Science • Technology • Quality • Regulatory • Community

PDA Letter

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June 2006

In This Issue…

PDA Parenteral Drug Association

Connecting People, Science and Regulation℠

A Supplier Approach to Ensuring Process and Product Quality

David Rubin, Robert Infinger, and Peter Eichert, Millipore Corporation

In order to ensure a manufacturing process can consistently produce a final product of predefined quality, that quality must be designed, developed and built into the process. To that end, the design and validation of an efficient manufacturing process must be based on a thorough understanding of the process itself, the materials utilized in the process and the ways the process affects the product quality and performance. Continuous, real-time quality assurance, within reach in today's technological environment, together with statistical and risk analyses, can ensure the quality of the final product and avoid costly delays and revalidation efforts.

Through its 2004 PAT guidance,[1] the U.S. FDA seeks to encourage industry use of tools that enable scientific, risk-managed pharmaceutical development, manufacturing and quality assurance. Such tools can help companies thoroughly understand and improve their products and their processes, reduce risk, and build on accumulated experience and knowledge. Examples include appropriate combinations of some or all of the following tools:

- Multivariate tools for design, data acquisition and analysis
- Process analyzers
- Process control tools
- Continuous improvement and knowledge management tools

Knowledge accumulated and understood from these processes can help support and justify innovations in manufacturing, validation and post-approval changes with FDA, as well as identify and evaluate factors that may affect product quality and performance.

The sum of experience and knowledge gained by a company, whether a pharmaceutical manufacturer or supplier, gives that company greater insight into the best possible methods for achieving the desired results. A thorough scientific understanding of both the multifactoral relationships and evaluation methods is crucial. Today's information technology makes the use of this knowledge base possible to help identify process and product variables and pinpoint the causes behind potential failure models.

continued on page 16

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Table of Contents

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President's Message

Bob Myers, PDA

PDA's New Showplace for Pharma Training and Education

I am very pleased to inform our members that we will be consolidating our U.S. operations, including the Training and Research Institute. This has been a long-term goal of the Association, and in April, a viable space which meets all of our requirements suddenly became available in Bethesda. The new PDA facility will occupy the first and second floors of the Bethesda Towers, only two blocks from our current headquarters.

First, and most importantly, this consolidation will allow us to improve our unique training and education facility. It is ideally sized and offers many advantages over our current operation in two locations. It will create synergies among our staff, enabling us to better serve the membership. The move also creates cost efficiencies for the organization, and, we believe, uniting TRI with our headquarters offers more exposure for our training and education participants and instructors to our headquarters staff and visitors. Our goal is to build a new showplace for pharmaceutical science and regulatory training and education.

Since the current TRI facility is ten-years old, we are taking advantage of this opportunity to modernize the laboratory and upgrade our technical training offerings. Of course, the new laboratory will feature "Aseptic Sterile Processing," an industry-standard, hands-on laboratory course that is the hallmark of TRI. We intend to improve TRI's cleanroom and make it a model sterile manufacturing operation. Our staff, especially those at our current campus in Baltimore, are excited by the prospects and already are approaching organizations about donating their services in designing and equipping the new facility.

We are also using the transition as an opportunity to add new laboratory and lecture courses that will help the industry understand and adopt advanced and emerging manufacturing technologies. We anticipate adding rapid microbiological tools to our micro lab and are planning courses on PAT (process analytical technology), disposable manufacturing systems, packaging development for cold chain operations and sterile compounding. We are also considering the establishment of a biopharmaceutical laboratory.

Plenty of opportunity exists for companies to participate. From the very inception of TRI, PDA's community of exhibitors and sponsors has supported the laboratory with generous donations. Creation of the new training facility generates even more opportunity for partnership with PDA, including laboratory design, new equipment for use in our programs, and in new course development. Since we hold almost weekly member meetings at our headquarters, there will be significantly more exposure and visibility for those who partner with us in this significant investment in our future. The current PDA headquarters will move to the new location in Bethesda in the third quarter of 2006. TRI is expected to be established in Bethesda by the first quarter of 2007.

PDA is proud to undertake this task of building this new showcase for training and education. Not only will it benefit the entire membership, it will benefit the industries PDA supports.

PDA's new headquarters at Bethesda Towers, 4350 East West Highway, Bethesda, Md.

PDA Parenteral Drug Association

June 2006

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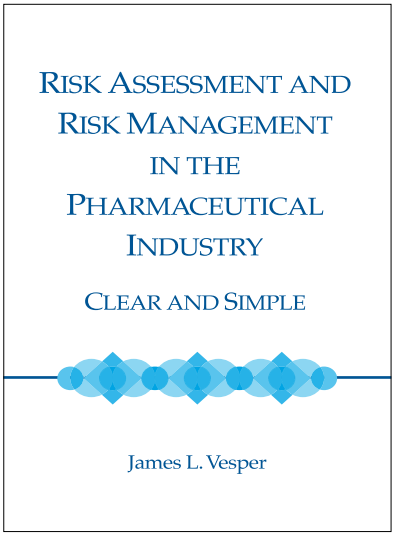

Risk Assessment and Risk Management in the Pharmaceutical Industry: Clear and Simple

James L. Vesper

This book begins with history, definitions, how we think about risks and hazards, it gives overview of the risk management process and commonly used risk assessment methods and tools. It also explores the phases of the risk management process in detail and examines how the various tools can be applied in identifying hazards and evaluating their potential impact and affects.

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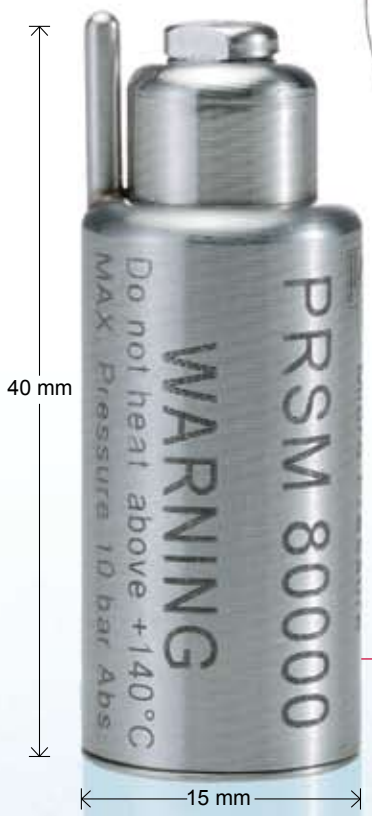

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PDA's In-Depth Look at Biopharmaceutical Validation

Workshop Planning Committee

On April 26-27, PDA held a 1½-day workshop on biopharmaceutical process validation in Anaheim, California. The scope of the workshop was to provide an overview on current process validation practices for drugs produced by r-DNA technology.

On the first day, speakers from the U.S. FDA and industry provided an overview of process validation practices and expectations and how they fit with post-validation process control strategies and process analytical technologies (PAT).

Kurt Brorson, PhD, Staff Scientist, CDER, FDA, addressed the importance of process characterization data for process validation and how process understanding built during development can help to design validation studies. He presented examples of how to define criteria for the collection of eluate fractions of a chromatography step for impurity reduction. The pros and cons of different approaches based on established process understanding were also presented. Next, **Norbert Hentschel**, Head of Compliance and Validation, Boehringer Ingelheim, reviewed the changing environment for process validation in the past 20 years. According to Hentschel, our industry appreciates the paradigm change to a more science- and risk-based validation approach. A clear pathway to advance this paradigm shift is desirable, e.g., how to demonstrate process understanding in a regulatory filing. The final speaker of the first day, **Christopher Watts**, PhD, Staff Fellow, CDER, FDA, talked about applications of PAT in process validation. He encouraged industry to apply PAT only to parts of the process if supported by process understanding.

The second day of the workshop began with a presentation on linking process characterization, process validation and process monitoring by **Anurag Rathore**, PhD, Principal Scientist, Amgen. Dr. Rathore emphasized that maintenance of the validated state requires process monitoring. A discussion of critical parameters followed the talk, and it was noted that a large number of critical parameters indicates a process is not robust. In some cases, parameters once deemed critical can be downgraded to a key or non-key category upon implementation of a more sensitive process control scheme.

Next, Norbert Hentschel returned to the podium to address the use of small-scale models in process validation. These models are particularly important for resin lifetime studies and evaluating new raw materials. Assay qualification, instead of validation, may be appropriate for process characterization studies. Hentschel acknowledged that demonstrating comparability by examining chromatographic profiles at two scales can be difficult, but evaluating shapes and retention times can be useful. A question arose regarding the number of resin batches that should be used for small-scale lifetime studies; generally, one batch is considered sufficient at small scale.

Gail Sofer, Director, Regulatory Compliance, GE Healthcare (and PDA Board member), next discussed resin and filter media lifetime. Validation costs reduced the savings gained by reusing resins over time. Sofer showed that, for one application, validating resin reuse up to 30 cycles was very cost effective, but validating reuse at 90 cycles did not offer as significant savings. Sofer also addressed concurrent validation for resin lifetime studies, measurable parameters for determining lifetime, and the use of surrogate parameters for viral clearance with reused resins. Sofer raised the possibility of using PAT in the future to potentially eliminate the need for blank runs in manufacturing.

In a talk on dealing with changes in raw material sourcing, **Anthony Mire-Sluis**, Head of Product Quality and External Affairs, Amgen, pointed out that the control of raw materials is essential to ensure robust processes and product quality. Raw materials need to be characterized, and their interaction with the process and impact on product critical quality attributes determined. The importance of supplier agreements was emphasized, along with the need to work with suppliers. A question arose about working with raw material vendors to help them understand how to be compliant, especially when they are the only source of a needed raw material. Inadequate raw material characterization can lead to a variety of problems, for example: changes in pharmacokinetics, increased leachables, misincorporations of amino acids in fermentation and viral contamination. The importance of change control to manage raw material changes was emphasized. Mire-Sluis also stated that developing a process and successfully transferring to a contract manufacturer requires process knowledge, which is gained from development, ➤

pilot scale experience, laboratory robustness studies and risk assessments.

Defining critical and key parameters is essential for process validation. Understanding and agreeing what is meant by these terms is essential for success. The next talk, by **Wendy Lambert**, Co-Development and Tech Transfer, Pfizer, provided an overview of definitions for the terms "critical" and "key" as established in the PDA Technical Report No. 42: *Process Validation of Protein Manufacturing and the ICH guideline Q7A*. Failure Mode Effect Analysis (FMEA) was explained as a tool for assessing process risks. Parameters with narrow proven acceptable ranges were deemed "critical." A margin of safety was established to reduce the risk of excursions.

Risk assessment requires identifying, analyzing and evaluating risks. Process validation risk assessment was presented by the next speaker, **Leslie Sidor**, Manager of QA, Amgen, a trained statistician. Potential hazards, or failures, need to be identified and linked with risks, such as consequences of the failure and its likelihood. Sidor presented an example of cell culture and purification FMEA. She also demonstrated how FMEA was used to identify risks, their effects, potential causes and severity. The importance of a secondary evaluation was discussed. A secondary evaluation may include factoring in elements like regulatory expectations.

Ted Gopal, Director of Validation, Genentech, followed Sidor and discussed the relationship of validation and FDA's PAT strategic initiative. In the future state, he asserted, fixed processes will be replaced by adaptive processes. Gopal shared details on the use of PAT to control galactosylation via monitored nutrient feeding. On-line biomass estimation was used to generate a feed profile that reduced waste accumulation and its concomitant increase in intracellular pH that decreases galactosylation. Potential benefits and challenges to PAT implementation were elucidated. Many advantages are foreseen, including a reduced number of discrepancies.

Extractables and leachables have become more of an issue during the last decade. With the use of disposables on the rise, it is essential for companies to address their capability to detect and remove potentially harmful materials. The importance of vendor support in this regard was discussed by **John Bennan**, President, ComplianceNet.

The final talk of the conference was delivered by industry consultant and PDA Board member **Rebecca Devine**, PhD, who presented, "Post-approval Changes: What to Do and Not to Do." The "Do's" include:

- expect the unexpected
- open a dialogue with FDA for major planned changes and request feedback
- identify additional characterization tests
- make the reviewer's job easy by preparing pre- and post-change flow diagrams

The "Don'ts" are:

- minimize the potential impact of a change
- ignore validation impact; and
- assume all will be as expected.

[**Editor's Note:** PDA thanks the program planning committee for developing the agenda for the Workshop on Biotech Process Validation and for collectively writing this summary of the event. The committee members are: Anurag Rathore, Amgen (co-chair); Norbert Hentschel, Boehringer Ingelheim Pharma (co-chair); Gail Sofer, GE Healthcare; Kurt Brorson, FDA; Chris Bussineau, Cambrex; and John Geigert, BioPharmaceutical Quality Solutions.]

PDA plans to continue the open dialogue on the future of biotech process validation on Dec. 4-5, 2006, in Berlin with a particular focus on PDA TR#42.

Recent Sci-Tech Discussions:
Manufacturing and the Use of SOPs

The following unedited remarks are taken from PDA's Pharmaceutical Sci-Tech Discussion Group, an online forum for exchanging practical, and sometimes theoretical, ideas within the context of some of the most challenging issues confronting the pharmaceutical industry. The responses in the Sci-Tech Discussions do not represent the official views of PDA, PDA's Board of Directors or PDA members. Join at www.pharmweb.net/pwmirror/pwq/pharmwebq2.html.

I am interested in others' view on the use of SOPs and EOPs (Equipment Operating Procedures) during the manufacture of drug products. I am aware that the GMPs require procedures for production and process control to be written and followed. I am also aware that most people would agree that these procedures should be followed carefully.

If the master batch record does not contain detailed information on the operation of equipment or performance of a manufacturing task, should the master batch record refer the operator to the SOP/EOP that contains the information? Also, what are your opinions on the philosophy/practice that once an operator is trained on a SOP/EOP that they are not required to actively use/refer to them unless they feel that they need to use them? Should SOPs/EOPs be required to be used during the manufacturing process, or can training and memory be relied upon? What is the industry and regulators perspective on this issue?

Respondent 1: The batch record should contain reference to the relevant SOP if sufficient detail is not supplied in the batch record (my suggestion is to avoid this if possible by putting the relevant information in the batch record in a condensed form, if applicable). If the operator is performing a task according to an SOP, then this SOP should always be available to him/her and be used. Recourse to memory is not acceptable when you consider there may be hundreds of SOPs in use at the site. I hope this helps.

Respondent 2: Use of EOPs for manufacturing of drug products is quite important in conjugation with training of the operators. Relying on memory for these procedures sometimes may create havoc if your facility has multi-products running at a time.

Respondent 3: Why call them EOPs ? It never ceases to amaze me the nomenclature folks try and introduce. Just call them what they are; i.e , SOPs. If you need to differentiate them, then number them such that it is obvious which group they belong to.

I do not agree that any procedure should be followed. For me they must be followed. Unless [manufacturers] feel they need to use them, they are standard operating procedures, not voluntary operating procedures, which, of course they must be followed. What if you introduce a change [and] what if their memory is not that good, how do you "validate" the memory of two individuals, and ensure they recall the same information correctly from memory? The answer is you cannot, which is why we have SOPs.

I believe there is a CFR statement that requires the production function to formally sign that "the batch" was made in accordance with GMP and that all appropriate SOPs/batch records, etc. were followed. Alas, I don't have my CFR pocket guide to hand.

Respondent 4: It is perfectly acceptable to reference SOPs for the operation of equipment and so on in the Batch Record. It is definitely not acceptable to allow the manufacture of any regulated drug product governed by 21CFR Part 210 and 211 to occur based on familiarity with a process or memorization. I am certain you will get 100% agreement on this.

Respondent 5: I am sure that there are some who would disagree with me regarding the use of SOPs, EOPs or whatever we choose to title them. My position has always been that in a regulated industry such as ours, the procedures for doing anything, including the operation of equipment, be followed each and every time.

The corollary that I would apply is probably familiar: Suppose you boarded an aircraft and were traveling from Los Angeles to San Francisco. Airlines are a regulated industry similar to pharmaceuticals. Their regulations require a checklist to be completed each and every time that an aircraft is flown. It begins with the pre-flight examinations and verification of the outside of the aircraft followed by an internal examination. Then the checklist takes the crew through an exhaustive process to provide assurance that the aircraft is not only safe but that it has been configured correctly for this particular flight. ➤

Now, suppose a crew that felt they knew what to do and decided to skip the checklist. Would anything happen to that aircraft on this flight? Unknown! Why, because it just does not happen. Everyone, including the crew has far too much to lose.

My reminder to everyone that I work with regardless of the company or product is simple. At some point during your lifetime, you, or someone that you care about will become a consumer of what you produce. Are you satisfied with what you do? To me, that is a very sobering thought. Given that, I believe that SOPs, EOPs, or whatever should be included in manufacturing records of whatever is made. Further, I believe that those documents need to be followed, precisely and exactly each and every time that the equipment and/or process is used.

Respondent 6: [Respondent 5,] great example. As for EOPs (equipment operating procedures)—just another variant on the term SOP, so let's just call everything relating to how to do a task and SOP (not an EOP, not a work instruction, not an operator guidance, etc.). If it is the company's officially approved method to perform a job it is an SOP.

Respondent 7: I totally agree with you regarding manufacture of any regulated drug product, but what is the general opinion for a phase I or phase II production? What about having a process based on familiarity with a similar process or memorization?

Respondent 8: For any manufacturing batch record, the exact item of equipment and exact procedure of use must be in the document. The procedure may be indicated by referring to an SOP. If you do not want to write a detailed procedure in the batch record, then write an SOP as per your approved procedure of writing and numbering SOPs.

"Similar process" or "familiarization" or any other explanation is not acceptable. The rule is, if it was not written it:

Was not done

No way to know if it was done right

You did not know what to do

You did not know what you were doing

That is not the message you want to convey. If you did it, you know how you did it. So you must write it. Using shortcuts is a sure way of documenting non-compliance.

Respondent 9: For the production of phase I/II IMPs I would use a documented process (specifications, SOPs, BPR etc.) as described in, or compliance with, EU GMPs (being based in the EU).

What do you mean by your second question? You could propose a process based on past experience (familiarity) but you would need to demonstrate that it is appropriate and reproducible with qualified equipment and documented (see EU GMP Annex 13).

Respondent 10: Whilst the investigation is ongoing I would point all to the recent events at Northwick Park Hospital in London during a Phase I study. I would advise that any quality system worth its salt requires written procedures that are trained and followed. Without wishing to abuse anyone personally, I can't help thinking that this is nothing but laziness on the part of those who are supposed to be following the procedures and abdication of responsibility on the part of management for allowing it. I would like to see any quality assurance (QA) guy sign off on the statement: "The batch was manufactured according to the best of my memory."

Respondent 11: First let me state, procedures must be written and must be followed. This is a basic rule of GMPs, written directly into the U.S. CFR and one of the "ten commandments." Basic GMPs also require that work must be documented. These things are not up for discussion.

Some day I'll learn to keep my mouth shut, but apparently today is not that day. I don't think there is any real disagreement here, I just want to clarify one thing. The original question was, if I read it correctly, with regard to if the operator needs to read through each step of the SOP each and every time they perform each and every step of the procedure. The answer is no. The operator is trained on the procedure. The procedure is available for the operator to reference as needed.

Following [Respondent 5's] Airline example, I want the flight crew to follow a checklist (similar to our batch record). I also want the flight crew to be fully trained on both how to fly the plane and appropriate emergency response. I want/demand/expect the pilot and all other members of the flight crew to have the appropriate education, training, and experience for them to perform their jobs properly. I expect them to keep their training current. I do not expect or want the pilot to have to pull out and read through the flight manual (his SOP) just prior to landing.

Respondent 12: We are in agreement though we probably differ on implementation cases. One of the things that always seems to plague me when I am writing protocols is that I tend to take the current operational SOP and utilize it as a roadmap for what to do.

I am one of those who knows how to fly, knows what the controls do but find a difference when I get into an identical aircraft after several months of being absent.

I have found that SOPs tend to change with time and that while the intent and even the requirement to train on the new SOPs is there, many don't seem to make it through that training. Depending on the equipment or process, it should be reviewed at a minimum just prior to the execution of whatever is being done. I also agree that it is not necessary to resort to the manufacturer's manual every time that we do something. Talk about a slow world.

If I offended anyone, I do apologize. I just feel that this is an important topic. I am glad to see that there are several people who are willing to share their own views as well.

Respondent 13: It is interesting that if you read the "Barr Decision" in its original, Judge Wolin recommended/required (I do not remember which) that Quality Control (QC) analysts document each step that they perform during an analysis as they did so—in the same way that production people document each production step as and when they perform it, as demonstrated by a batch production record.

I can see logic in having check lists for each and every operation currently performed under each and every facility Standard Operating Procedure (SOP). Logic: yes. Practicality: probably not.

PDA Interest Groups & Leaders

PDA Interest Groups are divided into five sections by subject matter. 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 and Manufacturing Sciences. Any PDA member can join one or more Interest Group by updating their member profile (www.pda.org/pdf/join_IG_instruction.pdf). Please go to www.pda.org/science/IGs.html for more information.

North American Interest Groups

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A Supplier Approach to Ensuring Process and Product Quality, continued from cover

In efforts toward innovation and process understanding, suppliers to the pharmaceutical industry need to be held to a new standard of quality, reliability and manufacturing. Biopharmaceutical customers want to understand how the variability of suppliers' products may impact the consistency of their process or their final product. Such variability can affect the process itself, as well as the controls applied and validation performed. The PAT risk-based approach can also be applied to scientific, application and process information.

Monitoring and controlling a process means actively manipulating it to get the desired results. In developing a process, a number of factors have to be considered: the attributes of the materials, the process analyzers' capabilities, and the endpoints—will the process result in the desired end product? This concept is establlished in the FDA PAT guide: "It is important to emphasize that a strong link between product design and process development is essential to ensure effective control of all critical quality attributes."

Just as pharmaceutical manufacturers can use PAT to improve their processes and the quality and performance of their end product, they can and should look for equal diligence from their suppliers.

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Strategic Materials Casting Plant Sets a New Standard

The cassette's membrane is the heart of the device. Consistent, robust and reproducible membranes are required for optimum performance. The current state-of-the art membranes are void free. When they were originally developed more than ten

continued on page 20

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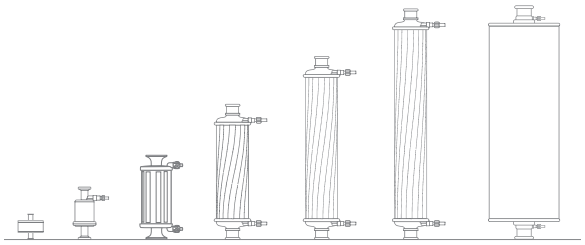

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Status of Moist Heat Sterilization: Revisions to PDA TR-1
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October 23-25, 2006
Prefilled Syringes and Drug Delivery Systems
(Conference and Exhibition)
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Training

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Microbiological Considerations for Oral Solid Products
Clark, New Jersey

May 16, 2006
PDA Southeast Chapter
Operational Excellence in Pharmaceutical and Biotechnology Manufacturing
North Carolina Biotech Center

May 17, 2006
PDA New England Chapter
FDA Inspections
Lexington, Massachusetts

May 18, 2006
PDA Midwest Chapter
Vendor Night and Discussion Groups
Northbrook, Illinois

May 18, 2006
PDA West Coast Chapter
Comparability Protocol Panel Discussion
Millbrae, California

June 7, 2006
PDA Metro Chapter
Viral and Mycoplasma Clearance
Clark, New Jersey

June 12, 2006
PDA Canada Chapter
Annual Meeting
Vancouver, British Columbia

Chapters (cont.)

June 28, 2006
PDA Capital Area Chapter
FDA Inspections and Quality Trends
Gaithersburg, Maryland

July 14, 2006
PDA Delaware Valley Chapter
Risk Assessment
Malvern, Pennsylvania

July 20, 2006
PDA Midwest Chapter
Application of Bacterial Spore Inactivation Kinetics to Risk Estimation in Sterilization Processes
Northbrook, Illinois

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May 23-24, 2006
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Moist Heat Sterilization
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June 7, 2006
Status of Moist Heat Sterilization: Revisions to PDA TR-1
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June 8, 2006
Status of Moist Heat Sterilization: Revisions to PDA TR-1
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Streamlining Success: Supply Chain Management
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May 10, 2006
PDA Update: Process Validation of Protein Manufacturing - PDA Technical Report #42
1:00 p.m.-2:30 p.m. EST

May 17, 2006
Validation of Bioreactors in a Biological Production Facility
1:00 p.m.-2:30 p.m. EST

May 24, 2006
Preventing OOS Deficiencies: A Guide to Regulations
2:00 p.m.-2:30 p.m. EST

A Supplier Approach to Ensuring Process and Product Quality, continued from page 16

years ago, the manufacturing process did not include today's sophisticated measuring and analytic tools. As a result, void-free membrane porosity and retention varied batch-to-batch. Tighter controls of key process variables with modern tools has enabled a new void-free membrane casting process that is producing more reliable membranes for biopharmaceutical processes.

Millipore broke ground for its multi-million dollar state-of-the-art UF casting plant in August 2002. Two years later, the plant was commissioned, and the process of qualifying individual membrane began. The deliverable from this plant was simple—more consistent, reproducible ultrafiltration membranes. To accomplish this goal, the membrane team designed a facility with advanced instrumentations, measuring technologies and controls. For example, the team implemented feedback control of membrane thickness, a critically important output. Measurements of the membrane's thickness are fed back upstream in the process so that adjustments can be made thus reducing the overall variability.

Another critical output from the process is membrane retention. Prior technology only allowed for accurately measuring 90% retention of molecules of a known size. The new facility increased this sensitivity 100 fold so that 99.9% retention can now be measured. This new capability detects more subtle shifts in the process thus enabling operators to respond before major shifts occur.

Product inspection also improved significantly. Visual inspection was replaced by incorporating digital imaging equipment which inspects every inch of membrane produced for surface defects.

Processes at the new facility include sophisticated, on-line tools that continuously measure key variables, enabling a more efficient operation. The automated measurements are more accurate, more consistent and are stored electronically.

Robust Device and Process

The cross-functional team charged with fulfilling the vision consisted of representatives from research and development, microbiology, manufacturing, industrial engineering, quality and product management. Their task was to deliver a robust device and manufacturing process that meets clearly defined performance specifications. Recognizing that only a well-understood process can be well-controlled, the team selected manufacturing techniques with which they had a fundamental understanding from years of manufacturing, and that could be monitored and controlled electronically.

The first step in the development process was to evaluate current TFF cassette manufacturing methods identifying inherent inefficiencies and difficult to control operations. The team set out to automate the process with the goal of reducing variability, increasing throughput and eliminating sources of error and potential product contamination. Additionally, they wanted to improve performance elements, such as increased temperature and pressure operating ranges, reduced extractables and small molecule diffusion.

continued on page 26

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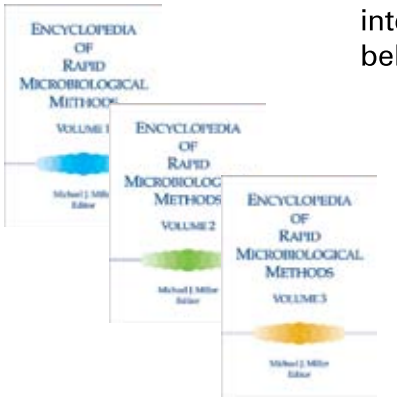

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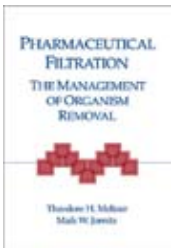

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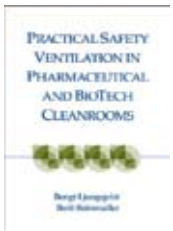

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Compendial Requirements for Automated Microbiological Method Validation:

The Role of USP Chapter <16> "Automated Methods of Analysis" and the Proposed Chapter <1058> "Analytical Instrument Qualification"

David Jones, Genomic Profiling Systems, and Scott Sutton, Vectech Pharmaceutical Consultants

Pharmacopeial microbiological tests detect and/or enumerate microbes that replicate in the presence of microbiological media. The challenge presented by adopting modern rapid microbiological methods is determining whether or not they represent the automation of a current compendial method or if they represent an "alternative" to a compendial method. The answer impacts how a firm should qualify and validate the new rapid method and may provide an opportuntiy for a more streamlined validation protocol.

The difference is critical because of two chapters in the U.S. Pharmacopeia. USP Chapter <16> "Automated Methods of Analysis" has been very useful to the chemistry community since its introduction in 1975. It provides a means to qualify new automation methods without engendering the full burden of a complete qualification/validation process, as described in USP Chapter <1225> "Validation of Alternative Methods." Chapter <16> provides examples of several tests that are amenable to automation in the chemistry laboratory, but does not address microbiological methods. A second consideration in the method validation is instrument qualification. Although a general GMP requirement, instrument qualification studies are not addressed in these chapters, a failing USP is addressing through the recently proposed <1058> "Analytical Instrument Qualification."[1]

With interest in rapid microbiological methods rising, there is a variety of new technologies available to the quality control (QC) microbiology laboratory that will move the microbiology lab into the 21st century. While many of the more widely discussed rapid methods are based on technologies completely dissimilar to the current pharmacopeial methods (PCR, viable dye, flow cytometry, etc.), several automated microbiological tests rely on traditional microbiological methodologies to detect and count microorganisms. There are several rapid micro systems currently available that automate detection and enumeration of cells replicating to form colonies on plates containing nutrient media. Examples of these technologies are the *QCount* from Spiral Biotech, the *ProtoCol* from MicroBiology International (MI) and the *Growth Direct™ System* from Genomic Profiling Systems (GPS).

The regional compendia are moving forward on the question of rapid microbiological methods. The USP draft chapter <1223> "Validation of Alternative Microbiological Methods"[2] will be official in August of this year, and the EP chapter 5.1.6 "Alternative Methods for Control of Microbiological Quality"[3] is now in force. Both regional compendia recognized the need to provide more appropriate definitions to the accepted validation criteria of accuracy, precision, limit of quantification, etc. This was required as it was recognized early on that the established terms, while appropriate for chemistry, were unworkable in the validation of microbiological assays due to the larger degree of variability in the system.[3,4] While these "validation guides" are useful, they assume that the new technology is in fact new and different from the compendial methods.

There is a need to distinguish between "automated compendial" methods and "alternative" tests, as they require different validation approaches. Automated compendial tests differ from alternative microbiological tests in that the automated tests are based on the same methods and principles and measure the same targets as the manual compendial tests. Alternative tests, on the other hand, use distinct methods and principles and measure distinct targets, such as ATP bioluminescence, "fluorescent events," etc., compared to compendial tests.

It is also worth mentioning that the compendial "method" under review may not actually be the title of the USP chapter. For example, the sterility test can be described as two discrete steps:

1) Filtration of the sample
2) Examination of the filter for the presence of viable cells.

A "rapid" sterility test will probably have the same design as the compendial test (now harmonized)—20 units of product will be filtered, and the filter will be assayed for viable cells.[6] The "rapid" part only comes in as you specify the method used to assay for viable cells. Similarly, many quantitative assays do not differ significantly from the compendial method except in the manner of determining the number of cells present. Here there may be more of a concern. The compendial method for enumeration is to grow colonies on or in an agar ➤

surface. The colony forming unit (CFU) may arise from one cell or several thousand; it becomes visible only after there are several tens of millions in the colony after replication.

Alternate methods of enumeration that are not based on the CFU are fundamentally different from the compendial method of enumeration used in the microbial limits tests, the antimicrobial efficacy test and others. For example, the AES Chemunex *ScanRDI* method measures the numbers of cells showing esterase enzymatic activity rather than the number of colony forming units—the quantity measured by the compendial methods. Consequently, the targets measured by the ScanRDI system can be very different than those measured by the compendial tests, since not all of cells with esterase activity can replicate in the presence of microbiological media[7].

Automated compendial tests differ from the manual compendial tests only in that some manipulations and/or detection steps are automated. For example, colony counting by GPS' *Growth Direct System*[8] and the *QCount* from Spiral Biotech uses the same method principles (growth of colonies on an agar surface) and measures the same colonies as do the tests described in several USP chapters. Both the manual and automated approaches enumerate colonies derived from microbes that can replicate on a media support. The automated system, however, uses digital imaging to detect the colonies, in contrast to the manual method in which colonies are detected by eye. The automated imaging is more reproducible and allows faster enumeration times.

For alternative tests, validation must be concerned with demonstrating that measuring different targets leads to equivalent or better results compared to the compendial methodology. However, USP <16> argues persuasively that an automated test need only demonstrate accuracy and precision. If we allow for the strategy and definitions in the proposed USP Chapter <1223>, application of the approach embodied in USP <16> for validation of automated methods in microbiology should be appropriate. In this approach, once the equipment is qualified, the method need demonstrate only accuracy and precision equivalent to the compendial method.

This does bring up equipment qualification as a concern. The 2005 Pharmacopeial Preview for the proposed USP chapter <1058> "Analytical Instrument Qualification" states:[1]

> *Good Manufacturing Practices (GMP) regulations require companies to establish procedures ensuring the fitness for use of instruments that generate data supporting regulated product testing. However, GMP regulations do not provide definitive guidance for the qualification of analytical instruments.*

The chapter's goals are described:

> *This chapter covers the initial part of the data quality acquisition process (qualification, validation, and verification), defines the roles and responsibilities of those associated with an instrument's qualification, and establishes the essential parameters for performing instrument qualification and a common terminology.*

In response to public concerns, USP published a revised draft which presents the opportunity to accept the system suitability test as proof of suitable performance for the PQ portion of the qualification.[9] This chapter is being finalized for publication. Once finalized, it will serve not only for automated microbiological methods, but all equipment qualification studies.

A major concern with acceptance of alternate microbiological methods is uncertainty over validation and the associated costs. However, the opportunities for these methods to streamline testing is enormous.[10,11] Clearly the different types of alternate microbiological methods have differing degrees of risk associated with them and should have differing validation burdens. Many of these automated technologies clearly fall in the same philosophical category as was envisioned by USP in the creation of a dedicated chapter describing the validation of an automated, rather than an alternative, method.

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continued on page 26

A Supplier Approach to Ensuring Process and Product Quality, continued from page 20

Next in the process was creation and review of a list of potential materials of construction for the jacket and internal sealing surfaces. Nine potential materials in ten common chemicals were tested for hardness, change in mass, total organic carbon (TOC) extractables, nonvolatile residue (NVR), and small molecule clearance. By individually testing all materials, the team was able to determine which provided the best combination of cleanliness and performance.

The original list of ten items was trimmed to three that met all acceptance criteria. These three materials were then introduced in alpha product samples and subjected to specific product tests. As a result, the team selected the two materials that not only met all acceptance criteria but also maximized performance.

Pellicon® 3 then moved into the detailed development stage. Manufacturing and development engineers, under the guidance of quality engineers, conducted experiments to help understand the contributions and interactions of process variables on the process and final product. One project requirement was to identify critical process parameters. The team conducted numerous designs of experiment (DOE) on isolated process steps to simplify the development process.

One basic building block for a Pellicon® 3 device is a membrane packet consisting of a permeate screen sandwiched between two membranes. Membrane packets are then separated by feed screens and stacked until the correct membrane area is achieved. To increase throughput while improving quality and cleanliness, the project team designed an automated packet assembly machine (APAM) that is fed rolls of membrane and precut screen, which are converted into finished packets. The APAM produces packets that are then in-line and on-line tested before robotically being stacked.

In determining the ideal machine operating conditions, the team conducted several DOEs to understand the impact of all process variables employed in manufacturing the packets.

For example, experiments were developed to measure the impact of each individual variable, as well as combinations of multiple variables, on selected outputs such as packet integrity or thickness (Figure 1, p. 28). Three critical heat sealing parameters were identified. This understanding allowed the engineers to focus on the most critical parameters and to establish appropriate operating specifications that result in a repeatable process that delivers packets of known performance characteristics (Figure 2, p. 28).

The knowledge gained from the DOEs enabled the proactive analysis of critical process parameters and will help in future development projects. Manufacturing engineers will continue to collect data and increase their understanding of the process. These steps will further reduce product variability by enabling modifications to the control methods and/or limits.

Delivering Quality

The final cassette manufacturing processes include design and manufacture to cGMP standards. These include cleaner design and manufacturing environments, use

continued on page 28

Compendial Requirements for Automated Microbiological Method Validation, continued from 24

[7] Yvon, P., "Viability-based Technologies: Solid-phase Cytometry Using Chemunex ScanRDI," *Encyclopedia of Rapid Microbiological Methods,* vol. 2, edited by M.J. Miller, pp 291-315 (PDA and DHI Publishing, LLC, 2005).

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About the Authors

David Jones, PhD, is the Director of Technical Services at Genomic Profiling Systems. He has many years experience with rapid microbiology methods, including time at Wyeth Biopharma were he helped evaluate and validate rapid methods and new technologies to improve laboratory efficiencies.

Scott Sutton, PhD, has had over 20 years of industrial experience with companies such as Bausch and Lomb and Alcon Laboratories before joining Vectech Pharmaceutical Consultants in 2004. Among his various affiliations, Dr. Sutton operates an information source on the internet—The Microbiology Network (http://www.microbiol.org) that provides services to microbiology related user's groups—and supports the PMFList, an e-mail list devoted to pharmaceutical microbiology (www.microbiol.org/pmflist_info.htm), and the Pharmaceutical Stability Discussion Group (www.microbiol.org/psdglist_info.htm).

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A Supplier Approach to Ensuring Process and Product Quality, continued from page 26

of robotics to eliminate human variations, in-line monitoring of critical process parameters, at-line testing of sub-assemblies and final products, and the use of precise controls and automation.

Just as pharmaceutical manufacturers strive to reduce batch variability in their products, these innovations have reduced batch variability in this filtration device. Biopharmaceutical manufacturers can be assured the UF cassettes they are using for their valuable product will perform as they expect them to.

Industry Gains

A number of gains in quality, safety, and efficacy can be seen as a result of Millipore's implementation of PAT principles in the manufacture of TFF devices.

- Reduced production cycle times through use of on-, in- or at-line measurements or controls
- Prevented rejects, scraps or reprocessing
- Increased automation to improve operator safety and reduce human errors
- Facilitated continuous processing to improve efficiency and manage variability

Manufacture in accordance with PAT guidelines will facilitate continuous learning through data collection and analysis over time, which will lead to further reduced product and process variability. Eventually, mathematical relationships between product quality attributes and critical material and process attribute measurements may result in real-time release.

State-of-the-art manufacturing under PAT principles using real-time control and quality assurance will reduce product variability. In the supplier arena, this will mean consistent, reproducible devices that have been manufactured using automated, continuous batch processes with robotics, continuous, in-line measurement of key variables, and in-line intermediate and final product testing. In the pharmaceutical manufacturing arena, this will result in TFF devices of high quality with repeatable performance.

Figure 1. Pareto Chart for L16 Array – Packet Thickness Results

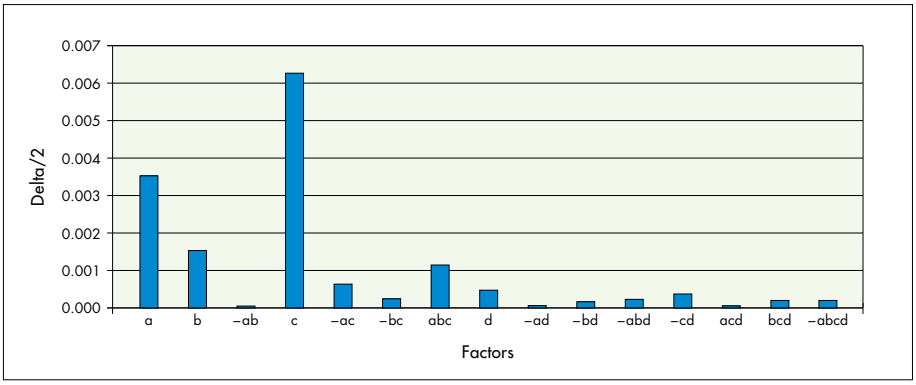
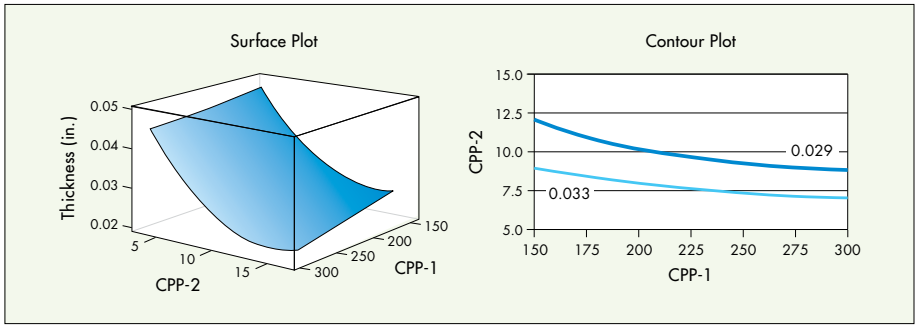


Figure 2. Surface and Contour Plots show effects of critical process parameters on packet thinkness



References

1. *PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance,* U.S. FDA Guidance for Industry, September 2004
2. Number of Monoclonal Antibodies on Market Nearly Doubles by 2008. *Biotechnology Healthcare,* pg. 64, June 2005.

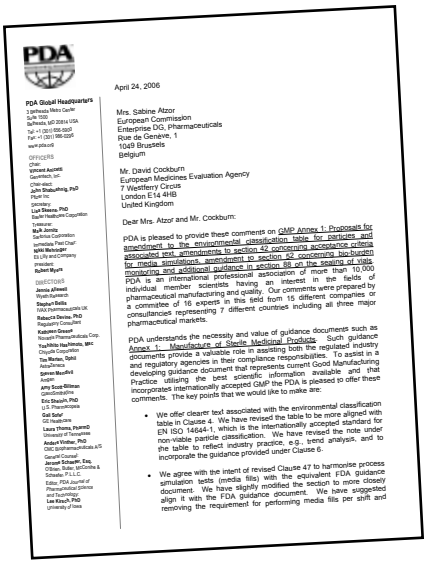
About the Authors

David Rubin has been with Millipore Corporation's Biopharmaceutical Division since 2002 responsible for Product Management of TFF devices. Most recently, he serves as a Program Manager responsible for the successful integration of new initiatives, products and facilities.

Robert Infinger is a QA Validation Engineer at Millipore. No further bio information was available at the time of publication.

Peter Eichert is the Quality Manager of Millipore's Jaffrey, NH facility, responsible for all quality aspects in the plant. He has 19 years experience in the quality field with 13 of that coming at Millipore.

PDA Comments on Proposed Changes to EU GMP Annex 1



PDA recently submitted comments on the proposed amendments to EU GMP Annex 1, Manufacture of Sterile Medicinal Products. The proposed changes were issued in late 2005 and included revisions environmental classification for particles, acceptance criteria for media fill simulations, bio-burden monitoring and sealing of vials, among other issues. The PDA working group, consisting of expert volunteer members from Europe, USA and Japan, commented on these proposals and even offered an alternative rewrite of the Annex incorporating the proposed changes.

The PDA suggestions embraced harmonization with EN ISO 14644-1, and the recent FDA final guidance on aseptic processing, where justified. A key comment addressed the proposed requirement that partially stoppered freeze dried vials should be maintained under Grade A conditions at all times, citing current aseptic practice in the industry that does not support the need for such a rigorous requirement. PDA thanks **Steve Bellis** and the working group (see below) who contributed their time and expertise to support the development of scientifically sound GMP guidance.

The full text of the PDA comments can be found on the PDA web site, www.pda.org/regulatory/RegComments.html

PDA Working Group

Steve Bellis, *IVAX* (Chair)

Mike Anisfeld, *Globepharm Consulting*

Martyn Becker, *Merck and Co.*

Jette Christensen *Novo Nordisk A/S*

Eric Dewhurst, *IVAX (on behalf of Blow/ Fill/Seal Operators Association)*

Volker Eck, *Nerviano Medical Sciences*

Dan Gold, *D. H. Gold Associates*

John Grazal, *AstraZeneca*

Klaus Haberer, *Compliance Advice/Services Microbiology*

Karl Hofmann, *Bristol-Myers Squibb*

Hirohito Katayama, *Astellas Pharmaceuticals*

William Miele, *Pfizer*

Stefano Salmieri, *Farmabios SpA*

Trudy Schots, *ZLB Behring AG*

Ian Symonds, *GlaxoSmithKline*

Frank Talbot, *FT Pharmaceutical Services*

April 24, 2006

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Enterprise DG, Pharmaceuticals
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1049 Brussels Belgium

Mr. David Cockburn
European MedicinesEvaluation Agency
7 Westferry Circus
London E14 4HB
United Kingdom

Dear Mrs. Atzor and Mr. Cockburn:

PDA is pleased to provide these comments on GMP Annex 1: Proposals for amendment to the environmental classification table for particles and associated text, amendments to section 42 concerning acceptance criteria for media simulations, amendment to section 52 concerning bio-burden monitoring and additional guidance in section 88 on the sealing of vials. PDA is an international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical manufacturing and quality. Our comments were prepared by a committee of 16 experts in this field from 15 different companies or consultancies representing 7 different countries including all three major pharmaceutical markets.

PDA understands the necessity and value of guidance documents such as Annex 1: Manufacture of Sterile Medicinal Products. Such guidance documents provide a valuable role in assisting both the regulated industry and regulatory agencies in their compliance responsibilities. To assist in a developing guidance document that represents current Good Manufacturing Practice utilising the best scientific information available and that incorporates internationally accepted GMP the PDA is pleased to offer these comments. The key points that we would like to make are:

- We offer clearer text associated with the environmental classification table in Clause 4. We have revised the table to be more aligned with EN ISO 14644-1, which is the internationally accepted standard for non-viable particle classification. We have revised the note under the table to reflect industry practice, e.g., trend analysis, and to incorporate the guidance provided under Clause 6.
- We agree with the intent of revised Clause 47 to harmonise process simulation tests (media fills) with the equivalent FDA guidance document. We have slightly modified the section to more closely align it with the FDA guidance document. We have suggested removing the requirement for performing media fills per shift and replaced it with the requirement that each person involved in aseptic processing should participate in at least one media fill per year. This is to address the need for each person, as part of their ongoing training/qualification requirements, to participate in at least one media fill and to address the point that with modern manufacturing practices it is becoming increasingly difficult to define a shift.

continued on page 31

Regulatory Briefs

Regulatory briefs are compiled by PDA member volunteers and staff directly from official government/compendial releases. Links to additional information and documentation are available at http://www.pda.org/regulatory/RegNewsArchive-2006.html.

Europe

EMEA Certificates of Medicinal Products

The EMEA released full guidance on the Certificates of Medicinal Products scheme. EMEA certificates confirm the Marketing Authorisation status of products and also confirm the GMP compliance status of the manufacturing site(s) producing the medicinal product and bulk pharmaceutical form (active pharmaceutical ingredient, API). EMEA can normally only certify a product if it has received a valid application for Marketing Authorisation via the Centralised Procedure. For products authorized *nationally* by EU Member States National Competent Authorities (National Authorisations and/or Mutual Recognition Authorisations), the certificates are issued by the national authority(s) granting the Marketing Authorisation. EMEA issues certificates within 10 working days following receipt of a valid application form.

Guideline on the Pharmaceutical Quality of Inhalation and Nasal Products

The EMEA published the final version of its guideline for inhalation and nasal pharmaceutical quality, which was prepared in collaboration with Health Canada. The guideline replaces all Quality Working Party (QWP) guidelines on pressurized metered dose inhalation products and dry powder inhalers. It is complementary to the existing EWP guideline on orally inhaled products. The guideline will come into effect on October 1, 2006.

GMP Info for the Qualified Person

The EMEA posted a "reflection paper" addressing compliance with the requirements of the Marketing Authorisation and the role of the Qualified Person (QP). Under EU rules, a batch of medicinal product, human or veterinary, that does not comply with the requirements of the Marketing Authorisation cannot lawfully be released for sale. From time to time a QP can be faced with a batch of product that does not fully comply with all the details described in the dossier. The competent authorities have been considering whether or not a QP is able to certify such batches, as required in Article 55(3)/51(3) of Directive 2001/82(3)/EC, thereby allowing them to be released for sale. The reflection paper intends to clarify, in the circumstances described, whether a batch complies with the requirements of the Marketing Authorisation or not. It is hoped that this paper will be helpful in dealing with cases where there has been some uncertainty. Cases of non-compliance outside the scope of this paper must continue to be dealt with by following the relevant national procedures.

The European Commission has signaled possible future support for an amendment to Annex 16 of the GMP Guide (Certification by a Qualified Person and Batch Release). This will partly depend on feedback from the industry on the practical implementation of the details in this reflection paper. EMEA is presently considering, together with the Commission, how this feedback should be collected and further information on this will be provided in the coming months.

PAT Information in Marketing Authorizations

The EMEA posted a "reflection paper" entitled, *Chemical, Pharmaceutical and Biological Information to be Included in Dossiers when Process Analytical Technology (PAT) is Employed.* The paper provides preliminary recommendations on how PAT related information should be presented in applications or variations to Marketing Authorisations. The EMEA notes that work on this topic is under continuing development. To avoid unnecessary barriers to improved product quality a flexible regulatory approach, rather than formal guidance, is important at this time. Nevertheless, the paper is intended to assist companies planning to file PAT-based submissions in the short to medium term. Feedback from the industry on the contents of the paper is welcome by the EMEA.

New Work Plans Published: GCP-GMP Inspectors Subgroup and GMP Inspection Services

EMEA posted new work plans for the GCP-GMP Inspectors Subgroup, which includes representatives of GCP Inspection Services and GMP Inspection Services. The Subgroup has been formed to consider a number of topics at the GCP/GMP interface identified by the industry or the regulatory authorities as areas where additional guidance or clarification would be helpful. The Inspection Services plan addresses: inspections under the centralized

system; co-ordination of re-inspections of manufacturers in third countries; mutual recognition agreements for GMP inspections; harmonization topics; GMP Topics including Annexes 1,2,3,6,7,14 and16; and collaboration with the European Commission and other groups.

United States

FDA Withdrawals Proposed Rule to Exempt Phase 1 Drugs from GMPs

FDA is withdrawing the direct final rule that published in the Jan. 17 Federal Register to amend its current GMP regulations for human drugs, including biological products, to exempt most investigational ``Phase 1'' drugs from complying with the requirements in FDA's regulations. FDA is withdrawing the rule because significant adverse comments were received.

FDA will now evaluate the comments received on the Direct Final and Proposed Final Rules, and will develop a Final Rule on this subject, following their normal notice and comment procedures.

FDA to Promote Best Practices Across Advisory Committees

In its broader effort to modernize approaches to managing the new drug review process, the Agency's Center for Drug Evaluation and Research (CDER) is launching an internal assessment of its Advisory Committee Meeting system in order to establish best practices surrounding this important process.

Led by senior management from the Advisors and Consultants Staff, within CDER, this comprehensive look at current practices will include the processes for nominating Members, choosing consultants with expertise specific to the meeting topic, developing competing products lists, screening for conflict of interest, and utilizing special government employees outside of an advisory committee meeting.

"This is part of an overarching quality systems improvement process within CDER designed to advance our approach to managing the review process, whether it is through process improvements in our own scientific work, through quality systems we adopt, or through technological improvements such as the incorporation of information technology to help us better evaluate the information we receive," said Dr. Scott Gottlieb, Deputy Commissioner for Medical and Scientific Affairs. "The idea is to identify best practices and adopt them center-wide to improve the consistency and predictability of the work we do."

"The advisory committee process is an increasingly important part of our work, and this effort is aimed at identifying and elevating the best approaches to take full advantage of the committees' function," said Dr. Steven Galson, Director, Center for Drug Evaluation and Research. "This, in addition to other recent commitments, such as working to adopt new quality systems for the way we manage post market studies and meetings with sponsors will allow us to continue to make improvements in how we approach our daily mission."

This review will begin immediately and is expected to take one year.

PDA Comments on Proposed Changes to EU GMP Annex 1, continued from 29

- We have suggested an adjustment to new Clause 57 to take account of the improved sterility assurance provided by the practice of using duplicate in-line sterilising grade filters for solution filling operations. When using duplicate in-line filters we believe it appropriate that the bioburden might be monitored only at suitable scheduled intervals.
- We have provided revised guidance on appropriate environmental conditions for the handling of lyophilisation vials between partial stoppering and final sealing. The new Clause 93 received the largest number of comments with all disagreeing with the requirement that: "Partially stoppered freeze dried vials should be maintained under Grade A conditions at all times, from the time of partial stoppering to capping". We offer a revised Clause 93 that represents proven good aseptic practice that is harmonised with other internationally accepted cGMP guidance documents.
- In general, we offer comments to more align Annex 1 with EN ISO 14644 and internationally accepted aseptic practice and GMP. We offer editorial comments to improve the continuity and clarity of some text.

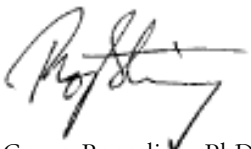
Attached please find a document that provides a Summary of PDA's Comments, as well as a second document where we have incorporated member comments into PDA Suggested Text for Annex 1.

PDA appreciates the work EMEA has put into revising Annex 1 and we offer these comments towards a joint effort for developing a scientifically sound GMP guidance document.

We would be pleased to discuss these comments with you at your convenience.

If I can be of further assistance, please feel free to contact me.

Yours sincerely,



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Europe Operations, PDA

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Annex 13 Two Years Later – Where Do We Stand?

Investigational Medicinal Products (IMP) & Clinical Trials in the EU

Susanne Keitel, PhD, BfArM

On May 1, 2004 both the EU Clinical Trial Directive and Annex 13 to the EU GMP guideline came into force. The directive is accompanied by a series of explanatory guidance documents, some of which are still being developed and discussed. The Annex emphasizes the role of the Qualified Person and the establishment of a Product Specification File. As regards submission requirements, the Joint CHMP/CVMP Quality Working Party has drafted a guideline which clearly differentiates between Investigational Medicinal Products Dossiers (IMPD) and Marketing Authorisation Applications.

After two years of implementation of the requirements, a number of questions still require answers:

- What are the first experiences since implementation?
- How well is the EU harmonized?
- Does the system allow enough flexibility to develop innovative drugs in the shortest time possible?
- Does it help to maintain and strengthen the EU as an attractive location for conducting clinical trials?

The PDA/EMEA joint conference will include discussion of this topic on. The session on "Investigational Medicinal Products" will summarize and discuss harmonization efforts for the quality part of the IMPD from both a regulator and industry point of view. This will include GMP aspects arising in inspections by the health authorities.

Investigational Medicinal Products

Thursday October 12, 2006
3:30-5:30 p.m. (15:30 – 17:30 h)

The Investigational Medicinal Product Dossier - Regulator View
Susanne Keitel, Bfarm

Investigational Medicinal Product Dossier – Industry View
Mike James, GSK

GMP and Inspection Aspects for IMPS
Richard Funnell, MHRA (invited)

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The aim of this conference is to increase understanding and awareness of GMP trends and expectations in Europe. Participants will include representatives from EMEA, member state health authorities and industry, who will share their expertise on recent developments in European GMPs and be available to meet and discuss topics with conference attendees.

Save the Date... Join us in London in October 2006 for the first ever **PDA/EMEA *Joint Conference!***

For further information please go to
www.pda.org/pdaemea2006

PDA℠ Parenteral Drug Association

emea

Vice President's Message

Gail Sherman

Mid-Year Review

With the first half of the year racing past us, I thought I would take this opportunity to do a "mid-year review" of TRI's activities and preview what's in store for the remainder of the year.

TRI had a hugely successful Annual Meeting course series in Anaheim at the end of April. There was a lot of good training offered, great instructors and positive feedback from the participants. We continued that into the Biennial Training Conference two weeks later; the content of new courses offered was well accepted. Our approach for this meeting focused on the trainer and what a trainer needs to do to develop, manage and provide training in a proactive environment. We plan to continue this approach into 2007, and maybe develop a course series for trainers in one of our selected venues. (And speaking of venues for 2007: We have selected those and are now filling them in with hot topics and on-going favorites. We will be in Houston, Tex.; Indianapolis, Ind.; Las Vegas, Nev.; Baltimore, Md.; Philadelphia, Pa.; Washington, D.C.; and San Diego, Calif. We also are planning, along with Georg Roessling, PhD, PDA's Sr. Vice President for Europe, to identify appropriate and timely topics to expand our services there.)

In May, we had the opportunity to provide Phase II GMP Training to 18 delegates from the Kazakhstan Ministry of Health, continuing an inspectorate training program we began last October. This training was at a more "expert" level than the first installment, with more senior-level participants. We spent much more time in laboratory functions and took the participants to Philadelphia to see facilities other than TRI. We are looking forward to an additional 20 delegates joining us in Baltimore in November for more focused inspectorate training.

The rest of the year continues with lecture series in St. Louis, Mo., and Boston, Mass., as well as with upcoming PDA conferences: the PDA/FDA Joint Regulatory Conference in September and the first ever PDA/EMEA Joint Conference. And of course our world-class, one of a kind laboratory training will continue through November.

And so the big news, of course, is the move of TRI to Bethesda (see Bob Myers' message). From a very personal perspective, I think this will be good for PDA, and we are all excited about participating in the design of the new space. Our focus is on building a facility that can provide more than one training program at a time, that has a "flow" that models a production facility, but is still a training facility, where students can actually see what is right and what is wrong—those concepts that only hands-on training can provide. We are excited about the potential for providing new types of training (biotechnology) and look forward to outfitting labs to respond to new initiatives. Stay tuned to future *PDA Letters* and updates as the move progresses. And I just got used to the commute up the interstate north! Guess I'll have to start rooting for the Washington Nationals baseball team (though the Baltimore Orioles will always have my heart)!

It is with mixed emotions that we look toward the end of 2006: We are sad to leave the comfort of the University of Maryland Baltimore County Tech Center, TRI's home since its founding, and, at the same time, we look forward to the challenges of our new home in Bethesda.

PDA Parenteral Drug Association

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Take home strategies to **build a better foundation for your organization's success:**

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www.pda.org/pdafda2006