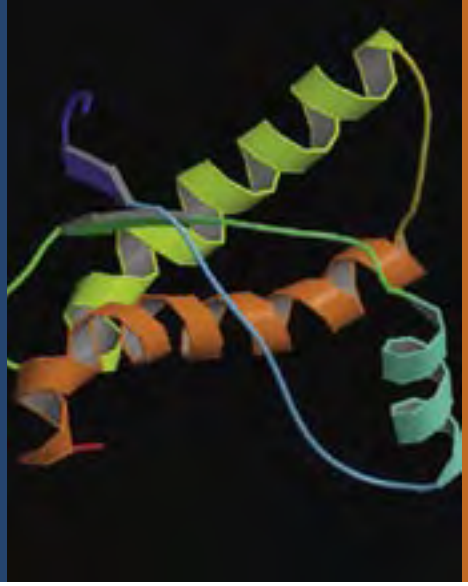
Science • Technology • Quality • Regulatory • Community

PDA Letter

Volume XLI • Issue #8

September 2005



In This Issue...

Special Issue

2005 PDA/FDA Joint Regulatory Conference

Keynote Speaker Manning, page 30

Exhibitors, page 31

Building a New Manufacturing Toolkit for Viral/TSE Safety

EMEA and U.S. FDA Cosponsor Unprecedented PDA Event

Three hundred and sixty participants from industry, academia and government met in Bethesda, Maryland in May, to contribute to the ongoing effort to improve the standards, the science and the regulations regarding viral and TSE safety.

The 2005 PDA Viral & TSE Safety Conference was the first cosponsored by the U.S. FDA and the EMEA. A 17-member Planning Committee set the agenda and goals to help contribute to the generation of new regulatory guidances, to identify potential areas of revision for current guidances, and to provide dialogue to help advance major regulatory and promising scientific initiatives.

The event also offered participants the chance to hear from Nobel Laureate **Stanley Prusiner,** MD, a pioneer of research into the biology and cause of transmissible spongiform encephalopathies (see the April 2005 *PDA Letter*, page 31, for more information on Dr. Prusiner and his work). Dr. Prusiner's keynote address focused on the latest thinking on prion biology, prion inactivation on surfaces and the science of prion detection and the development of more sensitive tests for detection of prions in animal and human tissues. He considered that the research priorities are the future role of diagnostics, disinfection of surfaces, the need to develop new drugs, and the need for more basic and clinical research.

In his opening remarks, program planning committee co-chair **Kurt Brorson,** PhD, Staff Scientist, FDA Center for Drug Evaluation and Research (CDER) identified a clear link between this historic meeting and FDA's Critical Path Initiative, announced last year. During the planning process, he explained, "it struck me that many of the meeting goals that we were conceptualizing and many of the sessions that we were trying to put together really were about building a better manufacturing toolkit."

One of the three goals in FDA's Critical Path Initiative is to encourage industry to develop and utilize a "better manufacturing toolkit"

continued on page 16

PDA Parenteral Drug Association

Quality. Consistency. Support.

For Peace of Mind, Specify Texwipe®

Take the stress out of specifying cleanroom consumables. At Texwipe our goal is to continuously improve our product offering, ensuring you receive the highest quality products available. All Texwipe products are rigorously tested and backed with a solid detailed traceability guarantee. We offer technical audits, product training and full customer support.

Texwipe, we work hard to ensure your peace of mind.

Dry Wipers • Pre-Wetted Wipers • Swabs • Sterile Products • Stationery • Mops

TW Texwipe®

Quality. Consistency. Support.

	North America	Europe	Asia
Tel	201 684 1800	+45 87 400 220	+65 6468 9433
Fax	201 684 1801	+45 87 400 222	+65 6468 6772
E-mail	info@texwipe.com	europe@texwipe.com	asia@texwipe.com

www.texwipe.com

Visit us at the 2005 PDA/FDA Joint Regulatory Conference in Washington, DC, September 11-14, 2005 at Table #39

This September,

the leading minds in Pharmaceutical Manufacturing, Quality Assurance, Compliance and Regulatory Affairs will be in Washington D.C...

Will you?

Since 1986, the PDA/FDA Joint Regulatory Conference has been the essential source for gaining valuable insights and success strategies from top FDA, industry and academic experts in an unbiased, science-based forum.

Specifically designed for mid- and upper-level pharmaceutical and biopharmaceutical professionals, this year's conference will present new information you can apply immediately to make your product development and continuous improvement processes more predictable, reliable and less costly.

2005 PDA/FDA *Joint Regulatory Conference*

The Product Life Cycle: Quality by Design, Implementation and Continuous Improvement

September 12-14, 2005

PLUS

Free visitor passes to the exhibit hall, the perfect venue to build relationships and learn about the latest products, services and technologies.

Eight interactive courses from the PDA Training and Research Institute, designed to improve processes, performance and the bottom line.

PDA Parenteral Drug Association

FDA

Register today!

www.pda.org/pdafda2005

Renaissance Hotel
Washington, D.C.
Conference - Sept. 12-14, 2005
Exhibition - Sept. 12-13, 2005
PDA TRI Courses – Sept. 15-16, 2005

Table of Contents

Coming Next Month...
Prefilled Syringes

PDA Training and Research Institute *presents:*

Rapid Microbiological Methods PDA #326

October 31 - November 4, 2005 • PDA TRI Baltimore, Maryland

This five-day workshop offers you a unique opportunity to evaluate several different Rapid Microbiological Systems in a laboratory-based environment. In addition to lectures covering several important issues regarding microbial systems, you will participate in informal discussions with other attendees about the positive and negative attributes of each system related to specific microbiological applications.

Vendors confirmed!

Gain Hands-on Experience!

Millipore
Biomérieux
MIDI
AES-Chemunex
Genomic Profiling Systems

Key topics

- Setting acceptance criteria
- What to expect during an inspection
- Ask the inspector
- Validation hardware and software for rapid methods
- USP perspective
- Regulatory submission overview

Plus: Multiple vendors each day!

Who Should Attend

QA/QC
✓ Director
✓ Manager/Supervisor
✓ Auditor

Manufacturing
✓ Director
✓ Manager/Supervisor

Validation
✓ Director
✓ Manager/Supervisor

Benefits of Attending

- Gain first-hand experience evaluating rapid microbial hardware to ensure the system you select is best suited to you application
- Hear directly from FDA regarding specific concerns related to your rapid micro program
- Informal discussions with other participants regarding pros and cons of each system related to specific applications guarantees you hear several perspectives
- Be sure you validation practices cover all aspects, including hardware and software, to be certain your program is ready for regulatory submissions

For more information contact:
James Wamsley
Manager, Laboratory Education
PDA Training and Research Institute
Tel: +1 (410) 455-5800
wamsley@pda.org

For registration inquires please call +1 (301) 656-5900

Robert Myers Named PDA President

Bob's Commitment to PDA Enticed Him to Pursue Position

On August 3, 2005, the Parenteral Drug Association named Robert Myers the Association's new president. Mr. Myers had served as the Acting President of PDA since April 2005.

"We are extremely pleased to announce that Bob Myers will serve as president of PDA. Bob's extensive leadership experience in the global pharmaceutical industry and in PDA will enable him to provide dynamic leadership for our Association. On behalf of the PDA community, we welcome him and look forward to working together to assure the Association grows in its mission to develop scientifically sound, practical technical information and resources to advance science for the pharmaceutical and biopharmaceutical industries," said Nikki Mehringer, Chair of the Board of PDA.

"I am extremely honored to be appointed President of the Parenteral Drug Association. Throughout my 30-plus year career, PDA has played an important role in my professional development and has helped me remain current with new technologies and regulations. I am committed to ensuring that PDA maintains the high quality of information, resources and services it provides both to its current members and to new participants from the global PDA community," said Myers.

Upon assuming the role of Acting President, Bob believed he would serve truly as an interim chief. Realizing that his respect for the organization was so strong , he threw his hat into the selection process for the permanent President.

Previously, Bob worked in a variety of positions at Schering-Plough for 28 years, including Vice President of U.S. Operations, VP of Offshore Operations and VP of World Wide Technical Operations. During these assignments, he had responsibilities at various times for the production of active pharmaceutical ingredients and sterile, solid, liquid and vaccine products in the United States, Europe and Asia. Since 2002, he has provided consulting services globally.

Bob rose through the ranks of volunteer committees to join the PDA Board of Directors in 1984.

Bob is a well-known PDA member and active volunteer. He was introduced to the Association in 1977 while working at Schering when his boss, PDA President **Nathan Kirsch,** asked Bob to present a paper on the validation of moist heat sterilization for manufacturing processes. At the time, Bob was the only validation expert at Schering and one of only a few in the pharmaceutical industry. He gained his expertise in validation from Irving Pflug at the University of Minnesota.

After presenting his paper at a 1977 PDA conference, he joined the Association. Demonstrating an unwavering commitment to the organization, his colleagues and the membership, Bob rose through the ranks of volunteer committees to join the PDA Board of Directors in 1984. He served on that body until 2003, a 20-year stint that included two years as PDA's Chairperson from 2000 through 2001. A firm supporter of PDA's Career-Long Learning activities, Bob was instrumental in the founding and oversight of the PDA Training and Research Institute.

In addition to Bob's many accomplishments with PDA, he was recently named to U.S. Pharmacopeia's International Health Expert Committee through 2010.

Over the last three months, PDA's Board of Directors undertook a comprehensive search process for the position of president of PDA. Applicants were sought through an announcement on the PDA Web site and e-mails to industry, including each of PDA's over 10,000 members. The response was very good, with applicants from the United States, Europe and around the world. A subset of the Board served as a Search Committee to screen applicants and conduct interviews. After long and careful consideration, this Search Committee recommended Bob to the Board of Directors, which approved the selection.

One of Bob's first priorities as president is to fill the vacant vice president positions for Science & Technology and Quality & Regulatory Affairs.

PDA Interest Groups Reorganization

Kathleen Greene (Novartis), PDA Board of Directors

The PDA Board of Directors recently approved the reorganization of PDA's Interest Groups.

The reorganization is intended to structure Interest Groups to represent PDA's strategic plan and maximize member benefits by improving networking and technical information flow, by providing relevant program topics for our meetings, by formalizing membership in Interest Groups, and by supporting Interest Groups though improved electronic communication.

In order to reflect current interests of our members and to assure the capability of PDA to support Interest Group logistics, some existing Interest Groups have been combined, some have been inactivated, and new Interest Groups have been added.

With this reorganization, PDA Interest Groups are divided into five sections composed of subject-related IGs. This aligns them for improved effectiveness, supports increased synergies between them, and provides opportunity for Interest Group members to play a more active role in Task Forces. The five sections are:

- Quality Systems and Regulatory Affairs
- Laboratory and Microbiological Sciences
- Pharmaceutical Development
- Biotechnological Sciences
- Manufacturing Sciences

We look forward to the increased benefits that this restructuring brings to members. Additionally, we thank all PDA members for their involvement in Interest Groups and extend a special thanks to Interest Group leaders for their hard work and dedication to PDA and to the needs of our community.

For more information, go to www.pda.org and click on "PDA Interest Groups."

Interest Group Steering Committee

Bob Dana
PDA

Don Elinski
Lachman Consultant Services, Inc.

Kathleen Greene (chair)
Novartis Pharmaceuticals Corporation

David Hussong, PhD
U.S. FDA

Frank Kohn, PhD
FSK Associates

Sandeep Nema, PhD
Pfizer Inc

Section Leader	Robert Dana	David Hussong	Sandeep Nema	Frank Kohn	Don Elinski
Section Title	Quality Systems and Regulatory Affairs	Laboratory and Microbiological Sciences	Pharmaceutical Development	Biopharmaceutical Sciences	Manufacturing Sciences
Related IGs	• Quality Systems • Inspection Trends/Regulatory Affairs	• Microbiology/ Environmental Monitoring • Visual Inspection of Parenterals • Analytical Labs/ Stability	• Packaging Science • Process Validation • Clinical Trial Materials • Combination Products	• Biotech • Vaccines • Lyophilization	• Facilities and Engineering • Pharmaceutical Water Systems • Sterile Processing • Filtration

Member Volunteer Opportunities

The PDA Audit Committee

PDA's Board of Directors is seeking new members to serve on the Audit/Finance Committee to ensure that PDA maintains the highest level of integrity in its financial governance and provides proper oversight to ensure the security of its financial reserves. Though associations are not subject to the requirements of the Sarbanes-Oxley Act, PDA has chosen to proactively conform with good audit oversight practices in anticipation of future regulation affecting not-for-profit organizations.

To comply with such practices, the Audit Committee is seeking PDA members who have significant understanding of accounting and related financial management. This requirement can be met by someone who has past experience in finance or accounting or other comparable experience or background which would result in financial acumen. The best candidate will have had experience as an operating unit manager or director with profit and loss responsibilities.

For additional information or to express your interest in this volunteer opportunity, please contact Lance Hoboy, VP, Finance & Strategic Planning, at +1 (301) 656-5900 (ext. 114) or hoboy@pda.org.

PDA Program Planning Committees

We are currently forming committees for the PDA Annual Meeting, PDA/FDA Joint Regulatory Conference, PDA International Congress and PDA Asia/Pacific Congress through 2008.

If you would like to volunteer, please forward a brief summary of your professional experience and your contact information to Wanda Neal Ballard, Director, Programs and Meetings, at +1 (301) 656-5900, ext. 111 or neal@pda.org

PDA Nanotechnology Interest Group: Call for U.S.-Based Volunteer

PDA is seeking a member volunteer from the United States to serve as a U.S. liaison to the European Branch of the PDA Nanotechnology Interest Group, which formed in 2004. The group has been very active and is planning a conference on nano-pharmaceutical products on November 10, 2005, in London. This intense one-day event will cover cutting-edge developments in nano-pharmaceutical product development and commercialization and will provide delegates insight into how nanotechnology is impacting and driving the pharmaceutical industry.

In addition, a delegation of EU officials is interested in cooperating with the PDA Nanotechnology IG. The U.S. liaison will join with the PDA European Director to meet this group sometime in the autumn.

PDA needs a representative from its U.S. membership to participate in these IG activities. If you are interested to serve as PDA's U.S. liaison and want more details about the opportunity, please contact Gautam Maitra, European Director, Science & Technology and Regulatory Affairs, at maitra@pda.org.

PDA Viral Filtration Task Force

The PDA Viral Filtration Task Force is seeking new members to assist in their work to establish a nomenclature system for small virus removal filters. The Task Force will produce an addendum to Technical Report 41, specifically addressing the removal of small viruses by filtration. The Task Force meets approximately four to six times per year and requires active participation and contribution.

If you would like to participate in the Viral Filtration Task Force, please provide a brief summary of your professional experience and your contact information to Iris Rice, PDA Coordinator, Quality, Regulatory Affairs and Science, at +1 (301) 656-5900 ext. 119 or rice@pda.org.

PDA Letter Editorial Committee (PLEC)

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

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

Visit us at the 2005 PDA/FDA Joint Regulatory Conference in Washington, DC, September 11-14, 2005 at Table #74

The reasons to use our flexible packaging are

PERFECTLY CLEAR

☎ : 1-800-845-3456 | : www.cryovacmedical.com | : cryovac.mkt@sealedair.com

©Sealed Air Corporation 2005. All Rights Reserved. The "9 Dot Logo" and "Sealed Air" are registered trademarks of Sealed Air Corporation (US)

Sealed Air
CRYOVAC®
Medical Products

Confirm Effectiveness of Cleaning Validation

U.G. Barad, PhD, Consultant

The process of cleaning and assuring the effectiveness of a cleaning program is an increasingly critical aspect of pharmaceutical manufacturing. Internationally, health authorities make cleaning a critical process and demand its validation. In spite of this, cleaning and cleaning validation continue to be a real challenge and a recurrent issue during regulatory inspections.

The fact that nothing remains clean forever is one that the industry is grappling with. Recontaminants could be potentially dangerous substances depending on the prevailing environment at the site. Cleaning validation should be performed in order to confirm the effectiveness of a cleaning procedure.

My new book, *Cleaning Validation: A Practitioner's Guide*, addresses health authorities' requirements and systematically guides the reader in meeting them, starting from defining a contaminant and cleaning validation right up to a continuing (ongoing) cleaning assessment program. The book emerges from my practical experience of directing cleaning and its validation over a period of 20 years, as well as from my constant interaction with different regulatory inspectors/authorities. The book, therefore, covers not only the requirements of different regulatory authorities but also their expectations.

In working with many international pharmaceutical companies over the years, I've learned that most failures in cleaning and cleaning validation (CV) are encountered more because of a lack of knowledge about the precise definitions of lexicons used in cleaning, as well as the lack of clarity about CV studies. Therefore, *Cleaning Validation: A Practitioner's Guide* starts with defining a contaminant as a "foreign" substance transferred in the form of residue(s) and proceeds to drug/drug products during processing. These foreign substances principally come from manufacturing equipment and or applications directly or indirectly or from the environment where the drug products are prepared. This definition also compels the reader to recognize that success in cleaning and CV also lies in knowing the theory of contamination and its dispersion.

The book further defines cleaning validation as "a process of providing a high degree of assurance through documented evidence that the cleaning methods employed consistently control the potential carryover of contaminants into subsequent product to a level which is below predetermined level." This definition stresses that in cleaning and CV, both the nature of the substance and the level of that foreign substance (contaminant) dictate the state of cleaning, and therefore, its validation.

Furthermore, the book guides the reader to scientifically establish the required sequential steps, namely: the CV master plan, cleaning procedure(s), validation of analytical procedure(s), sampling procedure(s), selection of sampling location(s), approaches to various grouping/bracketing and worst-case rating, acceptance criteria and formulas for limit calculation, levels of cleaning, CV protocol, change control procedure, deviation investigation reporting, monitoring records and/or trend reports, revalidation of cleaning procedures and the ongoing evaluation of a cleaning program.

About the Author

U. G. Barad, PhD, has worked with leading international pharmaceutical companies for 20 years in quality assurance, quality control, direction of validation activities, management of regulatory compliance, documentation and operations. He has framed and approved quality policies, guidelines, procedures and SOPs. He is the recipient of PDA's 2003 Distinguished Author Award and the author of three recent books that focus on quality: *The Essence of GMPs, Excellence Through Validation* and *Quality Assurance*, all co-published and distributed by DHI and PDA. His latest book, *Cleaning Validation: A Practitioner's Guide*, published in August.

To order a technical book, technical report or other technical resource from PDA, please visit the PDA E-Store at www.pda.org/estore.

PDA
Parenteral Drug Association

*Connecting People, Science and Regulation*SM

2005 PDA Visual Inspection Forum

Overview

Visual inspection continues to be an important element of the manufacturing process and the quality assurance of injectable products. This two-day interactive forum will closely examine:

- ✓ New developments in the field of visual inspection, including contributions to a basic understanding of the sampling and inspection process
- ✓ Preparation and use of inspection standards
- ✓ Practical aspects of manual and automated methods and the regulatory and compendial requirements that govern them

The forum will also provide a unique opportunity to discuss your inspection challenges with the experts.

Who Should Attend

This conference will be of value to mid- and senior-level professionals with specific interest in visual inspection in the areas of:

- ✓ **Manufacturing**
- ✓ **Research and Development**
- ✓ **Packaging**
- ✓ **Validation**
- ✓ **Quality**
- ✓ **Quality Standards Harmonization**
- ✓ **Parenteral Development**

What You Will Learn

PDA has organized this forum to provide the most current information for you to use immediately in your plant by enabling you to:

- Understand particulate inspection methods and equipment
- Identify critical parameters that effect the inspection process
- Gain practical experience in implementing inspection methods
- Learn about compendial requirements and regulatory trends
- Examine techniques to validate visual inspection methods
- Find out how to identify and control foreign material

Special features of this forum include "hands-on" exposure to exhibited equipment and instrumentation, as well as case studies and group problem solving.

Bethesda, Maryland

October 20-21, 2005

Venue

Holiday Inn Select
Washington-Bethesda
8120 Wisconsin Ave.
Bethesda, MD 20814
Tel: +1 (301) 652-2000
Fax: +1 (301) 652-3806

Rates: $139 for single/double
Book your reservation by October 6th to receive the PDA rate.

Registration Fees (US$)

PDA Member	$1,200
Nonmember	$1,395
Government/Health Authority	$495
Academic*	$495
Student*	$185

** Must be a PDA member to receive this rate.*

For more information and to register online visit:

www.pda.org/visualinspection2005

Or, print out a registration form and fax or mail it to:

PDA Global Headquarters
3 Bethesda Metro Center
Bethesda, MD 20814 USA
Fax: +1 (301) 986-1093

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

Recent Sci-Tech Discussions

The following unedited remarks are taken from PDA's Pharmaceutical Sci-Tech Discussion Group, an online forum that serves as a platform for exchanging practical, and sometimes theoretical, ideas within the context of some of the most challenging issues confronting the pharmaceutical industry. Join at www.pharmweb.net/pwmirror/pwq/pharmwebq2.html. Responses are from independent forum users and do not represent the views of PDA.

Spore Strips

Hi forum members,

I have the following query regarding the procedure followed with positive spore strips during validation. All responses will be helpful.

During the validation of autoclave loads, spores are placed in various locations, and following the cycle, these are removed and placed into TSB media for 14 days (checked at seven days). If any positive growth is observed, the samples are heat-shocked at 90° for ten minutes and then plated out. My questions are:

Is it acceptable to conclude that as there was no growth following heat-shocking that the result is a false positive?

What method do other companies employ when they get positive growth from their spores?

Thanks for all your help.

Respondent 1

You may also want to ID and show that the false positive is not B. stearothermophilus.

Respondent 2

I would suggest that you plate out the contaminated samples directly and then determine if it is the original BI organism.

Heat-shocking the vegetative cells could damage them—it is usually the technique applied to the spore suspension during preparation prior to germination in order to remove other vegetative organisms.

Respondent 3

I wanted to address the "False Positive" part of your statement. To quote a well-known sterilization expert, "BI's do not lie," it is just telling you the true story of what occurred in your cycle. You might have growth, if during transfer of the strips from their glassine to the TSB there was environmental contamination introduced, but if you then incubate at 55-60, there are not many bugs that will grow at that temperature. Geobacillus stearothermophilus is the bug used for steam, and growth at 55-60 is one of the acceptance criteria for this organism in our facility before use in a spore crop. A positive can indicate your vessel is not achieving the correct parameters, or the BI was placed in a manner that impeded the correct exposure. I have included below a link to an article that can give you insights into your positive BI's in a validated vessel.

Our in-house heat-shock is 15 minutes at 95-100, mostly for removal of any possible mesophiles and vegetative cells. There is one school of thought that this heat shock also "actives" the spores.

Respondent 4

Review sterilizer cycle printouts to verify cycle parameters.

Cycle temperatures and exposure times or accumulated lethality must be adequate.

Verify that the biological indicator placement, process challenge device assembly, chamber loading, cycle parameters, BI recovery methods, etc., are per S.O.P.

Verify that the biological indicator has the correct spore count and D-value for the application.

Review routine and unscheduled maintenance, incident log, and calibration documentation.

For prevacuum steam sterilizers, run a Bowie-Dick type test and/or a leak test. A Bowie-Dick type test can help detect inadequate air removal from the chamber. Utilize the sterilizer leak test cycle to determine the leak rate of the chamber, and compare the rate to previous leak test results performed during commissioning or validation.

Have the function of the sterilizer checked by qualified personnel.

Verify the calibration of temperature and pressure channels of the sterilizer.

Identification testing should be performed on subcultures of the positive biological indicator culture:

> Subcultures from the positive cultures should be incubated at temperatures 35°-37°C and 55°-60°C for 24 to 48 hours.

Microscopic examination may be performed on the smears of the incubated subcultures under Gram's stain.

G. stearothermophilus is suggested by growth at 55°-60°C (131°-140°F), and no growth at 35°-37°C (95°-99°F) and Gram-positive rods. ➤

SimpleMix RTU

DISINFECTANTS & SPORICIDES

- All chemical agents and the WFI Quality Water are filtered at 0.2 microns and manufactured in a Class 100 filling operation
- Eliminates regulatory concerns for mixing and sterility of the solution
- Lot sterility tested per current USP compendium
- The contents of the double bag package are sterilized through a validated gamma radiation cycle.
- The system assures the appropriate dilution is made each time in a closed, sterile system
- Concentrate solutions are never handled
- Available in 16 ounce and gallon containers

US and Foreign Patents Pending

Made for Veltek's DECON-PHENE®, DECON-PHASE®, DECON-CYCLE®, DECON-QUAT100®, DECON-Clean® and DECON-SPORE 200 Plus®

Visit us at the 2005 PDA/FDA Joint Regulatory Conference in Washington, DC, September 11-14, 2005 at Table #44

vai
Veltek Associates, Inc.
(610)-644-8335
www.sterile.com

INNOVATIVE CLEAN ROOM PRODUCTS

Respondent 5

The fact that a heat shock can kill vegetative cells after incubation does not prove that there were no viable spores present prior to incubation. So no, it would not be acceptable to conclude that this was a false positive.

If the ID of the organism in your media matches the ID of the BI organism, you need to conclude that it is a genuine positive and start investigating what is wrong with the sterilization cycle (e.g., inadequate air removal, inadequate condensate removal, some points not making temperature prior to the initiation of "dwell", too minimal a cycle, etc.).

Sampling of Incoming Chemical Raw Materials

Please advise as to current practice for OSD for sampling of incoming chemical RM. Is statistical sampling of containers still OK? Or have the requirements evolved so that we must actually ID every single package of chemical (FTIR)?

Are the requirements the same for active and excipient materials?

Respondent 1

As far as sampling of incoming RM is concerned, we can follow identification test for each container and complete testing as per the formula square root N+1. The requirements are the same for active and excipient materials.

Respondent 2

You could perform retrospective validation on your previous incoming raw material. You have to prove that your certain supplier for a certain raw material is reliable for time-to-time delivery. Then you could use the result as supportive data for not doing sampling for each container incoming raw material.

Respondent 3

EU guidance requires that there should be appropriate procedures to assure the identity of the contents of each container of starting material. This can be interpreted as single container ID. I would advise it for actives and for key excipients where mix-ups have been known to happen with catastrophic consequences for the end-users e.g., diethylene glycol mislabelled as propylene glycol or glycerin.

Respondent 4

The international standard body ISO 3951:1989 for inspection by variables is appropriate to use for a batch of a non-discrete materials like an APIs.

Respondent 5

The ANSI Z1.4 is indeed valid ONLY for the sampling of discrete populations of units. After one determines the number of sampled units (n) based on the total number of units (N) packed in Z boxes according to the ANSI Z1.4, one may randomly collect the n units from a selected number of these boxes if he does not want to open all boxes for whatever justifiable reason. This number of boxes can be a fixed percentage (e.g., 10%) of Z boxes, or alternatively from the square root of Z +1 boxes. While doing this, each randomly picked box is sampled with an equal number of units.

The total number of units sampled from the whole lot is still based on statistical principles as set in the ANSI Z1.4. The application of square root Z +1 is suggested as an example of following a simple practical index to minimize the number of boxes actually sampled when one does not want to open all boxes. If one wishes to partition the whole lot into, for instance, 3 sublots based on some logic that establishes a better representative sampling (bottom, middle and upper; or beginning, middle and end), he may apply the square root Z+1 on each sublot: i.e., n/3 is sampled from Square root Z+1 boxes out of all Z boxes in the sublot.

Examples of sampling from limited boxes or packages could be: testing for physical dimensions of sterile vials packed in trays of 100 units per tray and only Square root Z+1 of the trays will be opened for sampling and exposed to a non-sterile environment.

Respondent 6

I have not read the original question but from the replies given, the following ASTM standard may be appropriate.

ASTM 300-03, "Standard Practice for Sampling Industrial Chemicals." It addresses liquids, solids, slurries, bulk materials and packages.

2006 PDA Annual Meeting

Pharmaceutical Manufacturing Science in the 21st Century
From Innovation to Implementation

Anaheim, California ◆ April 24 – 26, 2006

Call for Papers

Dear Friends and Colleagues:

Have you or someone you know in the pharmaceutical and biopharmaceutical community done something special in the past year, something that would be of particular interest to the rest of the world? Examples include:

- Solved an unusually difficult technical problem
- Validated a difficult process or an unusual dosage form
- Submitted an MAA, BLA or an NDA which includes some of the "new" things we are hearing about: risk-based decisions, PAT, nanotechnology, etc
- Expanded upon ideas about what "risk-based" means and how it can be implemented
- Developed a new sterilization process or method

Why not let the world know about it? We encourage you to submit a scientific abstract for presentation at the **2006 PDA Annual Meeting**, which will be held April 24-26, in Anaheim, California.

Abstracts must be noncommercial in nature, describe new developments or work and significantly contribute to the body of knowledge relating to pharmaceutical manufacturing, quality management and technology. Industry case studies demonstrating advanced technologies, manufacturing efficiencies or solutions to regulatory compliance issues are preferable and will receive the highest consideration. All abstracts will be reviewed by the Program Planning Committee for inclusion in the meeting or in poster sessions.

ABSTRACTS MUST BE RECEIVED BY September 30, 2005 FOR CONSIDERATION.

PDA is seeking presentations 30 minutes in length, that present major challenges and practical approaches to resolution in the following areas:

- Aseptic processing of medicinal products
- International regulatory and harmonization initiatives
- Industry manufacturing/product trends
- Combination products
- Risk management and risk-based GMP
- Supplier quality management
- Use of disposables in manufacturing
- Packaging, labeling and anti-counterfeiting measures
- Glass defects and AQL
- Innovative biotech upstream and downstream processing
- Contract manufacturing issues and quality agreements
- Design and management of multi-product facilities
- Blend uniformity and solid dose manufacturing
- Validation of pharmaceutical and biotech processes
- Viral safety evaluation
- Process analytical technologies (PAT)
- Quality management systems for pharmaceuticals and biopharmaceuticals
- Industry case studies—compliance and quality issues
- Microbiology initiatives and trends
- Rapid microbiological methods
- Barrier isolation technology
- Sterilization
- Environmental Monitoring

Commercial abstracts featuring promotion of products and services will not be considered.

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

- ✓ Title
- ✓ Presenter's biography
- ✓ Additional authors
- ✓ Full mailing address
- ✓ Phone number
- ✓ Fax number
- ✓ E-mail address of the presenter
- ✓ 2-3 paragraph abstract, summarizing your topic
- ✓ The type of forum in which you can present your topic (traditional, case study, discussion/debate, panel)
- ✓ Target audience (by job title or department)
- ✓ Explanation of specific take-home benefits your target audience can use immediately on-the-job
- ✓ Key objectives of your topic and what new information you will present that has not been presented elsewhere

PDA also reaches a broad market with their signature audio conferences. If you are interested in submitting your abstract as a possible audio conference 1-2 months after the conference, please submit as well.

Upon review by the program committee, each submitter will be advised in writing of the status of his or her abstract after September 30, 2005. PDA will provide one complimentary meeting registration per presentation. Additional presenters will be required to pay appropriate conference registration fees. With the exception of health authority speakers, all presenters are responsible for their own travel and lodgings.

Visit www.pda.org/annual2006 to submit your abstract today.

Building a New Manufacturing Toolkit for Viral/TSE Safety, continued from cover

for healthcare products, stated Dr. Brorson. A better toolkit should facilitate the efficient and safe movement of new and innovative therapies from concept to the marketplace.

The 2005 PDA Viral & TSE Safety Conference, he noted, is an example of how industry, EMEA and FDA can work together to foster development of the new toolkit. "For example, we'll have sessions on TSE safety approaches, standardization of viral clearance studies, new technologies to enhance safety and improve robustness…on robustness in bioprocessing and controlling viruses in unconventional source materials…a session on risk assessment and mitigation." Each session focuses on and seeds ideas for building "a better manufacturing toolkit, [and] our hope is that a better manufacturing toolkit will spur product development and enable manufacturers to transition products from concept to market in an efficient and safe manner."

Program planning committee co-chair **Glenda Silvester,** Principal Scientific Administrator, EMEA, stated that it was a particular pleasure, in this 10th Anniversary year of the EMEA, to be holding the first conference with PDA that is cosponsored by the two health authorities. The conference will provide plenty of opportunity "to hear about the latest scientific developments and to discuss areas where updating of regulatory guidance may be desirable to take account of these developments." She stressed that EMEA "keeps viral and TSE safety under continuing review. Conferences such as this provide a strong scientific base to support that review." The EMEA also keeps in mind "the desirability of international harmonization wherever this is applicable."

The planning for this conference took account of issues raised during the 2003 PDA/EMEA Virus Safety Forum in Germany, anticipating further development at the 2005 meeting, explained Silvester.

Biopharmaceutical scientists are developing an understanding of key and critical operating parameters of viral clearance steps, a primary objective of the GMP initiative.

"Key questions" the conference would help answer include:

- Are all the virus tests required in the ICH guideline needed for well-known cell lines?
- To what extent can virus validation studies be extrapolated to similar manufacturing processes, often referred to as "generic" validation?

A "direct outcome" of the 2003 meeting was the initiation of work on a guideline on viral safety for investigational medicinal products. Likewise, Silvester said, "our team will follow up on key points raised" at this 2005 meeting. These "will be further discussed within the EMEA Scientific Committees and particularly the Biologics Working Party."

An Advancing Field

In his main talk, "FDA's Perspective Of Viral Safety For Biotech Products," Dr. Brorson noted that the field of viral clearance/inactivation has rapidly advanced in the past decade or so. These scientific advances coincide nicely with a second CDER initiative, the 21st century GMP initiative, announced in 2002. A major goal of the GMP initiative is to encourage manufacturers to adopt new technologies and risk-based approaches to biopharmaceutical quality. Additionally, a related goal is ensuring that FDA's review and inspection processes are based on state-of-the-art science.

Advances in bioprocessing science and technology, combined with FDA's evolving focus on this science, are moving "the viral safety arena" closer to the "ideal state" identified by the initiative, stated Dr. Brorson.

Dr. Brorson outlined a number of recent technological advances in the field. Q-PCR assays, for example, are "particularly good at quantifying characterized viruses—viruses where the genome sequence is known and specific PCR primers and probes can be designed for them." The assays possess improved precision relative to conventional assays and are "ideal for virus-removal validation studies" where well characterized viruses are used for spike/removal studies. They also have potential in the quantification of endogenous retroviruses in harvests of characterized cell-cultures, and can be used in multi-spiking validation studies ("evaluate the removal of up to three viruses at once"). Q-PCR assays have some limitations; they are not suitable for measuring virus inactivation or for screening for unknown viruses.

Biopharmaceutical scientists are developing an understanding of key and critical operating parameters of viral clearance steps, a primary objective of the GMP initiative. Dr. Brorson stated that the critical and key parameters

for viral clearance should be defined before deciding whether a unit operation is robust for viral clearance. The challenge is that the designation of key and critical operating parameters "is not always obvious."

There must be "strong scientific justification" behind the designation of which parameters are or are not key/critical. Justification can be acquired through small-scale studies, manufacturing experience and/or consultation of the peer-reviewed scientific literature. This field is active and fluid; advances in bioprocessing science might change a particular parameter's designation over time. Parameters deemed non-key/critical for one performance attribute, like step yield, may be "critical for other aspects of unit operation performance, like viral clearance; it is even possible for some parameters to be critical for clearance of one virus but not another. All of this must be understood in a scientific and mechanistic context."

A scientific understanding of robustness and inactivation/removal mechanisms opens the door to risk-based validation approaches. For viral safety, these include bracketing and "modular," or "generic," validation, approaches similar to the "design space" concept introduced by ICH Q8.

Quoting FDA's 1997 monoclonal antibodies "points to consider," Dr. Brorson explained that the modular and generic approaches involve "the application of clearance data from one product to another with identical unit operations." When appropriate, these approaches have been accepted for Investigational New Drugs, "based on a very careful evaluation and comparison of the unit operation between the model and new product to determine whether or not the parameters are equivalent. The key is robustness: One must really have confidence that the unit operation is robust…in order to decide whether product-specific effects are unlikely and that the generic (in-house experience) approach is acceptable; this relies on a scientific understanding of the critical parameters of the unit operation."

Chromatography and viral filtration are other elements where questions frequently arise during dossier evaluation.

Published examples of analyses of unit operations robustness in the scientific literature focused on a "careful evaluation of the impact of relevant parameters of the unit operation on its ability to clear viruses, and an evaluation of the removal or inactivation mechanism," said Dr. Brorson.

For chromatography, effectiveness over extended resin reuse is an area of specific concern, and has been studied extensively to determine under which circumstances it becomes critical.

The EMEA Perspective

In discussing EMEA's perspective, **Patrick Celis,** PhD, Scientific Administrator, EMEA, gave an overview of current guidance and summarized the approach to virus inactivation/removal seen in marketing authorization dossiers. He also outlined a number of issues that have arisen during the evaluation of viral safety data in dossiers for biologics products.

Dr. Celis listed areas that often cause problems during regulatory review, including questions about the reproducibility, reliability and specificity of inactivation/removal and about the validity of downscaling. Other problems frequently include lack of clarity regarding process parameters, uncertainty over the reduction capacity of the process for small, non-enveloped viruses and concern about the potential for viral contamination from culture media components, such as fetal calf serum and trypsin.

Chromatography and viral filtration are other elements where questions frequently arise during dossier evaluation. For the former, robustness/specificity, column reuse, mechanism of reduction and column sanitization can prompt reviewer questions. For viral filtration, robustness, virus aggregation and integrity testing are sometimes at issue.

Dr. Celis highlighted the activities of the EMEA Biologics Working Party (BWP) during the year-and-a-half since the 2003 PDA/EMEA Forum.

Among the issues considered by the BWP are "generic" (or in-house experience) validation, testing of well-known cell lines, and viral safety of novel technologies, e.g., cell therapies, transgenics and tissue engineering. The BWP considered that revision of current EMEA viral safety guidelines is "probably not" necessary. But the group did decide that there was a need for additional guidance (e.g. for clinical trials material and new technologies).

Dr. Celis stated that it is important for industry to communicate issues to the regulatory authorities and

continued on page 20

PDA Calendar of Events for North America

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

Conferences

September 12-16, 2005
PDA/FDA Joint Regulatory Conference, Courses and Exhibition
Washington, DC

September 15, 2005
Mycoplasma Contamination by Plant Peptones
Washington, DC

October 20-21, 2005
2005 PDA Visual Inspection Forum
Bethesda, Maryland

November 3-4, 2005
Aseptic Processing Guidance
Las Vegas, Nevada

April 24-28, 2006
PDA Annual Meeting

May 8-10, 2006
2006 Training Conference
New Orleans, Louisiana

Training

Lab and Lecture calendar events are held at PDA-TRI Baltimore, MD unless otherwise indicated.

Laboratory Courses

September 7-9, 2005
Advanced Environmental Mycology

October 4-5, 2005
Validating a Steam Sterilizer

October 6-7, 2005
Fundamentals of D, F and z Value Analysis

October 17-21, 2005
Aseptic Processing Training Program (Week 1)

October 31-November 4, 2005
Rapid Microbial Methods

November 7-9, 2005
Cleaning Validation

November 14-18, 2005
Aseptic Processing Training Program (Week 2)

Lecture Courses

September 7-9, 2005
Fundamentals of Pharmaceutical Filtrations and Filters

September 15-16, 2005
PDA/FDA Joint Regulatory Conference Courses
Washington, DC

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

September 26-28, 2005
Basic Skills for the Training Professional

Course Series

October 24-26, 2005
Medical Device Course Series
Denver, Colorado

November 29-December 1, 2005
***Career-long Learning*™**
New Orleans, Louisiana

Chapters

September 8, 2005
PDA Mountain States Chapter
Vendor Show

September 15, 2005
PDA New England Chapter
Dinner Meeting

September 22, 2005
PDA West Coast Chapter
Dinner Meeting

September 28, 2005
PDA Southeast Chapter
Vendor Show
Durham, North Carolina

September 28, 2005
PDA Capital Area Chapter
Rapid Microbiology and Contemporary Idenfification Systems in Support of Manufacturing
Gaithersburg, Maryland

October 4, 2005
PDA Southern California Chapter
Combination Products and USP Update
Irvine, California

October 5, 2005
PDA Delaware Valley Chapter
Vendor Show

October 20, 2005
PDA Midwest Chapter
Dinner Meeting
Northbrook, Illinois

November 10, 2005
PDA Mountain States Chapter
Speaker Dinner

PDA Calendar of Events for Europe/India/Asia Pacific

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

EUROPE

September 20, 2005
PDA and the PDA Italy Chapter
Rapid Micro TR 33
Milan Italy

September 21-22, 2005
PDA Training & Research Institute
Career-long Learning™
Basel, Switzerland

October 24-25, 2005
The Universe of Pre-filled Syringes - 2005
Munich, Germany

November 10, 2005
PDA and PDA Europe
PDA Nanotechnology Conference 2005
London, England

November 24, 2005
PDA and the PDA Central Europe Chapter
PDA EuroForum
Pharmaceutical Product Labeling
Vienna, Austria

November 30-December 2, 2005
PDA Training & Research Institute Laboratory Course
Practical Aspects of Aseptic Processing
Basel, Switzerland

December 7-8, 2005
PDA and the PDA France Chapter
Biosimilars/Extractables & Leachables
Paris, France

INDIA

October 7, 2005
PDA and the PDA India Chapter
Microbiology for Pharmaceuticals and Cleanrooms
Mumbai, India

ASIA/PACIFIC

September 8, 2005
PDA Australia Chapter

November 24, 2005
PDA Australia Chapter
Annual Meeting and Holiday Dinner

November 2005
PDA Japan Chapter
Annual Meeting
Tokyo, Japan

December 2005
PDA Korea Chapter

Building a New Manufacturing Toolkit for Viral/TSE Safety, continued from 17

for both regulators and industry to participate in forums like the PDA viral & TSE safety conferences.

Regarding the guideline on viral safety for clinical trials, Dr. Celis noted that its purpose is to harmonize the approach throughout the EU, which is "especially important for multicenter clinical trials." EMEA published a concept paper in December 2004, the public consultation period for which closed in March. The draft guideline is expected to be published during the second half of 2005. It will address:

- The extent of viral safety studies prior to and during clinical development
- Use of in-house experience concerning virus safety evaluation
- Criteria for the design of preliminary virus safety evaluation studies
- Risk analysis to be performed

Dr. Celis also pointed out that the European Pharmacopeia had published a general chapter on viral safety, and that consultation period was expiring at the end of June.

Following the presentations by Dr. Brorson and Dr. Celis on biotech products, the FDA Center for Biologics Evaluation and Research's **Mahmood Farshid,** PhD, Supervisory Biologist, and EMEA's **Glenda Silvester** spoke about the regulatory perspective on viral safety for plasma-derived products.

During a Q&A session following the four talks, an audience participant asked if FDA would follow EMEA's lead and develop guidance for clinical trials. Dr. Brorson replied that the biotech divisions are now more "settled in" at CDER (in the Office of Biotechnology Products/Office of Pharmaceutical Science) and may begin thinking about the possibility of creating guidance in this area or updating existing guidance like the monoclonal antibodies points to consider document. He noted that the latter document already suggests streamlining approaches at early clinical trials for life-threatening indications.

For plasma-derived products, there were questions on what log reduction is considered significant and on verifying the laboratory virus clearance model with multiple lab-scale runs and a statistical comparison to the manufacturing history. The questioner stated that the limited number of lab runs would not be statistically significant. Dr. Farshid advised that the small-scale data should be relevant to the actual process. He noted that FDA has seen "studies that are very clean and clear, but when we go to the actual manufacturing process, the firm changed some of the critical parameters." He asserted, "The only way you can say the clinical data is relevant is to provide sufficient data to show that it is actually relevant."

The number of times a firm should repeat a small-scale viral safety study "depends on what you are validating," explained Dr. Farshid. For some inactivation steps, "a couple of times is sufficient;" for others, "you have more variables… so it is case-by-case."

EMEA's Mrs Silvester added: "What we are dealing with is establishing whether the inactivation step is effective and then reproducibly effective." Companies must "do what is necessary to the understanding of that particular step." The process is "not strictly in terms of numbers, but what you are trying to show."

Exceeded Expectations

Following the opening regulatory session, the 2005 PDA Viral & TSE Safety Conference moved on to TSE issues. During the second day, the conference covered issues regarding standardization, cell substrates, new technology and robustness. On the final day, the conference addressed more issues regarding robustness, viral control in unconventional source materials, and risk assessment and mitigation.

Overall, the three-day event exceeded all expectations in terms of the quality of presentations, the energy of the panel discussions and the overall attendance figures. Several members of the program planning committee intend to participate in a PDA audio conference in late September to provide an overview of the science and technology presented at the May event. The co-chairs (**Rich Levy,** PhD, **Brorson** and **Silvester**) also intend to present meeting summaries at upcoming PDA conferences, like the 2006 Annual Meeting. They anticipate that a follow-up event, co-sponsored by FDA and EMEA, would be appropriate for either late 2007 or early 2008, depending on advances in the field. Keep an eye on the *PDA Letter* and www.pda.org for more information.

Walter Morris, PDA, in collaboration with Kurt Brorson, Rich Levy and Glenda Silvester

Please turn to page 30 for photos of the day-one speakers from the 2005 PDA Viral & TSE Safety Conference.

The EMEA's Annex 18: "Disharmonization?"

Enforcement of EMEA's Annex 18 at Issue

Stephen Bellis, IVAX Pharmaceuticals

In November 2000, the EU GMP Guide was modified to incorporate ICH Q7A, GMPs for APIs, as Annex 18. Recently, legislation in Europe has modified the legal recognition of Annex 18 so that it will become Part II of European GMPs, giving it the same force in law as the current GMPs for medicinal products for human or veterinary use. Specifically, Article 46f of Directive 2001/83/EC and Article 50f of Directive 2001/82/EC, as amended by Directives 2004/27/EC and 2004/28/EC, respectively, require manufacturing authorization holders (MAH) to use only active pharmaceutical ingredients (APIs) that have been manufactured in accordance with GMPs for starting materials. This aspect of the change is not particularly controversial, as it has been common practice in Europe to use APIs manufactured in line with GMPs What is controversial and needs to be understood by the PDA membership is how the competent authorities in Europe intend on enforcing this new requirement.

The requirement to use only APIs manufactured in accordance with the detailed requirements of GMPs comes into effect as of October 31, 2005. To assure compliance with this new directive, the competent authorities will inspect MAHs against the new requirements to ensure the legal requirements governing the use of APIs are being met. **Note that the competent authorities will assess the MAH, not the API manufacturer itself.** Manufacturers/Suppliers of APIs are only inspected under "certain circumstances" (Ref. 1) and do not constitute part of a competent authority's routine inspection program. It is the responsibility of the MAH to be able to demonstrate that APIs used post October 2005 have been manufactured per GMPs.

As part of the inspection process, the competent authorities will review the MAH's inspection process, i.e., the systems in place to adequately determine GMP compliance, and the competent authorities will review the MAH's written audit reports. The first part is not new, as European competent authorities and other regulatory agencies have had the right to review audit programs for years, but this has not been consistently done. What *is* new is the routine review of audit reports. The review of the audit report is multipurpose. First, the review is intended to determine if the MAH has addressed audit observations to ensure that corrective actions have been completed. Secondly, if the audit findings are so egregious that the MAH has determined the API supplier is not compliant with GMPs, the competent authorities will want to see what the MAH has done to replace that supplier. Thirdly, an adverse audit report can constitute a "certain circumstance" whereby the competent authorities can justify an inspection of an API supplier.

What *is* new is the routine review of audit reports.

Richard Andrews, Operations Manager, GMP, Medicines & Healthcare Products Regulatory Agency, stated the following regulatory expectations in a recent presentation to industry:

- Manufacturing authorization holders should have a process for supplier approval in place.
- The supplier approval program should cover the whole supply chain—manufacturer, repacker and/or broker.
  - All steps in the supply chain of the active substances in use by a manufacturing authorization holder will have been audited.
  - A report of each audit performed has been written and issued.
- Any deficiencies/noncompliances identified have been recorded and subsequently closed out.
- A statement as to the GMP compliance of each step in the supply chain is made.

Mr. Andrews also noted:

- *The ultimate responsibility for ensuring that the active starting materials used in any licensed medicinal product have been manufactured in accordance with GMPs therefore lies with the qualified person certifying the product for release.*

This final point needs to be clearly understood. With the change of Annex 18 into Part II of European GMPs, it becomes legally enforceable. Therefore, the qualified person releasing the product into Europe has to have knowledge that not only the medicinal product, *but also the API(s)* used in the product, have been made according to GMPs. If you are a company importing medicinal ➤

products into Europe, your local qualified person will now require more information about the APIs used in the products. The qualified person does not have to have audited the API supplier him/herself, but needs to have evidence that the supplier has been audited and is compliant with GMPs.

Marketing Authorization

The document discussed in Reference 1 also includes advice on the information that must be submitted with a marketing authorization or variation to change or add a new API supplier. The applicant must submit a declaration from the MAH that the API(s) concerned have been manufactured in accordance with GMPs. The document explains this further by stating: "It is expected that the holder will base such a declaration on carrying out, or having carried out on his behalf, an audit of the manufacturers/distributors of the active substances involved."

Harmonization Issues

With the changes to the GMPs for APIs, the applicability of Annex 18 (ICH Q7A) is expanded. Annex 18, section 1.3 (Q7A), excludes all vaccines, whole cells, whole blood and plasma, blood and plasma derivatives and gene therapy APIs. The proposed Part II, section 1.2 (Ref. 2), of the European GMPs excludes only blood, plasma and bulk packaged medicinal products. It includes active substances that are produced using blood and plasma. By omitting vaccines, whole cells and manufacturing and control aspects specific to radiopharmaceuticals from the new wording, it implies that they are implicitly included. This proposal significantly expands the scope of ICH Q7A within the European Union and to products imported into the European Union to APIs for veterinary medicines (except ectoparaciticides), vaccines (all types), cell substrates, medical gases and radiopharmaceuticals. Therefore, a situation has arisen which leads to some disharmony on the GMP requirements for APIs which was so carefully and painstakingly achieved with ICH Q7A.

Changes to other Annexes (Ref. 3)

When the EU guidelines are divided into Part I for Drug Products and Part II for APIs, the situation regarding the annexes to the EU guide will need to be clarified with respect to APIs in order to avoid confusion. Annexes 9, 10, 12, 14, 16 and 17 are not applicable to APIs at all. Annexes 8, 11, 13 and 15 are already covered in specific chapters of Annex 18 (new Part II), and therefore should not be applicable to APIs. The EMEA stated in a recent concept paper (Ref. 3) that some duplications and overlaps between the proposed Part II and the current Annex 2 (Biological Products for Human Use), Annex 3 (Radiopharmaceuticals) and Annex 6 (Medicinal Gases) will be identified and amended for the sake of clarity.

Certain Excipients

The changes to the European Directives required the EMEA to consider whether or not GMPs were required for "certain excipients," but there was no further explanation within the Directives as how to make this determination. Therefore, the EMEA published a questionnaire for both excipient users and excipient suppliers regarding the perceived need for GMPs for "certain excipients." The responses were mixed, but industry associations, including PDA, preferred the current state of self-regulation. The EMEA Inspectors Working Party considered the comments received and proposed a risk-based approach. Commission lawyers advised that a list of specific excipients was required. There is a team working within the Inspectors Working Party to define a list of criteria that would be used to determine if a specific excipient should be manufactured in accordance with GMPs. The Inspectors Working Party has agreed to accept public comment on their proposed criteria as part of the review process.

References

1. EMEA/INS/GMP/50288/2005, *Guidance On The Occasions When It Is Appropriate For competent authorities To Conduct Inspections At The Premises Of The Manufacturers Of Active Substances Used As Starting Materials,* London, 2 March 2005.
2. EMEA/INS/GMP/15202/2005, *Medicinal Products For Human And Veterinary Use: Good Manufacturing Practice, Basic Requirements Part II: The Principles Of Good Manufacturing Practice For Active Substances Used As Starting Materials,* London, 4 March 2005.
3. EMEA/INS/GMP/1477/2005, *Concept Paper On The Revision Of Some Annexes To The European GMP Guide In The Context Of GMP For Active Substances,* London, 25 April 2005.

About the Author

Stephen Bellis is European Quality Director for IVAX Pharmaceuticals and is a member of PDA's Regulatory Affairs and Quality Committee.

Regulatory Briefs

Europe

EMEA Publishes Two Annex Guidelines on Biosimilars for Comment

The EMEA Committee for Medicinal Products for Human Use published two draft Annex guidelines on biosimilars. One covers products containing recombinant erythropoietins; the other addresses products with recombinant granulocyte-colony stimulating factor.

The guidelines can be accessed at www.pda.org/regulatory/RegNewsArchive-2005.html.

United States

Stephen Galson Becomes CDER's Permanent Chief

Stephen Galson, MD, was named the permanent Director for FDA's Center for Drug Evaluation and Research (CDER). Dr. Galson will lead the more than 2,200 employees of CDER who work to evaluate and approve prescription and over-the-counter drugs for their safety and efficacy. Dr. Galson's charge includes overseeing the Center's broad national and international programs in pharmaceutical regulation.

"Dr. Galson's scientific and management experience will benefit all Americans as the FDA continues to advance and protect public health," said Commissioner Crawford. "Under Steven's leadership, CDER has formed the new Drug Safety Oversight Board announced by Secretary Leavitt, created a new office to strengthen the Center's review of drugs to treat cancer, and approved more than ten generic drugs under the President's Emergency Plan for AIDS Relief."

Dr. Galson joined FDA in April 2001 as the Deputy Director of CDER and most recently served in the role of the Acting Center Director. Prior to his arrival at FDA, he was the Director of the Office of Science Coordination and Policy, Office of Prevention, Pesticides and Toxic Substances, at the Environmental Protection Agency. Dr. Galson is the recipient of numerous Public Health Service awards, most recently the Outstanding Service Medal for his leadership and management of CDER while serving as Acting Center Director. Dr. Galson holds a BS from Stony Brook University, an MD from Mt. Sinai School of Medicine and an MPH from the Harvard School of Public Health.

FDA Commissioner Announces Important Personnel Changes

FDA Commissioner **Lester M. Crawford**, MD, is pleased to announce several personnel changes at the Agency designed to create an even more efficient and compact central organization.

"With this senior team of experienced public health professionals, FDA is well positioned to continue to improve our science," said Dr. Crawford. "We are now ensuring that we get safe and effective products to patients who need them, that we communicate clearly with patients and physicians so they have the best information available to make well-informed decisions about their health, and that we continue to take new steps through our Critical Path initiative to take advantage of changes in medical science and health care delivery to move our health care system from one focused on treatment to also addressing chronic needs and healthcare prevention through a more personalized approached to medical care."

Scott Gottlieb, MD, a former FDA and Centers for Medicare and Medicaid Services senior official, is returning as FDA's new Deputy Commissioner for Medical and Scientific Affairs. In this position, Dr. Gottlieb will coordinate medical and scientific affairs for the Office of the Commissioner, serving as senior policy advisor to the Commissioner in these areas. Dr. Gottlieb is a practicing physician who most recently worked as a Resident Fellow at the American Enterprise Institute, a prominent Washington, DC-based think tank and also spent time as an American medical correspondent for the *British Medical Journal*.

Janet Woodcock, MD, will become Deputy Commissioner for Operations and Chief Operating Officer (COO) on a permanent basis following her experience in this position as Acting Deputy Commissioner. As COO, Dr. Woodcock will be responsible for managing Agency-wide scientific and regulatory processes and will also oversee special initiatives that require close collaboration across the Agency's medical and scientific centers. An internist and rheumatologist, Dr. Woodcock was previously the Director of CDER and also has significant experience working in the Center for Biologics Evaluation and Research.

Murray M. Lumpkin, MD, will become Deputy Commissioner for International and Special Programs, also on a permanent basis, following his acting duties in this same position. He will oversee the Office of International Programs, the Office of Pediatric Therapeutics, the Office of ➤

GMP MANUAL

Good Manufacturing Practice & Implementation

New!

The most extensive GMP reference book in the world!

Maas & Peither
GMP PUBLISHING

3,000 pages expert knowledge for easy implementation of Good Manufacturing Practice

- Quality Management
- Personnel
- Quality Control
- Documentation
- Contract Manufacturing
- Quality Tools
- Premises
- Qualification
- Process Validation
- Cleaning Validation
- Computer System Validation
- Production
- Equipment
- Packaging
- Inspections

plus 25 Guidelines from EU, FDA, PIC/S, ICH, WHO

- ***Up-date-service***
- ***21 day test without charge***

Order now 5 files plus CD-ROM for only 595 € and save 100 €.

Subscription price until October 31, 2005 – two updates per year approx. 160 € each

www.gmp-manual.com

Combination Products, and will coordinate the FDA response to national public health issues that cut across programmatic centers at FDA. A pediatrician with an additional certification in tropical medicine, Dr. Lumpkin was previously the Deputy Center Director for CDER.

Patrick Ronan, currently Associate Commissioner for Legislation, will become Chief Staff Officer to Commissioner Crawford. Ronan will coordinate staff activities in the Office of the Commissioner and will serve as the principal liaison to Department of Health and Human Services. A former senior congressional staffer, Ronan has been active for the last decade in the legislative arena with a focus on public health issues.

Quality Problems Cause Headaches for Glaxo, Shut Down Able

Quality and manufacturing problems involving two GlaxoSmithKline (GSK) drugs, Paxil CR and Avadamet, forced the company to sign a consent decree in May. Under the terms of the decree, the company agreed to take measures to ensure that its Cidra facility and the two drugs fully comply with current cGMP requirements and to ensure that ongoing shipments have the quality attributes they are required to possess. The decree also requires that a third-party expert certify all corrections, as well as the firm's compliance with cGMP requirements. Additionally, FDA will continue to monitor these activities through its inspections. The company was not required to pay a disgorgement penalty, common to recent GMP-related consent decrees. However, GSK did post a penal bond of $650,000,000 contingent upon the company either successfully reconditioning drugs seized in March 2005 or destroying them and paying costs to the government. The decree provides 150 days for the firm to correct the manufacturing deficiencies.

Able Labs faces more serious challenges resulting from its cGMP infractions. The most serious FDA allegation is that the company failed to reject drugs failing stability testing. Rather than reject the products, the company either resampled and reinjected, or reprocessed. Other violations were reported on an FDA 483, which covered 29 inspections conducted from May 2 through July 1. Prior to these inspections, the company voluntarily suspended production of all its products following its own internal findings of serious GMP violations. Later the company withdrew all of its approved abbreviated new drug applications from the market.

In its inspection findings, FDA placed blame directly on Able's managers, citing their failure to assure the safety, identity, quality and purity of all drugs shipped. The company experienced serious shake-ups at the highest levels. First, CEO Dhananjay Wadeker resigned with Able's initial announcement regarding the internal findings. Next, interim CEO and President Robert Mauro resigned on July 7, following the issuance of the FDA 483. The company would like to enter into a consent decree with the U.S. Department of Justice and is considering filing for bankruptcy.

Links to FDA press releases regarding the GSK case and the Able 483 are available at www.pda.org/regulatory/RegNewsArchive-2005.html.

U.S. FDA Seeks Input on New Quality Assessment System

CDER is launching a pilot program to generate data needed to develop guidance on its new pharmaceutical quality assessment system (QAS). The Office of New Drug Chemistry (ONDC), led by **Mohed Nasr**, PhD, is working on the project.

Specifically, FDA is seeking 12 original new drug applications (NDAs) that will be ready for submission by Dec. 31, 2006. Interested sponsors will work with the Agency on an individual basis, with review of the application being the primary goal. The program to create the QAS guidance will focus only on the chemistry, manufacturing and control portion of the NDA.

When the new QAS is completed, the emphasis of CMC review will shift to critical pharmaceutical quality attributes—related to chemistry, formulation, manufacturing process design and product performance—and their relevance to safety and effectiveness. FDA outlined the groundwork for the new assessment system last fall with the release of a white paper, titled "ONDC's New Risk-Based Pharmaceutical Assessment System." The paper was developed as part of the Agency's pharmaceutical GMP initiative.

Dr. Nasr provided more details about the QAS at the 2005 PDA Extractables/Leachables Forum in May. The objective is to facilitate innovation and continuous improvement throughout the product life cycle and to provide regulatory flexibility for specification-setting and post-approval changes based on scientific knowledge and understanding of product and process by applying quality-by-design principles.

The deadline to submit requests to participate in the program is Oct. 31. For more information, go to www.pda.org/regulatory/RegNewsArchive-2005.html.

PDA Membership Off to a Great Start in 2005

Kelly Coates, PDA

2005 has been a great year for PDA membership. Over the first six months, PDA has welcomed more than 1600 new members.

Chapters Lead the Way

PDA's 24 Chapters worldwide have been instrumental in our recent membership growth. By providing local programming and networking opportunities, Chapters often are the first point-of-contact with PDA for many members. Their ability and willingness to educate pharmaceutical and biopharmaceutical professionals about PDA is an important part of our new member recruitment efforts.

The Israel Chapter is leading the way with 248 new member referrals so far this year. Thanks to their efforts, hundreds of industry professionals in Israel are realizing the benefits of PDA membership.

The Japan Chapter has also done their part by referring 51 new PDA members. Chapters like the Japan Chapter provide information and resources targeted to the local environment and culture. They assist in conveying PDA's mission and connecting local industry to the global association.

Other Chapters that have referred PDA members so far this year include:

- Australia Chapter
- Canada Chapter
- Capital Area Chapter
- Central Europe Chapter
- Delaware Valley Chapter
- France Chapter
- Italy Chapter
- Spain Chapter
- Taiwan Chapter
- United Kingdom and Ireland Chapter

Many thanks to our Chapters for supporting the association and enhancing the membership experience for thousands of PDA members!

New Membership Types Offer More Opportunities

The new membership types introduced in late 2004 have made it easier for a diverse group of professionals to join PDA and participate in scientific exchange. The "Developing Economy," "Academic" and "Student" membership types provide full member benefits and privileges at a reduced rate. These membership types were established to increase the diversity of our membership and thereby enhance interaction between academics, students and professionals worldwide.

Just the Beginning

2005 is far from over, and we are working to make it a banner year for PDA membership. In addition to recruiting new members, we are working to enhance the PDA membership experience. A redesigned welcome packet was sent to new members starting in July. This packet provides an introduction to PDA, including information on member benefits and services to help those new to our community attain the complete PDA experience. For our long-time members, we are now issuing lapel pins to recognize every five years of membership.

As an association, we realize our greatest asset is our membership. We are here to serve you and to provide resources that enable you to grow professionally and to advance the pharmaceutical and biopharmaceutical industries. To our long-time members, thank you for your years of participation. To all of our new members, welcome to PDA! We're happy to have you, and we look forward to working with you in the years to come.

Make the Most of Your PDA Membership

Participate in Your Local Chapter

PDA has 24 Chapters around the world, with local programming and resources to help you stay informed, interact with your peers, and influence the pharmaceutical and biopharmaceutical industry. Please see www.pda.org/chapters for more information.

Join an Interest Group

PDA Interest Groups allow people with common interests to interact, exchange information, and directly impact the science, technology and regulation of bio/pharmaceutical manufacturing; go to www.pda.org/science/IGs.html for details.

Participate in Member Opportunities

Join a PDA Board, Committee or Task Force. Take advantage of these opportunities to participate in our shared commitment to the advancement of science, technology and training, and to develop your own technical and managerial skills. Please see www.pda.org/volunteer for more information.

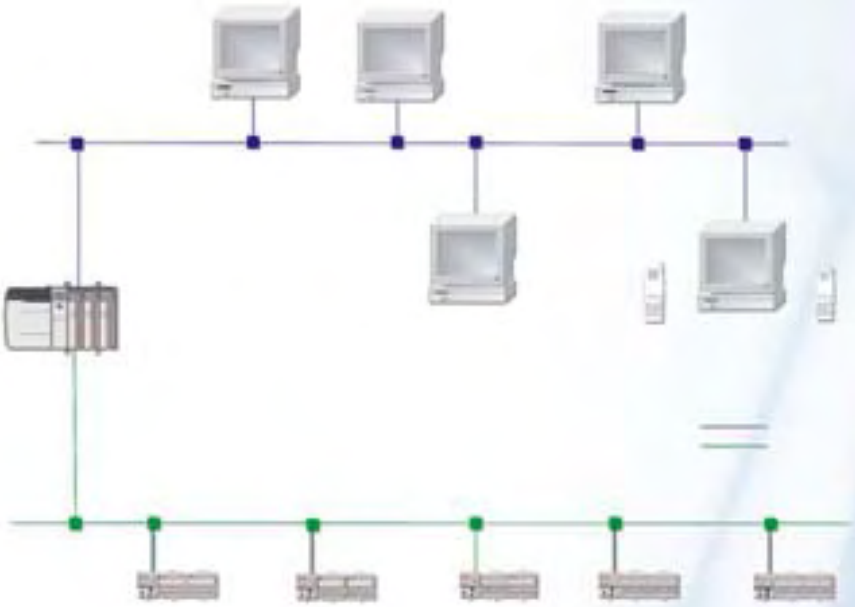
Submit Articles to PDA Publications

The *PDA Letter* and the *PDA Journal of Pharmaceutical Science and Technology* welcome article submissions from members. Go to www.pda.org/letter and www.pda.org/PDF/AuthorGuides-JPST.pdf for more details.

Thermal Validation Solutions

Temperature, Pressure & Humidity

For over 50 years Ellab has focused on manufacturing the highest quality temperature, pressure and humidity monitoring systems. The ValSuite software enables a complete solution integrating real-time monitoring, wireless data logging, and automated calibration in one validated software platform for applications requiring compliance with FDA guidelines and international GMP standards.



TrackView

Network data acquisition software designed for plant and process control monitoring

TrackView is designed with an Oracle database for safe storage of data that can be web enabled for off-site review and alarm notification. The user interface allows for multiple defined alarming with a variety of alarm actions and customized reports. Flexible features require minimal customization greatly reducing installation time and costs. TrackView encompass a full range of inputs, 0-5V, 0-10V, or 4-20mA. TrackView is compliant to 21 CFR, part 11 with a detailed audit trail and administrator control defining user access.

E-Val Flex

Real-time thermocouple monitoring system.

TrackSense Pro

Wireless data logger unmatched in accuracy, performance and versatility. Complies to the strict standards in the pharmaceutical industry.

Calibration Baths & Temperature Standards

The bath and temperature standard can be integrated into the software for automated multi-point calibration.

Thermal Validation Solutions

ellab
Building Confidence

Chapter Contacts

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

Asia Pacific

Australia Chapter
Contact: Greg Jordan
E-mail:
greg-j@bigpond.net.au

India Chapter
Contact: Darshan Makhey, PhD
E-mail:
dmakhey@nicholaspiramal.co.in

Japan Chapter
Contact: Katsuhide Terada, PhD
E-mail: terada@phar.toho-u.ac.jp
Web site: www.j-pda.jp

Korea Chapter
Contact: Woo-Hyun Paik
E-mail: whpaik@naver.com

Southeast Asia Chapter
Contact: K. P. P. Prasad, PhD
E-mail: prasad.kpp@pfizer.com

Taiwan Chapter
Contact: Shin-Yi Hsu
E-mail: shinyi.hsu@otsuka.com.tw
Web site: www.pdatc.org.tw

Europe

Central Europe Chapter
Contact: Erich Sturzenegger, PhD
E-mail:
erich.sturzenegger@pharma.novartis.com

France Chapter
Contact: Jean-Louis Saubion, PhD
E-mail: ufch@wanadoo.fr

Italy Chapter
Contact: Gabriele Gori
E-mail: gabriele.gori@bausch.it
Web site: www.pda-it.org

Prague Chapter
Contact: Zdenka Mrvova
E-mail: zdenka.mrvova@zentiva.cz

Spain Chapter
Contact: Jordi Botet, PhD
E-mail: jbotet@stegroup.com

United Kingdom and Ireland Chapter
Contact: Frank W. Talbot
E-mail: ftpharmser@aol.com

Middle East

Israel Chapter
Contact: Sigalit Portnoy
E-mail: sig@taro.co.il

North America

Canada Chapter
Contact: Hein Wick
E-mail: hwick@hwmr.ca
Web site: www.pdacanada.org

Capital Area Chapter
Areas Served: MD, DC, VA, WV
Contact: Barry A. Friedman, PhD
E-mail:
barry.friedman@cambrex.com
Web site: www.pdacapitalchapter.org

Delaware Valley Chapter
Areas Served: DE, NJ, PA
Contact: Art Vellutato, Jr.
E-mail: artjr@sterile.com
Web site: www.pdadv.org

Metro Chapter
Areas Served: NJ, NY
Contact: Nate Manco
E-mail: natemanco@optonline.net
Web site: www.pdametro.org

Midwest Chapter
Areas Served: IL, IN, OH, WI, IA, MN
Contact: Madhu Ahluwalia
E-mail: madhu@cgxp.com

Mountain States Chapter
Areas Served: CO, WY, UT, ID, NE, KS, OK, MT
Contact: Cathie Wilkerson
E-mail:
cathie.wilkerson@rtx-inc.com
Web site: www.mspda.org

New England Chapter
Areas Served: MA, CT, RI, NH, VT, ME
Contact: Myron Dittmer, Jr.
E-mail: mdittmer@hyaluron.com

Puerto Rico Chapter
Contact: Silma Bladuell
E-mail: bladues@wyeth.com

Southeast Chapter
Areas Served: NC, SC, TN, VA, FL, GA
Contact: Lisa Eklund
E-mail: lisa.eklund@hospira.com
Web site: www.pdase.org

Southern California Chapter
Areas Served: Southern California
Contact: Kikoo Tejwani
E-mail: kikoo.tejwani@bbraun.com
Web site: www.pdasc.org

West Coast Chapter
Areas Served: Northern California
Contact: Peter Rauenbuehler
E-mail: pbr@gene.com
Web site: www.wccpda.org

PDA
Parenteral Drug Association

Announcement and Call for Papers

PDA and the PDA Israel Chapter present...

Quality Tools for the 21st Century

Eilat, Red Sea, Israel ◆ May 17 – 18, 2006

Call for Papers

PDA and the PDA Israel Chapter are seeking presentation proposals for the 2006 *Quality Tools for the 21st Century* Conference that will take place in the beautiful resort town of Eilat on the Red Sea. Attendees will include Quality, Regulatory, Manufacturing, Laboratory, Engineering and Research & Development professionals within the international pharmaceutical, biopharmaceutical and related industries. PDA will consider abstracts of a noncommercial nature, with potential to significantly contribute to enhancing the knowledge and skills of conference attendees.

ABSTRACTS MUST BE RECEIVED BY September 30, 2005 FOR CONSIDERATION.

This conference will focus on quality issues of importance to personnel whose responsibilities include designing, improving, managing or participating in aspects of pharmaceutical / biopharmaceutical quality systems. Abstracts addressing recent trends and drafts or recently issued guidances, including but not limited to the following topics, are being sought:

- **Novel Approaches to Quality Systems** (ICH Q9, Q10, draft FDA guideline "A risk based approach to pharmaceutical cGMPS," etc.)
- **Mastering Manufacturing Science** (ICH Q8: case studies for implementation, design space models, quality systems in R&D as a tool to ensure quality in production, etc.)
- **Advanced Technologies and Tools** (Implementation and case studies using PAT, rapid microbiological methods, advanced aseptic processing technologies, advanced chemical tests, etc.)
- **Risk Management** (Models for managing risk; HACCP, FMEA case studies, hands-on approaches, use of Design of Experiments in managing risks associated with changes and product development, CAPA programs, root cause analysis, use of comparability protocols, etc.)

Submissions should state:

- ✓ Presenter
- ✓ Title
- ✓ Company
- ✓ Full address
- ✓ Phone, fax and e-mail address of presenter
- ✓ Presenter's biography (<100 words)
- ✓ Co-presenters
- ✓ Title
- ✓ Company
- ✓ Full address
- ✓ Phone, fax and e-mail address of co-presenter
- ✓ Co-presenter's biography (<100 words)
- ✓ Proposal title
- ✓ Target audience (by job titles, department and specialty areas)
- ✓ Session description
- ✓ Objective for the session
- ✓ Rationale: An explanation of how the participant and the organization will benefit from this session (<100 words)

Upon review by the program committee, submitters will be advised in writing of the status of their abstracts after November 30, 2005. Commercial abstracts promoting products and/or services will not be considered.

PDA will provide one complimentary meeting registration per presentation. Additional presenters will be required to pay appropriate conference registration fees. With the exception of regulatory speakers, all presenters are responsible for their own travel and lodging.

Abstracts should be submitted by e-mail to: **kstaylor@netvision.net.il**

Meredith Manning, JD, Keynote Speaker for 2005 PDA/FDA Joint Regulatory Conference

PDA is pleased to present **Meredith Manning**, JD, as our keynote speaker at the 2005 PDA/FDA Joint Regulatory Conference. Her legal expertise will provide valuable insight, in addition to the traditional regulatory and industry perspectives, to this year's conference theme—The Product Life Cycle: Quality by Design, Implementation and Continuous Improvement.

Manning is a partner in the Washington, D.C. office of Hogan & Hartson LLP and a member of the firm's Food, Drug, Medical Device and Agriculture Group.

Manning primarily counsels companies and trade associations in the pharmaceutical and biotechnology industry on an array of issues surrounding U.S. FDA review, approval, and oversight of drug and biological products. In addition, she counsels drug and biotechnology clients concerning enforcement matters threatened or brought by the FDA and other regulatory bodies, including issues surrounding advertising and promotion of prescription drugs. This includes counseling companies about anticipated enforcement, responding to FDA inspectional observations and warning letters, and negotiating consent decrees with FDA and the U.S. Department of Justice.

She has substantial government litigation experience, especially with respect to enforcement of the Federal Food, Drug and Cosmetic Act. Manning served as Assistant U.S. Attorney, Civil Division for the U.S. Attorney's Office in Washington, D.C. Prior to joining the U.S. Attorney's Office, she was Associate Chief Counsel in the Office of the General Counsel at FDA, where she handled a variety of litigation and litigation-related counseling issues.

In addition, she routinely assists major pharmaceutical and biotechnology companies in assessing their compliance programs and in reviewing and revising policies and procedures governing compliance with FDA's rules and regulations.

Building a New Manufacturing Toolkit for Viral/TSE Safety, continued from page 20

Day 1 speakers from the 2005 PDA Viral & TSE Safety Conference.

(l/r) Mahmood Farshid, Kurt Brorson, Rich Levy, Patrick Celis, Annemarie Moritz, Thomas Kriel and Glenda Silvester

(l/r) Lance Hoboy, Bob Myers, Stanley Prusiner and Rich Levy

(l/r) Steve Petteway, Philip Minor, Barbara Potts, Robert Rohwer, David Asher, Maria Sol Ruiz and Glenda Silvester

2005 PDA/FDA *Joint Regulatory Conference*

List of Exhibitors

COMPANY	TABLE
AAC Consulting Group	64
Accugenix, Inc.	28
Applied Biosystems	52
Aurical Company	77
Azopharma Contract Pharmaceutical Services	26
Bayer Healthcare, Biological Products Division	73
Biologics Consulting Group	53
bioMerieux	23
BioProcess International	75
Bio Reliance, Invitrogen Bioservices	79
Bioscience International	37
Biovigilant Systems, Inc.	71
Celsis International plc	50
Charles River Laboratories	41
Ciba Specialty Chemicals	58
Clarkston Consulting	60
Commissioning Agents, Inc.	49
Compliance Solutions, Inc.	51
Cryovac - Sealed Air Corporation	74
Dallas Semiconductor/Maxim	21
Dresser Instruments/EBO	72
Drumbeat Dimensions, Inc.	40
Dupont Qualicon	31
EMD Chemicals Inc.	70
Ferro Pfanstiehl Laboratories	56
Genesis Machinery Products	46
Genomic Profiling Systems	42
GxP Partners	55
Lighthouse Instruments	54
Lloyd's Register Serentec, Inc.	78
Micron Training	61
Millipore Corporation	24
Molecular Epidemiology, Inc.	30
NNE US, Inc.	45

COMPANY	TABLE
Novatek International	29
Pacific Bridge Medical	63
Pall Life Sciences	20
PAREXEL Consulting	22
Parenteral Drug Association (PDA)	7, 8
Perfex Corporation	62
Pharmaceutical Formulation & Quality (PFQ)	48
Pharmaceutical Services Corporation	65
Pilgrim Software, Inc.	18
PML Microbiologicals	47
Pharmaceutical Systems, Inc.	76
Quality is Learned, Inc.	33
Quintiles Consulting	10
Qumas	25
Sartorius Corporation	38
SGS Life Science Services	19
SL Pharma Labs, Inc.	59
Sparta Systems, Inc.	36
SynTegra, LLC	9
Texwipe (ITW)	39
Thomson Scientific	34
Validation in Partnership Limited	35
Vectech Pharmaceutical Consultants, Inc.	32
Veltek Associates, Inc.	44
Vetter Pharma-Fertigung GmbH & Co. KG	43
VTS Consultants, Inc.	57
Working Words, Inc.	27

September 12-13, 2005
Renaissance Hotel
999 9th Street NW
Washington, DC

Admittance to the Exhibit Hall is FREE

If Only Training Could be the Big Easy

Joanne Cochran, 2006 PDA Biennial Training Conference Chair

Is your GXP training effective?

Are you delivering the quality message you want?

Do you know what regulatory agencies are looking for in terms of compliance?

Come to the 2006 PDA Biennial Training Conference, May 8-12, 2006 in the "Big Easy"—New Orleans, Louisiana—to get the answers to these questions.

Based on your feedback, the 2006 conference has been expanded to include more concurrent sessions with opportunities to learn from other training professionals.

- Network with your peers from across the training community.
- Find out what training is working and producing the results you want.
- Learn from our keynote speaker, **Stephen Smith**, Rummler and Brache, about how to enhance performance in your organization. Discover what his company's studies have shown regarding GXP learning.
- Brush up on your presentation techniques, too! See how other companies are managing their GXP training.

We invite you to this thoroughly informative, innovative and interactive training event. Upon completing your registration, you will receive a survey about the most pressing compliance issues you are facing. This will help us structure our regulatory sessions to best meet your needs.

Register now at www.pda.org.

We'll be looking for you in the Big Easy!!!

Joanne Cochran, Consultant, JWC Training Associates, Chair of the 2006 PDA Biennial Training Conference

PDA Letter Deviation Report: July/August 2005

Our first 48-page issue in quite a while increased the chances for errors. A misplaced page with edits resulted in two embarrassing misspellings in the announcement about the change to PDA's name and logo, page 6. We apology to Michael Korczynski, former PDA President, Board member and Director of TRI, for omitting the "y" in his name. Likewise, we apologize to Irving Pflug for spelling his name "Pflag."

An unexpected quirk in our new production software caused a swap in photos when the press plates were created. For those wondering why Nikki Mehringer and Glenn Wright appear as the "TSE: Current Developments and Safety Approaches Panel" on page 41, now you know. We apologize to that panel and included their photo with the cover story of this issue (see page 30).

A handwritten note resulted in a bad caption for the TRI Advisory Board photo on page 43. First off, we misidentified the group. To make matters worse, we spelled Barbara van der Schalie's last name "Vander Schalie"; Gregory Meyer's last name "Myer"; and Surat Baloda's first name "Saraj."

Our apologies to all.

The *PDA Letter* is published 10 times per year, exclusively for PDA members. Subscriptions are not available. Articles in the PDA Letter may be reproduced with permission—contact the *PDA Letter* Editor for details. © PDA 2005

***PDA Letter* Editor**
Walter Morris
+1 (301) 656-5900, ext. 148
morris@pda.org

Advertising
Dorothea McGuire, Sales
+1 (301) 656-5900, ext. 150
mcguire@pda.org

Layout
Lisa Baehr

Printing and Distribution
H&N Printing and Graphics, Inc.

Executive Staff
Robert Myers, President
Lance Hoboy, VP, Finance & Strategic Planning
Gail Sherman, VP, Education
Matthew Clark, Director, Marketing, Membership & Chapters
Nahid Kiani, Associate Director, Sales
Gautam Maitra, European Director, Sci./Tech./Reg. Affairs
Wanda Neal Ballard, Director, Programs & Meetings
Robert Dana, Sr. Advisor, Science & Reg. Affairs

PDA Officers
Nikki Mehringer, Chair
(Eli Lilly and Company)
Richard Levy, PhD, Chair-elect
Stephanie R. Gray, Secretary
(Pharmaceutical Strategies)
Georg L. Roessling, PhD, Treasurer
(Schering AG)
Floyd Benjamin, Immediate Past Chair
(Keystone Pharmaceuticals, Inc.)

Board of Directors
Jennie Allewell (Wyeth Research)
Vince Anicetti (Genentech, Inc.)
Rebecca Devine, PhD
(Independent Consultant)
Kathleen Greene
(Novartis Pharmaceuticals Corporation)
Yoshihito Hashimoto, MSc
(Chiyoda Corporation)
Maik Jornitz (Sartorius Corporation)
Tim Marten, DPhil (AstraZeneca)
John Shabushnig, PhD (Pfizer Inc.)
Eric Sheinin, PhD (USP)
Lisa Skeens, PhD
(Baxter Healthcare Corporation)
Laura Thoma, PharmD
(University of Tennessee)
Anders Vinther, PhD
(CMC Biopharmaceuticals)

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

PDA Office of European Director
R-1059.747 Postfach
Schwarzwaldalle 215
CH-4002 Basel, Switzerland
Tel: +41 61 321 56 30
Fax: +41 61 321 83 48

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

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

Vice President's Message

Gail Sherman, VP, Education

Moving Ahead into 2006

Last month I wrote about my first year with PDA, with all of the associated challenges and what I would like to call successes. To keep building the momentum, we have already planned most of our 2006 curriculum. Maybe we were a little bit ambitious, or maybe we finally got the hang of this thing called "marketing," or maybe a little bit of both. In any case, we intend to publish a TRI catalogue for the very first time, which should be available in time for the PDA/FDA Joint Regulatory Conference in September, and will be distributed to participants. We are still planning a few course series and are actively pursuing potential instructors. When final, the complete schedule will be posted on www.pda.org/tri. And before we know it, we'll be planning 2007; we would like to start sometime in January 2006. We hope that the catalog and Web site will better assist you in the preparation of your training schedules for 2006 and forward.

To further strengthen our services, we have hired **Jessica Petree** as our new Lecture Education Manager and have permanently borrowed **Megan Lahti** from PDA Headquarters as our new Education Coordinator. Partnered with **James Wamsley**, our Laboratory Education Manager (whose articles you have come to expect in the *PDA Letter*), we feel that we have a pretty strong team to keep TRI moving forward!

In building our 2006 course schedule, we heavily mined current TRI faculty and the PDA Chapters for creative ideas. Many of our instructors obligingly provided new angles for both the laboratory and lecture circuit. The Chapters were a great resource, especially those in cities where we are planning our 2006 course series. We received great feedback from the Southeast Chapter (Raleigh) and the Midwest Chapter (St. Louis), as well as offers of assistance from the New England Chapter (Boston). In addition, we talked with the Canada Chapter about presenting courses in conjunction with their 2006 Annual Meeting. This is the first time that TRI has gone to the Chapters for input into our course development. Along with PDA Membership & Chapters Manager Kelly Coates, we also created guidelines for Chapter collaboration with PDA TRI to increase the accessibility of continuing pharmaceutical education programs to PDA members and others in our community.

The TRI Advisory Board developed a new course concept for the 2006 PDA Biennial Training Conference on "training as a business." We already developed four courses for the event, and hope to offer several more. We want to depart from the typical "how to train" model and delve deeper into the real issues of training—the avoidance of training-related 483 observations; the metrics that are needed in evaluating training; the issues of quality systems in an aseptic environment; the question of what the training function looks like; and the issues surrounding risk-based training and compliance. We are very excited about this new approach to training.

The PDA Computer Validation Modernization Task Force is another excellent source for TRI's 2006 curriculum. This Task Force is developing a framework of core competencies for training the employee involved in the management and implementation of good systems practices. We hope to evolve this into a certificate program, whereby a number of courses would be developed and offered to our members. This project is still in its infancy, and the Task Force will be refining it in the upcoming months. Once the framework and competencies are developed, TRI will be looking for instructors to further develop and deliver the content.

So, while TRI's traditional course series and laboratory courses are almost completely scheduled for 2006, we are still exploring new ideas. And while our planning has moved forward to 2006, we still have a lot happening in 2005, at TRI's facility in Baltimore, as well as in Basel, Denver and New Orleans.

And, if you think you have an idea for a course that we can't offer in 2006, we can certainly add it to our 2007 calendar!

PDA TRI's Supplemental Aseptic Processing Offerings

James Wamsley and Amanda Olsen, PDA

PDA TRI has established itself as an expert in aseptic processing training. As showcased in the last issue of the *PDA Letter*, PDA TRI is esteemed for its ten-day interactive Aseptic Processing Training Program. What is lesser known is that we offer supplemental courses to pharmaceutical and biopharmaceutical professionals interested in gaining a wider knowledge-base in aseptic processing in order to advance their careers.

We recognize the importance of this continuing education, and we offer four laboratory courses that specifically tie into aseptic processing, presenting a more detailed look into specialized topics:

- **Design and Validating Cleaning and Disinfection Program for Controlled Environments**—An invaluable component of a successful aseptic processing program is an appropriate cleaning and disinfection program to control contamination within your classified environment. This two-day, hands-on course is designed to provide you with the tools necessary to develop an appropriate plan of action to control contamination within your aseptic environment.
- **Fundamentals of D, F and z Value Analysis**—This two-day course is designed to give you a background in the determination of D, F and z values, along with a working knowledge of these principles that you can use immediately on the job. By using knowledge gained during this course, you will be able to develop a more robust and successful sterilization program at your own facility. Therefore, you will be better able to assure the sterility of your aseptically processed products.
- **Pharmaceutical and Biopharmaceutical Microbiology 101**—To be successful in producing a sterile product, you must know what you are up against in your facility and how to collect, identify and control it. This three-and-one-half day, hands-on course is intended to provide lab personnel, with or without extensive microbiological experience, a comprehensive overview of current microbiological sampling, testing and identification techniques currently used throughout the industry. In addition to current lab practices, you will learn the theory behind those practices in order to better understand the methods that are used.
- **Validating a Steam Sterilizer**—This two-day course provides you with hands-on experience validating a steam autoclave. To ensure the success of your aseptic manufacturing program, you must be able to prove that your steam sterilizer and the cycles used to sterilize components, media, buffer, etc., meet the criteria you set for your program. The course curriculum takes full advantage of both classroom and laboratory-based teaching techniques in applying the life cycle approach, including Cycle Development; Installation, Operational and Performance Qualification; and Revalidation Activities.

These four courses are held at PDA TRI's state-of-the-art laboratories in Baltimore, Maryland. Registration for some of these courses is still available for 2005; please check www.pda.org/calendar for details.

The Foundation for Pharmaceutical Education, Training and Research is looking for donations and/or loans of the following equipment:

- Bioreactor - small scale/benchtop; 3-5 liter
- Filtration equipment
- Chromotography equipment for different resins and columns

This equipment will be used for new PDA Training and Research Institute training courses in Bioproduction with a focus on both upstream and downstream processing.

If you have questions, please feel free to contact James Wamsley, Manager, Laboratory Education at 410-455-5946 or wamsley@pda.org.

Picky about particulates?

Manic about microbes?

Count on Biotest

The HYCON® System for Environmental Monitoring: RCS Air Samplers, APC Particle Counters and Contact Slides.

APC Airborne Particle Counters and RCS Microbial Air Samplers combine to give you a clear picture of airborne contamination. Biotest Diagnostics Corporation offers a full line of reliably accurate, technically-advanced, hand-held, air monitoring devices. When you're picky about maintaining air quality standards, count on Biotest. Call today or visit our website at www.BiotestUSA.com.

Biotest

CE

Biotest DIN EN ISO 9001 HYCON

BIOTEST DIAGNOSTICS CORPORATION
66 Ford Road, Suite 220, Denville, New Jersey 07834
Phone: 973.625.1300 • 800.522.0090 • Fax: 973.625.9454
www.BiotestUSA.com

Visit us at the 2005 PDA/FDA Joint Regulatory Conference in Washington, DC, September 11-14, 2005 at Table #36

The Quality Management System trusted by most life science companies!

- Scalable
- Easy to use
- Fully configurable (no custom code required)
- Rapid, predictable implementation
- Proven results meeting cGxP requirements
- Pre-configured, out-of-the-box
- Unlimited applications on the same platform
- Comprehensive validation package
- Domain expertise

TRACKWISE®

The Ultimate Quality Management Software

TrackWise is the only software with out-of-the-box functionality and flexibility to implement your organization's cGxP applications: Deviations, CAPA, Complaints, Change Control, Commitments, Audits and more, with flexible workflows based on industry best practices. It's the only QMS solution that comes with a full-featured, built-in business rule engine, and with powerful query, reporting and trending capabilities! Add to this, proven, scalable and load tested web-based architecture.

Superior functionality and flexibility, combined with our expertise, is what has made TrackWise the industry standard.

Let Sparta Systems' experience and technology assure the success of your quality management system too!

The "best in class" solution for
quality and regulatory compliance.
Why more than 100 life science companies with over 250 installations use TrackWise!

Sparta Systems, Inc. *Quality Management Solutions*

2137 State Highway 35, Holmdel, New Jersey 07733 • (888) 261-5948 • (732) 203-0400 • FAX: (732) 203-0375
e-mail: info@sparta-systems.com / europe@sparta-systems.com • www.sparta-systems.com

SW-1082