared (unless probably in powder handling rooms).

Respondent 2

What I normally do is set up the particle counter by an extract duct and "set off" a smoke pencil in a distant corner and note the time at which the counter goes out of limit. If your particle counter has an audible alarm this may help. I then remove the smoke pencil and determine how quickly the room (at the measurement location) comes back into specification.

This parameter is particularly useful in determining changing room clean up rates which in accordance with EU GMP only have to meet their spec in the "At Rest" condition. Obviously one needs to understand room performance in the operational state and the test as described is ideal. Room recovery rate (I believe) was a requirement of the old BS 5295 for clean room classification I do not know if it made it to the new ISO standard.

Respondent 3

The recovery is tested usually after dynamic operation at the room and not when you simulating the particles. You can use British MCA guideline that giving exact limits for particles and recovery time. www.mca.gov.uk

PDA Interest Groups & Leaders

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

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

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University of New York
E-mail: twilkin@citytech.cuny.edu

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

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

Visual Inspection of Parenterals
John G. Shabushnig, PhD
Pfizer Inc.
E-mail: john.g.shabushnig@pfizer.com
European Branch
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APSYS GmbH
E-mail: markus.lankers@apsys.de

PDA Launches Training Program On FDA Aseptic Processing Guidance, from cover

work on short notice to organize the events. **Richard Johnson,** Director, Quality Center of Excellence – Drugs, Abbott Laboratories and **Martin Van Trieste,** Vice President Quality, Bayer HealthCare, co-chaired the committee (*see sidebar*).

Koller emphasized that the forum was a "perfect example of the PDA Mission at work and of what PDA is all about."

Program planner Van Trieste stressed that "a core competency of PDA and its members [is] how to do sterilization and aseptic processing."

PDA training on the new FDA aseptic conference continues this year. In the tradition of PDA's training workshop for the International Conference on Harmonisation (ICH) quality guideline on cGMPs for active ingredients (Q7A), the Association is holding the *Aseptic Processing Guidance: Training Workshop,* in four different locations in the first half of 2005: San Francisco (Feb. 17-18), Philadelphia (March 14-15) and London (May 3-4).

Building on the one-day forums in Washington and Frankfurt, the 2005 training workshops will have an expanded agenda and cover nearly every section of the final guidance. FDA will continue to lend its expertise to the training effort.

Previewing the workshop at the 2004 forums, Van Trieste explained, "The two-day conferences next year will go into a lot more depth about each of [the] topics covered in the guidance document." The limited number of topics covered in the one-day forum "was a matter of time. We decided we needed to do something quickly to help the membership in terms of how to interpret the guidance document and how to move forward."

Setting the Tone for Implementation

By offering the aseptic guidance forum on two continents within sixty days of the document's publication, PDA set the tone for how the community should view the guidance. Rather than use the forum as time to rehash issues debated during the guidance development process, the focus was squarely on strategies for implementing key provisions.

Van Trieste emphasized this philosophy during his discussion of differences between the original 1987 guideline and the 2004 guidance. The purpose of the forum, he stated, is to "help us interpret" the document. "The time to debate has passed. The document is done. This is a conference on how to implement."

There is little in the aseptic document that should surprise or trouble PDA. Many of the suggestions and comments provided by the Association and its Aseptic Processing Task Force throughout the guidance development process were accepted by FDA.

For example, PDA's *Points to Consider for Aseptic Processing* had a large impact on the evolution of the guidance. "If you look at it," Van Trieste pointed out, "37 of the issues that PDA talks about in the points to consider, the FDA's guidance document is in harmony with them. [The guidance] doesn't endorse [the points to consider]. It doesn't say this is what you do, but the interpretations of the PDA said here is how you handle a specific subject matter is not in disagreement with what is in the FDA guidance document…. Five of the PDA points to consider I would say were partially in harmony with the FDA guidance."

FDA did reject one item in the points, noted Van Trieste. "One was actually

Aseptic Processing: The New Guidance Program Committee & Faculty

Program Committee

Richard Johnson (co-chair) *Abbott Laboratories*

Martin VanTrieste (co-chair) *Bayer Healthcare*

Martyn Becker, *Merck & Co.*

Stephen Bellis, *IVAX Pharma.*

Nancy Berlin, *PDA*

Victoria Dedrick, *PDA*

Neal Koller, *PDA*

John Lindsay, *Aseptic Solutions*

Terry Munson, *PAREXEL Consulting*

Wanda Neal Ballard, *PDA*

George Robertson, *PDA*

Glenn Wright, *Eli Lilly & Co.*

Faculty

Martyn Becker

Stephen Bellis

Richard Friedman, *CDER, FDA*

Richard Johnson

Carol Lampe, *Baxter Sterility Assurance*

Terry E. Munson

Martin Van Trieste

Glenn Wright

Robert Sausville, *CBER, FDA*

Ian Symonds, *GlaxoSmithKline*

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Richard Johnson
Abbott Laboratories

rejected….Talking about environmental monitoring and incubation temperatures of environmental monitoring samples, PDA scientists believe you only need one temperature for environmental monitoring—that is sufficient. And the FDA is recommending two different temperatures—one for yeast and molds and one for everything else. That is the big difference."

An additional six items in the points to consider are not addressed in the FDA guidance, making the points to consider "still the only document out there that provides guidance on those issues," stated Van Trieste. The PDA points to consider "is a very good document. Even today it stands the test of time. So it is a good document to go to look for how to interpret certain things in the guidance document."

PDA's Aseptic Processing Task Force had similar success with its comments on the draft version of FDA's aseptic guidance, issued in 2003.

"PDA made over a 100 comments to the agency," explained Van Trieste. In 39 cases, "FDA accepted our comments and changed the document. There were 19 of our comments that the FDA didn't take…but took alternative approaches [to those] originally written in the draft document, which I think is a success for PDA."

Overall, he said, "about 50% of what PDA thought should be changed in the guidance document was actually changed."

Van Trieste also briefly discussed the strong contribution the Product Quality Research Institute made to the guidance through its working group on aseptic processing, which was populated largely by members of PDA's Aseptic Processing Task Force.

Implementation Tool Created

Van Trieste created a project management tool to facilitate implementation of the document and generously has given it to PDA.

Delegates at the both the Washington and Frankfurt events received a CD-ROM with the project management tool.

The Microsoft Excel spreadsheet will help firms track how many of the 477 requirements in the document they comply with and which company SOPs fulfill a requirement.

For guidance provisions where the company is not compliant, the spreadsheet allows easy tracking of actions to be taken, responsible personnel and expected dates of completion.

"This is a basic project management tool that will take every one of the requirements in the guidance document, put it in a spreadsheet, and you can put in there if you comply or don't, if you have an action to do or not, and use it as a project management tool," explained Van Trieste. In addition, "if you then look at the requirement or the recommendation from FDA, it is hyperlinked to the FDA guidance document and it takes you to that text in the guidance document so you can see it in its entire context."

Delegates at both the Washington and Frankfurt events received the project management tool on CD-ROM. Attendees at all four of the 2005 workshops will also recieve the management tool as part of their registration.

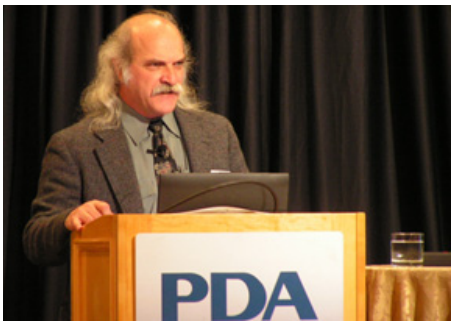
Different Continents, Different Practices?

The survey distributed at both events, though far from scientific, revealed some interesting differences in the way aseptic processing is performed by firms in Europe and the United States. Van Trieste summarized the results following the Frankfurt event and compared and contrasted the findings. He intends to present the data at the four workshhops in 2005.

At the Washington forum, 74 out of 197 delegates returned a completed survey. In Frankfurt, 46 out of 95 delegates completed the survey. In some cases, delegates from the same company collaborated and filled out one survey, and in other cases, multiple representatives of a company submitted surveys. For a survey of this type, the response rate is exceptional and quite diverse.

Van Trieste notes in his summary that the data *provides useful insights to the participants so they can compare their firms practices versus others* and *into the differences between U.S. and European participants.*

Carol Lampe
Baxter Sterility Assurance



Robert Sausville
CBER

One of the larger discrepancies between the European delegates and the U.S. delegates involved air monitoring practices in Class A areas: 86% of the participants in Frankfurt stated they monitor for non-viable particulates in Class A areas, whereas 63% of the participants in Washington monitor for non-viable particulates.

Another interesting discrepancy was found regarding disposition of batches. In Washington, 89% of participants disposition batches based on the investigation results with a micro count on a critical surface; 69% of the Frankfurt participants did the same.

In other areas, strong similarities were found. For example, 33% of the respondents at both the Frankfurt and Washington forum used isolators for aseptic filling operations.

Three Important Areas

The forum was designed to cover three important areas of the guidance: process simulation, environmental monitoring and isolators.

On process simulation, the Washington event featured presentations by CDER's Friedman, **Glenn Wright** (Eli Lilly) and Abbott's Johnson. In Frankfurt, IVAX's **Stephen Bellis** spoke in place of Wright.

As part of his presentation, Friedman reviewed CDER's new quality system guidance, and demonstrated how the new aseptic guidance fits into the quality system framework. Wright provided an overview of the process simulation section of the guidance. He stressed that firms should "clearly define" the rationale for the conditions and activities simulated during the media fill. "This is something I think industry has struggled with for quite a long time," he said.

Wright spotlighted a list of "key points" to be considered included in the aseptic guidance. "This is a great list," he said, "and I think it was very good for this list to be incorporated in the guidance because it gives very good direction on things you are looking for." The list is not "all-inclusive," but provides information on "some of the more normal lines you'll see."

Wright cautioned that "every single line and filling operation is slightly different, so you are really going to have to think about your own filling line and other things that you are going to need to add and things you are going to be worried about as you go through it."

Good media fill design is not only a matter of good science, but also good business, said Wright. "Media fills are expensive activities and so from a business standpoint…you should really think about the design of how you execute media fills because you do want to get the most value" from them.

Environmental monitoring was addressed by Friedman, Baxter's **Carol Lampe** and Van Trieste in Washington. In Frankfurt, Friedman (via videotape), Merck's **Martyn Becker** and GSK's **Ian Symonds** spoke.

Isolators were addressed by CDER's Sausville and PAREXEL's **Terry Munson** at both conferences (Sausville via videotape).

The aseptic processing forum in October served as the perfect kick-off to PDA's training program for the FDA aseptic processing guidance. The program continues in 2005 with the four workshops and the aseptic processing laboratory course offered by the PDA Training and Research Institute, which has been updated to reflect the guidance.

Walter Morris, PDA


Forum delegates during a Q&A session

PDA Calendar of Events for North America

Please visit www.pda.org for the most up-to-date event information, lodging and registration.

Conferences

February 17-18, 2005
Aseptic Processing Training Workshop
San Francisco, California

March 14-15, 2005
Aseptic Processing Training Workshop
New York, New York

April 28-29, 2005
Aseptic Processing Training Workshop
Chicago, Illinois

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

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

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

September 11-14, 2005
PDA/FDA Joint Regulatory Conference, Courses and Exhibition
Washington, DC

Training

Laboratory Training and Lectures are held at the PDA TRI facility in Baltimore, Md., unless otherwise indicated.

Laboratory Training

January 25-28, 2005
Pharmaceutical and Biopharmaceutical Microbiology 101

February 7-11, 2005
Aseptic Processing Training Program (Week 1)
Week 2: March 14-18

February 24-25, 2005
Environmental Mycology Identification Workshop

March 3-4, 2005
Developing and Validating Cleaning and Disinfection Programs for Controlled Environments

March 7-9, 2005
Cleaning Validation

March 22-23, 2005
Validating a Steam Sterilizer

April 7-8, 2005
PDA Annual Meeting
Chicago, Illinois

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

May 25-27,2005
Cleaning Validation

June 2-3, 2005
Environmental Mycology Identification Workshop

Lectures

February 17-18, 2005
Computer Products Supplier Auditing Process Model: Auditor Qualification

June 13-14, 2005
Computer Products Supplier Auditing Process Model: Auditor Qualification

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

Lecture Course Series

March 7-9, 2005
Biopharmaceutical Course Series
San Francisco, California

May 2-4, 2005
Pharmaceutical Course Series
Princeton, New Jersey

November 29-December 2, 2005
Career-long Learning™
New Orleans, Louisiana

Chapters

April 11, 2005
PDA Canada Chapter Annual Meeting
Toronto, Ontario, Canada

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

PDA Calendar of Events for Europe and India

Please visit www.pda.org for the most up-to-date event information, lodging and registration.

EUROPE

January 24, 2005
PDA EuroForum
PDA and the PDA Prague Chapter presents
Technology Transfer and Contract Manufacturing
Prague, Czech Republic

January 31, 2005
PDA and the PDA Central Europe Chapter presents
Clinical Manufacturing — Sterile Dosage Form
Basel, Switzerland

February 2, 2005
PDA and the PDA UK/Ireland Chapter presents
Biotechnology Conference: Risk, Regulation and Resource
Oxford, United Kingdom

March 1-4, 2005
2005 PDA International Congress,Courses and Exhibition
Rome, Italy

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

June 2, 2005
PDA EuroForum
PDA and the PDA Prague Chapter presents
PAT - Industry, Regulator and Academic
Budapest, Hungary

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

June 13, 2005
PDA EuroForum, Risk Analysis
London, England

June 20, 2005
PDA EuroForum
PDA and the PDA Italy Chapter presents
PAT / Rapid Micro TM 33
Milan, Italy

November 3, 2005
PDA EuroForum, Complete Stability Testing for a Successful Applicaton
Lisbon, Portugal

INDIA

January 21-22 , 2005
PDA and the PDA India Chapter presents
Common Technical Document (CTD): Learn by Doing
Hyderabad, India

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

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

July 19-20, 2005
PDA IndiaForum
PDA and the PDA India Chapter presents
Q7A Update
Location TBD

September 16-17
PDA IndiaForum
PDA and the PDA India Chapter presents
Certificate of Suitability CEP
Location TBD

November 22-23
PDA IndiaForum
PDA and the PDA India Chapter presents
In-Licensing
Location TBD

Victoria Ann Dedrick
Vice President, Quality and Regulatory Affairs

Vice President's Message

2004: Banner Year for PDA's Regulatory Activities

As we begin a new year and as I approach the end of my first year at PDA, I thought it appropriate to thank a number of people who have made 2004 a great success for the quality and regulatory department.

The quality and regulatory group at PDA had a banner year in 2004 that can be directly contributed to its great volunteers. The Regulatory Affairs and Quality Committee (RAQC) and its task forces worked hard all during 2004 to ensure that PDA continued its leading role in the application of science-based approach to the global regulatory scene. Commenting on 15 documents to regulatory authorities was a great feat; five sets of comments are highlighted in this issue of the *PDA Letter:*

- **AS/04.066/Rev. 3, *WHO Guidelines for Sampling of Pharmaceuticals and Related Materials: Risk Assessment with Respect to the n, r, p Plans,*** Task Force Chair: **Don Elinski**, Eli Lilly and Company
- **FDA White Paper*: Defining the Customer in a Regulatory Agency,*** Task Force Chair: **Cindy Rockel**, Millipore
- **FDA White Paper: *Risk-Based Method for Prioritizing CGMP Inspections of Pharmaceutical Manufacturing Sites – A Pilot Risk Ranking Model,* Marie Breen**, Schering Plough Corporation
- ***Draft Guidance for Industry and FDA: Good Manufacturing Practices for Combination Products,*** Task Force Chair: **Michael A. Gross**, QLT, Inc.
- ***Draft Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations,*** Task Force Chairs: **Michael Van Der Werf**, Consultant, and **Zena G. Kaufman**, Pfizer Inc.

I would like especially to thank **Suzanne Levesque**, Sabex, who was the RAQC Chair when I arrived at PDA and helped get me off to a great start with the group, and our current Chair, **Amy Scott-Billman**, GlaxoSmithKline, for her tireless work, support and great meeting preparation. I have noted task force chairs and sub-committee chairs above, but I would also like to recognize **Steven Bellis**, IVAX Pharmaceuticals UK, **Tim Marten**, AstraZeneca, **James Lyda**, PAREXEL Consulting, and **John Towns**, Eli Lilly and Company, who also headed up groups during 2004. Each and every member of the RAQC contributed during 2004 to ensure PDA's success.

PDA's RAQC closely monitored the work of FDA during 2004 as it sought to complete the first phase of its 21st Century Initiative: A risk-based Approach to Pharmaceutical Good Manufacturing Practices (cGMPs) and move to phase 2 implementation. The September 20-22 PDA/FDA Joint Regulatory Conference provided PDA with an unprecedented opportunity to work with FDA to roll out their phase two plans for this landmark regulatory initiative. FDA provided 23 senior staff persons from four centers to present the next steps to industry at the meeting. Attendance at the conference was over 800 and the Program Committee, that included several RAQC and task force members, is to be commended for their excellent work in designing a landmark meeting for PDA.

I would also like to thank our Chapter members who contributed comments to many documents and welcomed me to their meetings. It was a pleasure to meet and work with them, and I look forward to expanding those activities during 2005.

All in all, 2004 was a great year, and we are looking forward to a more successful and productive 2005.

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2. Pharmaceutical Quality (2004)
   Edited by Richard Prince—Item No. 17207, PDA member: US$ 240, PDA nonmember: US$ 299
3. Good Practice and Compliance for Electronic Records and Signatures - Part 3: Models for Systems Implementation and Evolution (2004)
   —Item No. 13003, PDA member: US$ 95, PDA nonmember: US$ 190
4. Quality Assurance: A Practitioner's Guide (2004)
   By U. G. Barad —Item No. 17212, PDA member: US$ 185, PDA nonmember: US$ 229
5. Steam Sterilization: A Practitioner's Guide (2002)
   Edited by Jeanne Moldenhauer —Item No. 17183, PDA member: US$ 215, PDA nonmember: US$ 269
6. PDA CD Archive Set (includes 2003 CD Update)
   PDA CD Archive Set: Item No. 01101 PDA member: US$ 395, PDA nonmember: US$ 590
   2003 CD Update: Item no. 01002, PDA member: US$ 95, PDA nonmember: US$ 290
7. Cleanroom Clothing Systems: People as a Contamination Source (2004)
   By Bengt Ljungqvist and Berit Reinmuller —Item No. 17206, PDA member: US$ 135, PDA nonmember: US$ 169
8. Points to Consider for Cleaning Validation, Technical Report no. 29 (1998)
   —Item No. 01029, PDA member: US$ 75, PDA nonmember: US$ 270
9. Cleaning Validation: A Practical Approach (2000)
   By Gil Bismuth and Shosh Neumann —Item No. 06118, PDA member: US$ 170, PDA nonmember: US$ 199.95
10. Endotoxins: Pyrogens, LAL Testing, and Depyrogenation, Second Edition, Revised and Expanded (2001)
    By Kevin Williams —Item no. 05003, PDA member: US$ 120, PDA nonmember: US$ 150

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PDA Comments On Five Regulatory Documents

PDA's 2004 regulatory activities ended in a flurry with the submission of written comments addressing a WHO guidance, two FDA draft guidances and two FDA white papers. Listed below are the PDA members who sat on the commenting Task Forces, followed by a portion of each cover letter. Go to www.pda.org/regulatory/regcomments.html for the complete set of comments.

FDA Customer White Paper
Cindy Rockel (Chair), Millipore
David Miner, PhD, Eli Lilly
Michael Van Der Werf, Consultant
Amy Scott-Billman, GlaxoSmithKline
Robert Dana, Elkhorn and Associates
Zena Kaufman, Pfizer

FDA Risk-Based White Paper
Marie Breen (Chair), Schering Plough
Rafiqah Williams, PhD, Eli Lilly
Robert Dana, Elkhorn and Associates
Tony Horton, Mylan
Amy Scott-Billman, GSK
Victoria A. Dedrick, PDA

FDA Combo Products GMP Guidance
Michael Gross (Chair), PhD, QLT
Amy Giertych, Baxter
Doris Conrad, GSK
Michael Porter, Eli Lilly
Tom Hutchinson, Pfizer
Gordon Munro, PhD, Watson

FDA QS Approach Guidance
Zena Kaufman (Co-Chair), Pfizer
Michael Van Der Werf (Co-Chair), Consultant
Amy Giertych, Baxter
Michael Porter, Eli Lilly
Tom Hutchinson, Pfizer
Gordon Munro, PhD, Watson
Robert Kieffer, PhD, RGK Consulting
Tony Horton, Mylan
Marie Breen, Schering Plough
David Miner, PhD, Eli Lilly
Amy Scott-Billman, GSK
Robert Dana, Elkhorn Associates
Cindy Rockel, Millipore
Michael Anisfeld, Globepharm
Jeffrey Levy, PhD, Eli Lilly
Rafiqah Williams, PhD, Eli Lilly
Doris Conrad, GSK Biologicals
Victoria Dedrick, PDA
Michael Gross, PhD, QLT
Richard Johnson, Abbott
Tim Marten, DPhil, AstraZeneca
Nikki Mehringer, Eli Lilly
Lisa M. Skeens, PhD, Baxter

WHO Sampling Guidance
Don Elinski (Chair), Eli Lilly
David LeBlond, Abbott
Mark Varney, Abbott
Jerry Planchard, Patheon
Russ Madsen, Williamsburg Associates
Wayne Taylor, PhD
Steven Bellis, Ivax
Lynn Torbeck, Torbeck Associates
Janet Stevens, Eli Lilly

Cover Letters • *Note: The complete cover letter and comments are available at www.pda.org/regulatory/regcomments.html.*

November 24, 2004

US Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref.: FDA White Paper: "*Defining the Customer in a Regulatory Agency"* submitted to Docket #2003N-0059 - Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach

PDA is pleased to provide comments on the recently issued white paper*: Defining the Customer in a Regulatory Agency*. PDA is an international professional association of more than 10,000 individual member scientists having interest and expertise in pharmaceutical and biopharmaceutical manufacturing and quality. A committee of interested industry representatives prepared the comments that follow.

PDA is encouraged and applauds FDA for issuing this white paper presenting a mechanism to define and characterize internal and external customer relationships. Defining customer relationships is a complex undertaking by FDA and at times can be "uncomfortable" given the many different roles, responsibilities and relationships FDA has with the identified customer base. We believe FDA's effort and the ultimate benefit of this white paper will support other FDA initiatives including, but not limited to:

- First and foremost, the use of a "quality system" approach to FDA operations that defines procedures that may guide these FDA customer relationships going forward.
- International Harmonization
- Promotion of the use of scientific principles that clarify and provide a common platform to discuss the execution of FDA's roles and responsibilities with its variety of customers (i.e. ranging from other governmental agencies to *compelled customers*).
- Setting the context for dialog regarding the application of risk management principles to assure that safe and efficacious drugs are available in support of the FDA's public welfare mandate.

November 24, 2004

US Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref.: FDA White Paper "Risk-Based Method for Prioritizing CGMP Inspections of Pharmaceutical Manufacturing Sites – A Pilot Risk Ranking Model" submitted to Docket #2003N-0059 - Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach

Dear Sir/Madam:

PDA is pleased to provide these comments on the White Paper issued September 2004, entitled "Risk-Based Method for Prioritizing CGMP Inspections of Pharmaceutical Manufacturing Sites – A Pilot Risk Ranking Model." PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological and device manufacturing and quality.
PDA is encouraged by the Agency's efforts to move ahead with this program to aid in the fulfillment of one of the goals of Pharmaceutical CGMPs for the 21st Century, which is to maximize the Agency's limited resources while providing the most health promotion and protection at the least cost for the public. PDA supports the approach and process that the Agency is taking and agrees this model should be implemented now and modified as improvements are identified. The following list of comments and conclusions reached by the PDA is provided to the Agency for consideration of inclusion in this program.

Point #1
Risk Filtering and Model Summary
In the section "Risk Filtering and Model Summary" it is stated "FDA does not intend to publish or disclose such details of a site's individual score or ranking". Without a site knowing the factors that were considered in their risk ranking, the site will not have the benefit of the agency's analysis in order to focus on those areas representing the highest risk. It is PDA's opinion a site should not have to guess if they have been determined to be high risk and what factors put them in that category. Incorrect assumptions could occur and continuous improvement opportunities might be missed.

November 23, 2004

US Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref.: "*Draft Guidance for Industry and FDA: Current Good Manufacturing Practices for Combination Products*," September 2004 submitted to Docket No. 2004D-0431, OC 2004219

Dear Sir/Madam:

PDA is pleased to provide comments on the FDA *Draft Guidance for Industry on Current Good Manufacturing Practices for Combination Products*, issued in September 2004. PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological and device manufacturing and quality. A committee of interested industry representatives prepared the comments that follow.

PDA commends FDA's initiative to develop guidance for the application of quality system principles in the development and manufacture of combination products. We recognize that the diversity of combination product types make it necessary to begin by addressing fundamental principles in broad terms. We encourage FDA to develop additional and more detailed guidance on quality topics which, due to their complexity, are not addressed at this point in the evolution of thinking about quality systems for combination products. Since the initial guidance is of a general nature our comments have been kept to a high level. We have also included some suggestions indicating where more specific guidance is needed. PDA stands ready to participate in a process that will provide more detailed guidance in the future.

The following comments are provided for the Agency's consideration.

Point #1
Introduction (lines 14-30)
In the Introduction and elsewhere in the draft guidance, current Good Manufacturing Practices are described as intended to ensure that "the product complies with performance standards as appropriate for the marketed combination product." It is PDA's opinion that the term "performance standards," should be used cautiously since it has a specific regulatory meaning in the context of medical devices.

December 1, 2004

US Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

REF: Draft Guidance for Industry: Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations, September 2004, submitted to Docket # 2004-22206

Dear Sir or Madam:

PDA is pleased to provide comments on the FDA Draft Guidance for Industry "Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations," issued in September 2004. PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological and device manufacturing and quality. PDA wishes to thank the Agency for the opportunity to provide comments on this document.

We believe this guidance provides industry a significant impetus to change their manufacturing philosophy from a reactive post-manufacturing quality testing regimen into one directed toward a manufacturing operation based on science and technology, with quality designed into the process and product. It is important for both industry and the Agency to have flexibility when applying this guidance irrespective of the size of the firm. As PDA is a member-based organization, this is an important consideration, since its members can be employed at large, medium and small manufacturing firms.

Please find detailed comments in the attached spreadsheet (Appendix A) and suggested revisions to Section III F (Appendix B). In addition, PDA would like to offer the following general comments:

Point #1: Globalization (reference lines 94 to 97)
PDA applauds FDA in its support of efforts to harmonize quality systems approaches to drug manufacture across the globe. PDA looks forward to participating in the effort through the pre-established mechanisms for global harmonization.

September 28, 2004

Dr. Sabine Kopp
Quality Assurance & Safety: Medicines (QSM)
World Health Organization
Avenue Appia
CH-1211 Geneva 27, Switzerland

Re: AS/04.066/Rev.3, WHO Guideline for Sampling of Pharmaceuticals and Related Materials: Risk assessment with respect to the n, r, p plans.

Dear Dr. Kopp:

PDA is pleased to respond to your request of 30 July 2004 for a risk assessment with respect to the proposed n, r, and p sampling plans in the above referenced document. PDA is an international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical and biopharmaceutical manufacturing and quality. This risk assessment was prepared by a committee that included recognized experts in statistics and the practice of pharmaceutical acceptance sampling.

Risk #1: No defined acceptance criteria or associated decision risk levels.

Appendix 1 in the guidance document properly defines a sampling plan as including acceptance criteria. It then provides the n, r and p sampling plans but these do not include acceptance criteria. All 3 plans indicate a vague requirement that results be "concordant" with respect to identity; but it is not clear that users would agree on the meaning of "concordant." If the n, r and p procedures are really sampling plans, clear and specific acceptance criteria must be given.

The CBER Update

Christopher Joneckis, PhD, Center for Biologics Evaluation and Research, U.S. FDA

Christopher Joneckis, PhD, is a Senior Advisor for CMC Issues at CBER. He has agreed to periodically provide updates of CBER activities most related to PDA member interests in future issues of the *PDA Letter*. Dr. Joneckis has spoken at many PDA events, most recently at the 2004 PDA/FDA Joint Regulatory Conference in September. He will be speaking at the PDA International Congress: *Bringing Practicality To Science,* March 1-4. Please visit www.pda.org/rome2005 for a complete agenda.

As part of its mission, CBER participates in broad FDA efforts and develops approaches on manufacturing and chemistry, manufacturing and controls (CMC) issues in order to facilitate development of new products, and improvements to existing products.

CBER actively participated in the Pharmaceutical cGMP for the 21st Century initiative, which explored pharmaceutical quality from a review and inspection perspective, and yielded a significant number of announced initiatives. Some of theses new initiatives do not impact CBER, largely because there were similar practices and systems already in effect. For example, the newly formed Pharmaceutical Inspectorate for the Center for Drug Evaluation and Research (CDER) and the Center for Veterinary Medicine adopts many of the principles of CBER and the Office of Regulatory Affair's Team Biologics program, including participation of product specialists during inspections.

CBER has lived with technological change and continues to encourage manufacturing and testing innovation and improvement, including implementation of Process Analytical Technologies (PAT), through its longstanding, integrated system of review and inspection. For example, CBER has been evaluating rapid microbial methods that are critical for testing many cellular products, and recently (August 2003 and February 2004) approved a rapid microbial method for use with two cellular products. CBER will participate as an observer on the FDA PAT group to facilitate information sharing on approaches and technical issues. Lessons learned from the Team Biologics program, particularly the more recent inclusion of Quality Systems, will be used by the PAT Team and the Pharmaceutical Inspectorate.

We also recognized that advances in manufacturing and testing technologies when applied effectively could provide appropriate assurance of product quality and safety when manufacturing products using spore-forming microorganisms. A revision to the existing regulation [21 CFR 600.11(e)(3)] provides for alternatives from the separate, dedicated facility approach. This will allow increased flexibility for manufacturers using spore-forming microorganisms in production (*Federal Register*, vol. 68, no.249, pg. 75116 (effective June 1, 2004).

In October, CBER held two public workshops that included discussion on manufacturing and CMC issues. CBER with CDER, co-sponsored a public workshop "Specifications for Biological and Biotechnological Products" that explored the scientific and statistical basis for establishing and refining specifications, including the impact of manufacturing capability. A public workshop on the FDA Critical Path Initiative for CBER products was also held, and we received many useful suggestions from stakeholders. We encourage submitting additional suggestions to the docket [2004-N-181].

The Good Tissue Practice (GTP) regulations that govern the methods, facilities and controls used for; the manufacture of human cell, tissue, and cellular and tissue-based products (HCT/Ps) were finalized in November. These risk-based regulations are aimed at preventing the introduction, transmission, and spread of communicable diseases by HCT/Ps, by reducing the risk that the HCT/Ps transmit communicable disease agents. Together with the establishment registration rule, which is already in effect, the Donor Eligibility and GTP regulations become effective for HCT/Ps recovered on and after May 25, 2005.

The CBER Web site (www.fda.gov/cber) has additional details on these and other important activities.

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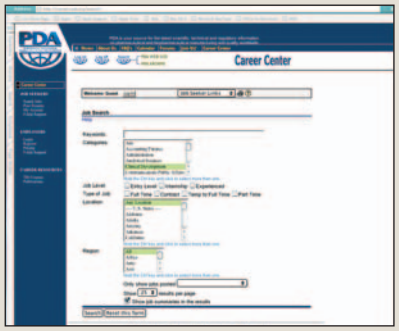

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An International Association For Pharmaceutical Science And Technology

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Delegates Call For Repeat of Prefilled Syringe Conference

Prefilled Syringes Conference Confirms Technology An Innovative and Thriving Field

Guy Furness, Contributing Writer

PDA and its Central Europe Chapter held a hugely successful conference, entitled "*The Universe of Prefilled Syringes,*" in Hanover, Germany, Oct. 18-19. The popularity of the event, together with the positive content of the presentations and a buoyant atmosphere both within and outside the meeting hall, confirmed that prefilled syringe manufacture remains an innovative and thriving field.

"The aim of the PDA is to provide a framework that members can use to enable them to communicate, interact and bring ideas into being. We are therefore happy that this conference, which was conceived and led by members, has been so well received. We can now look forward to planning further PDA events," commented **Georg Roessling,** PhD, PDA board member and Head of CMC Technology and Drug Delivery Systems at Schering AG, who opened the conference and welcomed attendees.

Twenty-two speakers from across the spectrum of companies and organizations involved in the field, including manufacturers of prefilled syringes and syringe components, contract fillers, equipment manufacturers and international regulatory authorities, presented to a packed meeting room. Over 120 people from across the globe were present at the event—significantly exceeding original attendance expectations.

"The high interest in the conference confirmed that the success story of the prefilled syringe has just started. There is an abundance of innovations around the prefilled syringe—this exciting tool responds to many needs of the pharmaceutical industry like product differentiation and easy processing and registration," said **Mathias Romacker,** Director of Business Development, Buender Glas GmbH. The prefilled syringe manufacturer invited a party of delegates on a post-conference visit of its prefilled syringe production facility in the nearby town of Bünde, Germany.

Of note was the abundance of new ideas coming out of companies operating in the prefilled syringe space. Among the innovations discussed were advanced treatments for glass syringes and rubber closures, which decrease interactions between the device components and the drug formulation contained within and increase stability, as well as reducing friction between the components, making administration easier and reducing the risk of sticking.

Delegates want more conferences on prefilled syringes

Other new technologies and processes discussed included: novel needle-tip designs for painless injection; enhanced sterile filling processes and equipment, which increases productivity while decreasing the risk of contamination; novel labelling technologies including peel-off label sections that can be inserted directly in to patient records; and entirely new device concepts for safety syringes that eliminate the risk of sharps injury.

This two-day conference was the first on this topic that the PDA had organized, but delegates and speakers have called for a repeat of the event on an annual basis.

For more information about this meeting (including how to obtain a copy of the proceedings) or to be kept informed about future PDA conferences, please contact PDA or visit www.pda.org.

A panel of speakers (from left to right): Graham Crowther, Marc Belien, Laurant Caburet and Gerhard Mayer

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Whether you're looking to round out your subject-matter knowledge or need the latest scientific publication, you'll find it in PDA's E-store collection. Here is just a sample of what you'll find:

Aseptic Processing

Points to Consider for Aseptic Processing, Supplement Volume 57 Issue 2
(2003) 72 pages. Member: US$ 75, Nonmember: US$ 270 – Item 03004

Current Practices in the Validation of Aseptic Processing – 2001, Technical Report No. 36
(2002) 34 pages. Member: US$ 75, Nonmember: US$ 270 – Item 01036

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

Microbiology in Pharmaceutical Manufacturing
Editor: Richard Prince
(2001) Hardcover, 900 pages. ISBN: 1-930114-32-X. Member: US$ 240, Nonmember: US$ 299 – Item 17185

Laboratory Validation: A Practitioner's Guide
Editor: Jeanne Moldenhauer
(2003) Hardcover, 1224 pages. ISBN: 1-930114-58-7. Member: US$ 250, Nonmember: US$ 309 – Item 17201

Media Fill Validation Environmental Monitoring During Aseptic Processing
Author: Michael Jahnke
(2001) 108 pages. ISBN: 1-930114-35-4. Member: US$ 90, Nonmember: US$ 109 – Item 17181

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

Training Video:

Understanding Sterile Production (Tutorial J)
English only. Video running time 33 minutes. Member: US$ 320, Nonmember: US$ 395 – Item 15022

Quality Systems

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

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

The Essence of GMPs: A Concise Practitioner's Guide
Author: U.G. Barad
(2003) Hardcover, 280 pages. ISBN: 1-930114-57-5. Member: US$ 185, Nonmember: US$ 229 – Item 17203

GMP in Practice: Regulatory Expectations For The Pharmaceutical Industry Third Edition
Author: James Vesper
(2002) 253 pages. ISBN: 1-930114-17-6. Member: US$ 105, Nonmember: US$ 129 – Item 17199

Understanding GMP: A Practical Guide
Author: Martyn Becker
(2001) 237 pages. ISBN: 1-930114-22-2. Member: US$ 170, Nonmember: US$ 209 – Item 17174

The Japanese GMP Regulations 2003
(2003) Paperback, 181 pages. Member: US$ 195, Nonmember: US$ 250 – Item 12002

Pocket Booklets:

Pocket Code of Federal Regulations GMP Guide – 2003 Edition
21 CFR Part 210 & Part 211. Member: US$ 4, Nonmember: US$ 10 – Item 13004

Pocket Code of Federal Regulations
ICH Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
Q7A. Member: US$ 4, Nonmember: US$ 10 – Item 13005

Training Videos/CDs:

Introduction to Microbiology & GMP (Tutorial H)
Video running time: 32 minutes. Member: US$ 390, Nonmember: US$ 485 – Item 15254

Also available in Video CD module at same price Item 15253 and Interactive CD-Rom. Member: US$ 620, Nonmember: US$ 775 – Item 15271

Good Manufacturing Practice Regulations, 21 CFR Parts 210-211 (Sub-Parts B thru K) training CDs. A total of 140 minutes and 414 slides in the 10 sub section training sessions.
Set of 10 programs. Member: US$ 1500, Nonmember: US$ 4500 – Item 11014

Cleaning Validation/Environmental Monitoring

Cleaning and Cleaning Validation: A Biotechnology Perspective
by Roger Brunkow, David DeLucia, Shane Haft, John Hyde, John Lindsay, Jill Myers, Robert Murphy, John McEntire, Karen Nichols, Brenda Terranova, Jon Voss and Edward White.
(1995) Hardcover, 190 pages. ISBN: 0-939459-50-7. Member: US$125, Nonmember: US$ 320 – Item 13002

Points to Consider for Cleaning Validation, Technical Report No. 29
(1998) 23 pages. US$ 75 member, Nonmember: US$ 270 – Item 01029

Environmental Monitoring: A Compilation of papers from the PDA Journal of Pharmaceutical Science and Technology
(1996) 220 pages. Member: US$ 100, Nonmember: US$ 295 – Item 01151

Cleanroom Clothing Systems: People as a Contamination Source
Author: Bengt Ljungqvist and Berit Reinmuller
(2004) Hardcover, 110 pages. ISBN: 1-930114-58-3. Member: US$ 135, Nonmember: US$ 169 – Item 17206

Training Video:

Validating Cleaning (Tutorial N)
English only. Video running time 28 minutes. Member: US$ 340, Nonmember: US$ 425 – Item 15042

New This Month!

Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations, Technical Report No. 32 revised (2004) 150 pages.
Paper version: Member: US$ 100, Nonmember: US$ 295 – Item 01032
CD-Rom version: Member: US$ 75, Nonmember: US$ 270 – Item 01132

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France Chapter Presents Bio/Pharmaceutical Manufacturing Conference

Kelly Coates, PDA

PDA together with the PDA France Chapter presented an oustanding conference, entitled **New Success Factors for Bio/Pharmaceutical Manufacturing in Europe,** on December 6-7, 2004 in Paris, France. This event provided two days of in-depth discussions and practical insights on regulatory compliance and implementation challenges for European manufacturers.

The efforts of the France Chapter resulted in an impressive event. The speakers presented a diverse body of knowledge that attendees could immediately implement in their careers.

Session topics covered:

- GMP for Active Substances and Excipients – Revision Directive EC/2001/83 (2003/84)
- Quality Systems & Risk-Based Inspections
- Risk Management
- The Role of the Qualified Person in Europe
- Parametric Release
- FDA Aseptic Processing Guideline

Featured speakers included:

- **Emer Cooke**, EMEA, Head Inspection Sector, London, UK
- **Joyce Ramsbotham**, Solvay, The Netherlands
- **Jacques Morénas**, Director Adjoint, International Affairs, AFSSAPS, Saint-Denis, France
- **Ian Thrussell**, Inspector, Medicines Inspectorate, MHRA, UK

Congratulations to the France Chapter for planning this excellent event!

PDA Letter Deviation Report

In the rush to launch the new look for the *PDA Letter,* a few mistakes were made in the November-December issue. First off, PDA Director John Shabushnig, PhD, Pfizer, was mistakenly omitted from the list of the 2005 Board of Directors on page 7. On the same list, Eric Sheinin's name was erroneously spelled, *Sheinen.* The caption for the photo on page 19 mistakenly identifies Louise Henry (standing, right), Vertex Pharmaceuticals, as PDA Board member Kathleen Greene.

PDA apologizes for the errors and any inconvenience caused by them.

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Under terms of the secondary membership agreement between PDA, the Parenteral Society (PS) and the Nordic Association for Contamination Control (R³-Nordic), PDA members may "add on" membership to either association for a nominal fee. This secondary membership feature entitles PDA members to receive full Parenteral Society and R³-Nordic membership benefits. The membership will begin January 2005 for a 12-month period*.

Here is how it works: **1)** use this page or a photocopy, **2)** fill in the requested information, **3)** attach a check in US dollars, drawn on a US bank, net of all bank charges, for US$ 150 (Parenteral Society), US$ 50 (R³-Nordic), or complete the credit card information and **4)** mail or fax to PDA. Parenteral Society secondary membership forms must be received by January 31, 2005. Applications for R³-Nordic will be accepted year round.

PDA will forward all secondary membership applications directly to the Parenteral Society administrative offices in England, or directly to the R³-Nordic administrative offices in Sweden. Under the terms of the agreement, this application must be renewed each year. If you have any questions, please contact Kelly Coates at PDA, +1 (301) 656-5900, ext. 149.

**Full Parenteral Society membership benefits (excluding voting rights) include the quarterly newsletter, discounts on meeting registration and publications, membership directory, and the Society's quarterly European Journal of Parenteral Sciences.*

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2005 PDA International Congress: *Bringing Practicality To Science*

Paul McKellips, PDA

The "eternal city" of Rome, Italy serves as the backdrop for this year's PDA International Congress, Courses and Exhibition—a three day exchange of solutions to meet regulatory compliance in a changing, global market.

This year's International Congress features:

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- Biological Safety
- Cleaning Validation

15 Presentations on **Regulatory Compliance:**
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- Post-approval Changes
- CAPA

6 Updates from **International Regulatory Authorities**
- CBER & the Critical Path
- EU Clinical Trials Directive
- FDA cGMP Clinical Trials

9 Presentations on **Risk Management**
- Case Study: Aseptic Processes
- ICH Q8 & Q9
- Case Study: Sterilization

9 Presentations on **Regulatory Quality Inititiatves**
- ICH Q10
- Case Study: QS Risk Analysis
- FDA 21st Century cGMPs
- EU 2004/2005 QS Initiatives

8 Presentations on **Aseptic Processing Technologies**
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Rome Cavalieri Hilton

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The Congress will take place at the Five Star Rome Cavalieri Hilton. Situated on a 15-acre Mediterranean private park, the Cavalieri overlooks the Colosseum, St. Peter's Cathedral, Trevi Fountain and the historic city center. The Catacombs, Vatican and Spanish Steps are only minutes away.

Contact Nahid Kiani for exhibit opportunities: +1 (301) 656-5900, ext. 128, or kiani@pda.org.

2005 PDA International Congress Exhibitors List

(Partial list of Exhibitors at press time)

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Vice President's Message

Gail Sherman

TRI's New Focus, New Courses—Come Soar With Us in 2005

As this publishes, I will have been at TRI for five months, and am proud of the team that has emerged over these last few months. There is a true commitment to making TRI the premier training organization that it can be.

Our "new" organization includes not only the Education Manager (lecture)—Strother Dixon—and our two Laboratory Education Coordinators—Juner Torres and James Wamsley—but also two full-time dedicated staff to support our marketing efforts and logistics—Al Jordan and Takiyah Jefferson. As a team we work together to define (and refine) our training programs so that the needs of our communities are met through our offerings.

In 2005, we will focus our lecture training course series geographically and in support of the industries in the selected geographic locations. For example, our first course series is in San Francisco, Ca., on March 7-9, and will feature training in biopharmaceutical and pharmaceutical sciences. On May 2-4, we head to Princeton, N.J., where we will be offering training for the pharmaceutical industry. Denver, Colo., follows on October 23-25, and New Orleans, La., from Nov. 29 to Dec. 1, where we will have courses relevant to all of our respective communities, including the medical device industry. At all of our course series, we will provide at least one course for the trainers in the pharmaceutical industry.

In addition to the traditional lecture course series, TRI will offer training at the International Congress in Rome in March, the Annual Meeting in Chicago in April, and the PDA/FDA Joint Regulatory Conference in Washington, D.C. in September. For the first time ever, we will sponsor a lecture course series in Europe, specifically in London on June 14-15. TRI is also in discussion with both the EMEA and the EMDQ for potential additional training in the months to come.

Our laboratory courses are as vibrant as ever—each being updated to correspond with new FDA guidances, especially our industry renowned 10-day Aseptic Processing Training course. We will also again offer *"Aseptic Europe"* twice in 2005. A new, first-time ever lab course, *"Pharmaceutical and Biopharmaceutical Microbiology 101,"* will be offered in January, with a subsequent offering in July.

We continue to dialogue with pharmaceutical companies for opportunities to develop and deliver training for in-house staff, and we are in ongoing discussions with our European counterparts to design programs relevant to the European industry needs.

To continue to offer new and exciting programs, we are looking forward to input from our industry partners for both development of new training courses and for the opportunity to teach. I invite all or you to attend our **Open House** on Feb. 1 (9 a.m. to 11 a.m. or 2 p.m. to 4 p.m.). Let us show you can benefit from our organization. Those who attend will automatically recieve a US$ 100 credit for one 2005 TRI course (excluding the aseptic processing course) and can enter a raffle to win reduced price courses. RSVP for the **Open House** by Jan. 21 by contacting me at sherman@pda.org..

We look forward to an exciting New Year and would love to have you join us! Look for more news from TRI in future *PDA Letters*. Please feel free to contact us at +1 (410) 455-5800 or tri@pda.org.

PDA

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April 4-8, 2005
Chicago, Illinois

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  - Rapid Methods
  - Viral Filtration
  - PAT
  - Combination Products
- 3 New PDA Technical Reports
  - Viral Filtration
  - Validation of Protein Manufacturing
  - Sterile Filtration of Gasses
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