PDA Southeast Chapter

SOUTHEAST CHAPTER
www.pdase.org

Letter From the President

August, 2004

Hello! My name is Lisa Eklund, and I am the new President of the PDA Southeast Chapter. Elections were held in December 2003 for the 2004 – 2005 terms. On behalf of the Executive Committee, I would like to thank all of you for your support and participation. Our officers are Lucia Clontz (Vice-President), Anita Garrett (Secretary), and Tony Pavell (Treasurer). The committee chairs are Pam Webb and Patrick Sabourin (Programs), Steve Podolski (Sponsorship), Christine Cramer (Communications), and Kip Lopez (Membership). All of these volunteers work hard and provide a lot of help.

I look forward to serving you for the remainder of my two year term. The Executive Committee's purpose is to meet the needs of the chapter members. My mission is to continue the fine traditions established over the years and to establish some kind of philanthropic activity for the chapter. I encourage all of you to contact anyone in the Executive Committee with your comments and suggestions. We strive to keep improving our meetings and services to the chapter. Remember to visit the website, www.pdase.org, for information on PDA Southeast Chapter and national chapter activities. We hope to see you at our Fall Meeting and Vendor Show on October 20, 2004 at the Sheraton Imperial in Research Triangle Park.

Remember to visit the website, www.pdase.org, for information on PDA Southeast Chapter and national chapter activities.

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Environmental Monitoring Data: Adverse Trends and Product Impact

By **Kenneth H. Mulvich, PhD**, **Principal Consultant, Micro-Reliance LLC**

Summary By Kodi Michaux, Data Quality Auditor I, and Talsker Dixon, Control Scientist III, DSM Pharmaceuticals, Inc.

Kenneth H. Muhvich, PhD, Principal Consultant for Micro-Reliance LLC gave a presentation on Environmental Monitoring at the Spring PDA Southeast Chapter Meeting. This event was held on April 20, 2004 at the NC Biotechnology Center in Research Triangle Park, North Carolina.

Ken began his presentation by emphasizing the sources of microbial contaminants in an aseptic facility, which includes environmental air, inanimate surfaces (and objects), raw materials, packaging components, and personnel (i.e. operators and mechanics). Environmental air refers to HEPA filtered, Laminar air. Contamination can result from turbulent air flows (identified through smoke studies), patched filters, and/or leaks around HEPA filters. Inanimate surfaces include tools and supplies for the aseptic core, areas under working height of the filling line, and items frequently touched by operators (i.e. control panel). Contaminants associated with raw materials can include organisms associated with WFI (which is not sterile), Bulk antibiotics (which can be a source for Fungi), and materials with high moisture content (high moisture promotes microbial growth). Packaging components include cardboard boxes, wooden pallets, and packing materials. Ken suggested that incoming lots of packaging components be monitored for Bioburden. In addition, he also indicated that wooden pallets should never be found near the aseptic core. Furthermore, Ken emphasized that personnel is the major source of microbial contamination (i.e. common human skin contaminants). Contributing factors include

continued on page 3

PDA Golf Social
Rain Date: Friday, Oct 8
Details to follow

continued from page 2

poor aseptic and gowning technique, and poor clean room conduct. In addition inadequate cleaning and sanitization can lead to the formation of bio-films in aseptic areas.

Some of Ken's other highlights included the importance of establishing good sample sites. Sample sites are usually determined by reviewing data sets from "commissioning samples" (i.e. mapping studies). Hazard analysis and critical control points can be used to help establish good sample sites. Sample sites can include rotated sites, but should also include fixed critical sites. Everyone should know the rationale for the sites they sample.

Along with establishing sample sites, you must also establish limits or levels for the sites. Ken recommended using the terms "limits or levels" and not "specifications" (which are tied to lot release). Various documents like USP and FDA guidelines provide some Environmental monitoring limits/levels. Limits/levels can also be set based on historical data and capabilities of the facility. More commonly it has been found that limits for clean rooms are consistent as where limits/levels for personnel are often inconsistent. There are two theories that are usually true about limits/levels:

- If limits for viable particulates are not exceeded, and there were no interventions, the product produced will more than likely meet requirements for a sterile product.

- Exceeded limits imply that the cleaning and sanitization program is inadequate or that some breach in aseptic handling or technique has occurred.

An excursion, as presented, refers to a failure of an Environmental monitoring sample to meet predetermined limits/levels. In addition, an excursion may also be an unexpected finding (i.e. a new microorganism, an increased incident of a particular microorganism, and/or failure to detect any microorganisms). Excursions should be investigated in a "Scientific" manner within 30 days, but not to exceed 60 days, of the occurrence. Suspect product should not be released until safety issues are resolved. Excursion investigations should be thorough, encompassing all details during the particular activity, because a common error is not identifying the actual root cause, which could lead to a potential microbial contaminant to persist.

Several factual case studies were presented to support an emphasis on performing thorough investigations:

- One case study focused on the identification of a new microbial isolate (gram negative rod) in a facility. The new microbial isolate persisted because the microorganism was disregarded due to the microbial recoveries being within the facility's allowable limits, and proper corrective action was not taken. The result was batch failures due to lack of sterility.

continued on page 4

continued from page 3

- Another case study was for Mold, which was isolated in a clean room several times in a 30-day time span. Corrective action was not taken (i.e. no cleaning with a Sporicidal agent). Ten days after the manufacturing of the product, visible growth of Mold was evident in the product.

- An additional case study dealt with a Microaerophillic contaminant. The contaminant was isolated from FTM broth tubes, but was never isolated during routine Environmental monitoring of the room or personnel. Early on, the probable cause was attributed to gowning technique; however, conducting a media fill with FTM found that the organism was resident in the aseptic area.

Several other factual cases were also presented to emphasize the importance of a timely, thorough investigation.

Ken concluded his presentation with some questions that you should be able to answer pertaining to your EM program. Some of those were what is the overall "hit rate" in your Grade A/Class 100 areas (the FDA expectation is <0.5%). How does your contamination rate this year compare to last year? How do they compare quarter to quarter? What are the "top five" bugs in your facility by percentage? Have you seen any new or unusual microorganisms in the last 12 months? These questions should be addressed in your EM trending reports.

In conclusion, an adequate Environmental monitoring program gives critical information to the manufacturer about the operational state of a facility and also provides a basis for making decisions about the safety of the product that is being produced. A well thought out Environmental monitoring program in concert with effective data analysis will also go a long way in preventing product contamination. Failure to recognize negative trends in EM data will ultimately result in product sterility failures.

PDA Southeast Chapter Sends Most Chapter Information Electronically.

If you have a new email address, please send this information to PDASE at proflink@bellsouth.net

Two Foundations of Understanding Risk: Variability and Process

Presented by Karen Welch, Sr. Partner, Center for Risk-based Strategies, Inc..

Summary Written by Melinda K. Light, Microbiology/ aaiDevelopment Services

With today's technology we can measure low potency, non-conforming, non-uniformity and/or low dissolution of our manufactured product lots. This allows us (the manufacturer) to reject or re-call these lots. Unfortunately, we cannot always determine root cause(s) of the failure or prevent recurrences.

One aspect to review as a root cause analysis is: Do we have sufficient process knowledge and are we measuring ALL critical quality attributes during the development AND manufacturing stages of the product. A trend in the process development and manufacturing of products is Risk Based Processes.

In determining whether to pursue a risk-based process we need to know and understand the "risks" involved. Are there risks to the consumer i.e. Patients, regulator or the industry?

Karen discussed two foundations of risk, Risk Assessment and Risk Management.

Risk Assessment: The process by which the form, dimension, and characteristics of risk are estimated.

Risk Management: The overall and continuing process of mitigating (or minimizing) risks throughout a product's lifecycle to optimize its benefit/risk balance.

We must employ Good Science and Engineering Principles to eliminate variation and understand the process before we can effectively assess and minimize risk. By increasing our knowledge we are able to more effectively assess risk. Minimizing variations will also reduce risk. Without using

continued on page 6

continued on page 5

any new technology we are able to decrease risk by reducing variation.

A process is considered well understood when:

- All critical sources of variability are identified and explained
- Variability is managed by the process
- Product quality attributes can be accurately and reliably predicted

In order to achieve process control regulatory policies must be tailored to recognize the level of scientific knowledge supporting product applications, process validation, and process capability. Product specifications need to be based on mechanistic understanding of formulation process in all variation factors that could impact manufacturing process. This will achieve continuous assurance of quality of your product.

For more information on Understanding Risk: www.crs-roi.org or kwelch@crs-roi.org.

PDA/FDA Joint Conference September 20-22, 2004 Washington, DC

By Lisa Eklund, PDASE President, Hospira

The PDA/FDA Joint Conference will be held September 20-22 in Washington, D.C. The focus will be upcoming regulatory guidances.

The national chapter has established a Volunteer Program. This program is open to anyone who wishes to participate. If you agree to volunteer 6 hours of your time at a national meeting, you can get your conference registration fee reduced by 50%. It is a very worthwhile program. I have done this myself, and it was a great opportunity to meet new people, help the national chapter, and save on registration costs.

Additionally, the national chapter has started a Chapter Points Program. Each chapter that earns at least 250 points in a year will receive $1000 from the national chapter. The top chapter will receive $5000. There are many ways to earn points including the following:

- Hosting regional chapter meetings and events
- Having new members join the national chapter
- Getting members to attend the national meetings
- Getting members to write articles for the national newsletter

These are just a few of the ways that we can earn points. We will provide more details at a later date. This program just started this year, and the Executive Committee is still trying to formulate a strategy to help the chapter. The important thing is that all of you can help us earn some money for the chapter which will benefit everyone.

The national chapter is also allowing the regional chapters to use their credit card services. We are still discussing this at the Executive Committee meetings. We welcome any feedback from the members because there is a processing fee involved with this service.

The Fall Meeting and Exhibitor Show will be held Wednesday, October 20, 2004 at the Sheraton Imperial Hotel and Convention Center in RTP, NC.

This is typically the most well attended meeting PDA Southeast Chapter presents.

Please mark your calendar and follow the PDASE website, pdase.org for registration information.

In addition, if you know of a company who might be interested in exhibiting, please direct them to the site, http://pdase.org/pdf/vendor_show_2004.pdf

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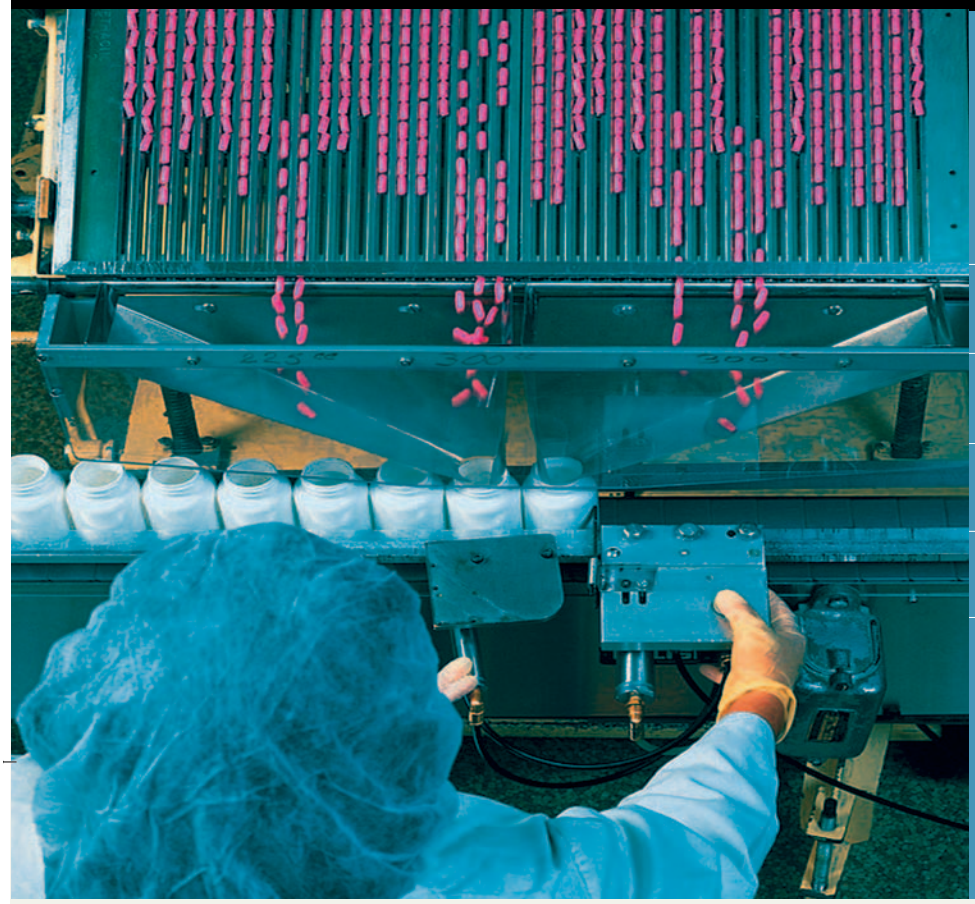

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