

Delaware Valley Chapter of PDA Newsletter



***Connecting People, Science, and Regulation
In Pennsylvania, Southern New Jersey, and Delaware***

In this Issue:

- ❖ Breaking the Rapid Microbiological Method Financial Barrier
- ❖ Current Good Tissue Practices Draft Guidance
- ❖ 5S – Learning to Ask "Why?" from www.theleanthinker.com
- ❖ Letter from PDA DelVal President, Art Vellutato, Jr.

Upcoming Meeting:

Rapid Micro Methods

Date: June 16th 2009

Location: The Desmond at
Great Valley

Future meeting dates:

FDA Directives & Vendor Night
30-Sep-2009

Regulatory Inspections
11-Nov-2009

For more info, visit our website:
www.pdadelval.org

***Interested in contributing to
the Delaware Valley PDA
Newsletter?***

***Have ideas you would like us
to cover?***

Want to provide feedback?

Email mattschmidt1@gmail.com

Upcoming Event: Breaking the Rapid Microbiological Method Financial Barrier with Dr. Michael J. Miller

By Matthew Schmidt

The introduction of new rapid microbiological methods has been increasing for a number of years; however, there is a continued hesitancy with respect to implementation. While many concerns regarding regulatory acceptance have been answered, many still want to be convinced that the return on investment justifies the time and expense of implementation.

On June 16th Dr. Michael J. Miller will be sharing his insights into this obstacle. Dr. Miller has authored over 90 technical publications and presentations in the areas of rapid microbiological methods, PAT, ophthalmics, disinfection and sterilization, and is the editor of PDA's *Encyclopedia of Rapid Microbiological Methods*. He currently serves on a number of PDA's program and publication committees and advisory boards, and is co-chairing the revision of PDA Technical Report #33: Evaluation, Validation and Implementation of New Microbiological Testing Methods.

We were lucky enough to have time to hear a little bit about his experience with rapid micro methods.

When did you first learn about rapid micro methods, and how long did it take you to "buy-in" and believe that rapid micro methods will work, and benefit our industry?

I have been actively working with suppliers of rapid methods for the pharmaceutical industry since the early 1990's. I have always "bought-in" to novel technologies that provided microbiology results faster and with greater accuracy and precision than the conventional methods that have been in use for hundreds of years. Rapid methods do work; however, it is important for potential end-users to understand what their true requirements are for each application that a rapid method could be used for. The benefits are many – technical, quality, and even economically.



Continued on Page 2

Delaware Valley Chapter of PDA Newsletter



Upcoming event – from page 1

How many different options do companies have when looking to implement a rapid micro method?

There are a number of currently available technologies for the detection, enumeration, and identification of microorganisms that companies have installed and are using today. Furthermore, there is now guidance from the PDA (Technical Report #33, which is currently under revision) and the USP and EP on how to validate these new systems for routine use. Another reference is PDA's *Encyclopedia of Rapid Microbiological Methods*, which provides dozens of examples of the science behind the technologies, and how rapid methods have been qualified and installed within the lab and manufacturing environments.



Lasers are used in the real-time detection of airborne microorganisms. Image courtesy of BioVigilant Systems, Inc.

Are advances still being made in the methods themselves?

Absolutely. Today, there are new rapid method suppliers who are in the process of developing the next generation technologies. For example, future systems will be able to instantaneously enumerate the number of organisms in a liquid sample (in real time) and others will provide simultaneous detection, counting, and identification in a contaminated sample. I anticipate most of the newer methods will provide for single cell detection, increased accuracy, better precision and the introduction of in-line sampling capabilities.

From your perspective, how is the industry accepting the new technologies?

The industry is accepting these new technologies, but at a slower pace than what I had originally envisioned. The industry's hesitancy can be traced to three areas: validation guidance, regulatory acceptance, and economic justification. First, many in the industry are unaware that there exists guidance documents to help companies develop meaningful validation plans, and examples have been provided above. There have been numerous case studies on rapid method qualification presented in print and at technical meetings around the world. Second, regulatory agencies have embraced rapid methods and have also provided a framework for implementing these new systems, including the use of comparability protocols and PAT strategies. I briefly discussed the regulatory environment in an article entitled, "It's Time to Get Rapid" in the April 2009 PDA Letter. Lastly, it should come as no surprise that manufacturing site heads are looking to cut the cost of product sold and to introduce new manufacturing efficiencies in their day to day operations. Rapid methods can certainly play an important role in meeting these goals; however, it is important to fully understand the return on investment that these systems can provide in order to demonstrate a solid economic justification for moving your program forward. But I am not going to spoil the show! If you want to learn more about developing a business case for rapid methods, and learn how to use return on investment and payback period financial models for this purpose, you will have to join me during the Delaware Chapter dinner on June 16, where I will present an overview of each!

Regional News:

- ❖ **Greater Philadelphia Region Life Sciences Cluster Attains Top Rankings** - A comparative study conducted by the Milken Institute ranks the Greater Philadelphia region second in the study's Overall Composite Index, after only Boston and ahead of Greater San Francisco. (www.milkeninstitute.org)
- ❖ **Regional Life Science Companies Needed to Help College Graduates Get "Ready for Work"** - Recent college graduates with a diversity of degrees ranging from Associates to Doctorate will have an opportunity train with regional companies focused on life science, biology, chemistry, physics, bioengineering, or bioinformatics from September - December 2009. The Training Program's goal is to give college graduates the real-world experience they need to obtain quality jobs in the life sciences. (<http://www.delawarevalleyinnovationnetwork.com>)

From Press Releases at www.pennsylvaniabio.org

Delaware Valley Chapter of PDA Newsletter



Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue – Based Products (HCT/Ps) Draft Guidance

By Michelle Oravis

This draft guidance was released in January 2009 and addresses manufacturing human cells, tissues, and cellular/tissue-based products. Both cGMP and cGTP regulations govern the processing and recovery of HCT/Ps. The general rules dictated by the cGMP requirements in 21CFR parts 210 and 211 cover the quality and purity aspects of the drug, as well as the facilities, packaging, manufacturing, and holding of the drug to ensure safety to the consumer apply to HCT/Ps as they would any other drug product. cGTPs (§ 1271.150(b)) cover the facilities and controls employed in the manufacture of HCT/Ps. The goal of the cGTPs is to prevent the introduction, transmission, or spread of communicable diseases by HCT/Ps.

Specific biological and medical device HCT/P requirements outside of the scope of CGMPs and CGTPs are detailed in this draft guidance. The issues specific to working with HCT/Ps can be seen in the box to the right.

The bottom line is that HCT/Ps follow the same rules for facilities, equipment, cleaning, environmental monitoring, and aseptic techniques for processing as traditional pharmaceuticals. Specific regulations are in place for Transmissible Spongiform Encephalopathy contamination and recovery steps relating to donor eligibility. This draft guidance serves as a comprehensive guide the recovery and manufacture of HCT/Ps.

Specific HCT/P Issues:

- Information about the possibility of a communicable disease transmission must be communicated to other facilities that received HCT/Ps from the same donor.
- Equipment soiled with HCT/P from various donors can be loaded into the same washer and cleaned at the same time. There are no requirements for separating the equipment by donor or by equipment use.
- The sterility of certain products and HCT/Ps are regulated. Reagents that are used in conjunction with the processing and preserving of HCT/Ps are to be sterile. However, HCT/Ps are not required to be sterile. Aseptic techniques are the industry standard when working with HCT/Ps.
- Samples from various donors must remain separated. Also, samples from the same donor taken at different time points should also be segregated for the purposes of preventing cross-contamination.
- Pre-processing cultures are critical to ensuring donors meet all the requirements. They are also a good in-process control measure. These cultures can eliminate donors with cultures positive for *Clostridium*, *Streptococcus pyrogenes*, and any other microbiological agent that would prevent the recovery of workable HCT/Ps.
- Determining an expiration date for HCT/Ps requires evaluating the HCT/P type, processing, preservation, storage conditions, and packaging. Two expiration dates should be generated: one for fresh samples and one for cryo-preserved samples.
- Packaging and shipping of HCT/Ps is not required to be a validated process. The main goal of packaging and shipping is to prevent contamination. If the packaging and shipping procedures prevent contamination they are acceptable.

In each newsletter, we will provide an overview of a recently-updated, or draft guidance document from the FDA.

News from PDA National:

- *PDA/FDA Joint Regulatory Conference is coming up! Are you registered Yet?*
- *PDA Technical Report 15 "Validation of Tangential Flow Filtration" is now available*

Delaware Valley Chapter of PDA Newsletter



5S Learning To Ask "Why?"

By Mark Rosenthal

This photo could have been taken anywhere, in any factory I have ever seen. The fact that I do not have to describe what is out of place is a credit to the visual control. It is obvious. But one of my Japanese sensei's once said "A visual control that does not trigger action is just a decoration."

What action should be triggered? What would the lean thinker do? The easy thing is to put the tape where it belongs. But there is some more thinking to do here.

Ask "Why?"

Why is the tape out of place? Is this part of the normal process? Is the tape even necessary? If the Team Member feels the need to have the tape, what is it used for? If the Team Member needs the tape *there* has the process changed? Or did we just design a poor shadow board?

That last question is important because when you first get started, it is usually the case. We make great looking shadow boards, but the tools and hardware end up somewhere else when they are actually being *used*.

Our hope is that the lean concepts here will provide motivation and knowledge to continually improve our understanding of quality, efficiency, and our industry.

Too often, we use a "lean" tool, and fail to see the larger purpose behind it - we fail to ask "Why?"



"5S - Learning To Ask Why?" is taken from www.theleanthinker.com - a blog by Mark Rosenthal where he shares his thoughts and insights from the shop floor.

Why? Where is the natural flow of the process?

Before locking down "point of use" for things, you need to really understand the POINT where things are actually USED. If the location for things like this does not support the actual flow of the normal process, then you will have no way to tell "the way things are" from "the way they should be."

The purpose of 5S is *not* to clean up the shop. The purpose is to make it easier to stand in your chalk circle and see what is really happening. The purpose is to begin to ask "Why?"

By the way - if you see an office chair being used as an assembly bench, you need to spend a little more time in your chalk circle.

Delaware Valley Chapter of PDA Newsletter



Message from the President

How does a GMP firm assure both compliance and quality? Questioning the current best practice is probably the most frequent endeavor. Unfortunately, most times this question has many answers. And even when a decision is rendered from a corporate consensus, doubt remains as to whether the decision is the correct one.

So what do firms do? One methodology that is all too familiar is to read each line of a regulatory document and imagine the multitude of meanings that can be deciphered. And even though we know what we are doing by such a time consuming exercise, we repeat such steps for our entire careers. We read it one day and it means this, the next day and it means that, and if we hold it sideways, it means something else. Another methodology is to conduct a best practice survey of other firms or seek the advice of consultants in the industry. In the end we attain satisfactory information in which to render a decision but the path to get there was very difficult. Understandingly, the lack of access and assured meaning of content is an enormously problematic and costly situation.

While the multitude of avenues nets some satisfaction, many do not take advantage of the obvious. As a PDA member, you have the opportunity to be part of a task force for writing industry technical reports, commenting on technical reports, or simply reviewing the finalized technical report. Such technical reports have been compiled to discern best compliant industry practice by peers in the industry. This valuable asset is sometimes forgotten. Few firms have the attention and support of regulatory agencies. The PDA is one organization that has had the careful ear and support of regulatory agencies worldwide for over 50 years.

Countless technical reports exist for a multitude of disciplines. Some of the upcoming or recently released documents include:

- *PDA TR No. 15 (Released Jun 2009): Validation of Tangential Flow Filtration in Biopharmaceutical Applications*
- *PDA TR No. 13 (In Revision): Fundamentals of Environmental Monitoring*
- *PDA TR No. 22 (In Revision): Process Simulation*
- *PDA TR No. 33 (In Revision): Evaluation of Validation and Implementation of New Microbiological Methods (Rapid Methods)*
- *PDA TR No. TBD (In First Revision): Fundamentals of Cleaning and Disinfection Programs in Controlled Environments*
- *PDA TR No. TBD (Currently In First Revision): Validation of Manual Aseptic Processes*

These technical reports and many others may serve as an invaluable source for your organization for the most up to date compliant industry practices with the added advantage of having ability to comment or contact committee members to clarify any confusion in interpretation. As President of the Delaware Valley Chapter of PDA I would strongly encourage you to either become a part of the creation of these documents or to know that they are readily available to you through PDA at <http://www.pda.org>.

We thank you for your continued support of the Delaware Valley Chapter of PDA and look forward to serving you for years in the future.

Sincerely,
Art Vellutato, Jr.
President of the Delaware Valley Chapter of PDA

Advertising Available!

We offer vendors, consultants, operating companies, and other organizations the opportunity to promote themselves and also support the Delaware Valley Chapter of PDA by purchasing advertising in our newsletter.

Please email jason.c.mattis@gsk.com for more information