PMF NEWSLETTER

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Investigations and Contamination, with the Return of an Old Friend

This month we are fortunate to have an article written by Frank Settineri describing in detail a case study for an investigation he performed into a potential sterility test failure. This case study is remarkable for its candor and thoroughness. Frank Settineri does an excellent job of describing a fairly complicated situation, where the product was filled by a contract manufacturer, and the sterility test performed by a different contract organization.

Important Links:

Information on the PMFList at
http://www.microbiol.org/pmflist.htm

Past Issues of the *PMF Newsletter* at
http://www.microbiologyforum.org/news.htm

To continue with the topic of contamination, we also present for your summer reading a review of the role of microbiology in development of a facility Contamination Control Plan. This document is a useful one, no matter the manufacturing process or finished product dosage form.

Also in this issue we find the *Call for Abstracts* for the PMF Fall Forum. Those who have attended in the past remember this conference for its intimate discussion opportunities. Presentation slots are limited (as are the limited registration opportunities) so do not miss out on the opportunity to present and lead discussion on a topic of interest to you or your company.

Finally, we have great news! The LAL User's Group is joining with PMF and re-launching the *LAL User's Group Newsletter*. Karen McCullough will be once more leading this organization, and those of us old enough will remember the outstanding service this organization has offered the industry. Welcome back to an old friend!

Scott Sutton scott.sutton@microbiol.org

A Practical Approach to Conducting Microbiological OOS Investigations

Frank Settineri
Veracorp LLC

Few microbiological events are more disconcerting than an out-of-specification result, commonly referred to as a Microbial Data Deviation (MDD). In the November Microbiology Forum Newsletter[1], Dr. Sutton detailed the process for conducting an MDD investigation, predicated upon the guidance documents including the FDA Out-of-Specification (OOS) guidance[2] (which essentially excludes microbiological and biological assays) the ICH Q7A OOS guidance[3] (which states that OOS investigations are not necessary for in-process tests) and USP <1117>[4] which intimates the difficulties associated with resolving a MDD. In the absence of a definitive guideline for conducting a MDD investigation, how is it possible to conduct a microbiological investigation that is scientifically sound and meets regulatory requirements?

I propose that the FDA Aseptic Processing Guidance[5] can be invoked to provide a rational, methodical, scientific approach to address the issue. Although this guideline addresses sterility issues, since sterility is the most critical attribute of a product, application of the stringent investigational principles in the document can be applied to any other product or raw material characteristic, thus ensuring that the decision to retest or fail a product has been made with the greatest scientific scrutiny and the lowest risk. Although invoking sterility attributes to non-sterile raw materials, products and assays may appear to be excessive, if applied judiciously and in conjunction with the approach provided by Dr. Sutton, they can be effective tactics in performing MDD investigations.

I would like to outline how a client used the Aseptic Processing Guideline to resolve a potential sterility test failure and how the incident can be used to model non-sterility related MDD investigations. This real life example involved a sterility failure on day 12 of an aseptically filled antibiotic ampule. Of course panic ensued throughout the organization because it was the first sterility test failure in three years of operation. To complicate matters, the client had recently been purchased by a larger company (complete with all the political ramifications), the active ingredient was sourced overseas, it was sampled and preweighed in New Jersey and it was shipped to another state where it was compounded and filled by a contract manufacture; the raw material and final product were tested by a contract laboratory. This event was the beginning of a long, protracted learning experience.

After the initial panic, as any microbiologist knows, the microbiology department was blamed for the failure and the product was slated for rejection. Before we proceeded down this road I intervened and requested that the product be placed on hold pending an investigation. We reviewed all the data from the last three batch records and reviewed the historical data from the last three years to determine if we should halt production. Due to the superlative recent and long term product history, and after some rather poignant discussion, we decided to continue with production since this

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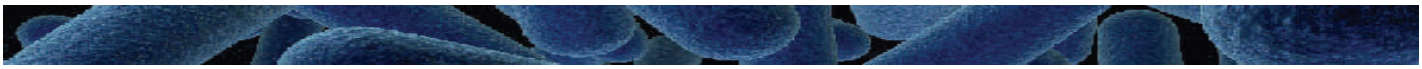

The Importance of Microbiology in the Contamination Control Plan for Aseptic, Terminally Sterilized and Non-sterile Manufacturing

Scott Sutton, Ph.D.
Vectech Consultants, Inc.

Introduction

The development of a contamination control program is critical to the effort to get a new facility qualified, and to maintain the facility in a state of control once qualified. The design and successful execution of a contamination control program requires a plan. The creation of a specific document allows the company philosophy, goals, and expectations to be formalized and agreed to by all parties. It also provides the goals and metrics by which the state of control for the facility can be measured in the annual review. The business reasons for this are obvious in terms of reduced regulatory risk and reduction of rejected/recalled batches (Lowry 2001).

This plan is important no matter what type of facility is being developed. Although it is most frequently used in the Quality plan for commissioning an aseptic facility, this is also important and should be used for commissioning and controlling facilities using terminal sterilization, and for non-sterile manufacturing facilities.

Why be concerned with contamination control in a non-sterile manufacturing facility? In many ways contamination control is more of a concern in a non-sterile facility than in sterile product production facilities. The sterile production facility knows there is a problem with contamination and cross-contamination of batches, the non-sterile facility has a great temptation to belief they are not touched by these issues. This can lead to an extremely cavalier attitude about contamination control by the operators and management. The non-sterile manufacturer is responsible for all aspects of his product, including any objectionable organisms present (Sutton, 2006) as described in a recent newsletter (*PMF Newsletter* v12 n7).

The API manufacturer is also concerned with contamination control. The FDA has explicit instruction on this score (FDA 1998) out of CBER. The EMEA guidance on API manufacture also includes guidance on control of bioburden and cross-contamination of batches (EMEA 2000)

This essay will not be able to provide more than an overview of issues in the space available this month. However, it is hoped that the need for an adequate contamination control plan for a facility will be made clear, and the beginnings of the content of such a plan explained. The interested reader is referred to the articles listed in the "References" and the "Further Readings" sections.

Scope

The Contamination Control Plan should be developed as part of the facility commissioning effort. As such, there will be four distinct phases of the facility operations that will need to be addressed:

1. Commissioning and initial start-up
2. Ongoing Operations
3. Shut-down for regular maintenance
4. Start-up after scheduled shut-down

These phases will not have the same level of contamination control. In fact, the third and fourth phases may well have different levels of control to be addressed. A good plan will discuss the concerns specific to each of these phases.

This program, and the protocol governing the program, are essential documents useful in documenting the rationale and methods used to accomplish three tasks:

- Minimizing the bioburden throughout the manufacturing processes
- Minimizing the level of batch residual cross-over contamination
- Minimizing the level of cleaning material residual contamination

As the SME (Subject Matter Expert) in microbiology, we will be most heavily involved in the first of these three tasks, minimizing bioburden. However, all three will be discussed (at least briefly) in this essay for context.

Minimizing Bioburden

Validated methods

All measures of bioburden in a facility will be indirect. We cannot count bacterial cells on a surface or in the air. We must transfer the microorganisms to an agar plate (or some other mechanism) and count colony forming units. If we make the assumption that the transfer of microorganisms from the air or from a surface to agar is consistent, then we can use these numbers to estimate trends over time. This

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assumes that the nutrient agar is capable of growing the microorganisms to visible colonies. As residual disinfectant on a surface may impede the growth of microorganisms, neutralizers are frequently incorporated into the growth media (Dey-Engley agar, MCTA, etc.). All sampling methods must be validated for the conditions of use.

The facility should be disinfected regularly using validated sanitizers and sporicides. The contamination control plan should describe the methods for testing and rationale for acceptance of materials to be used in the ongoing program of disinfection. The plan should ideally describe the *in vitro* or laboratory tests to evaluate the sanitizers, including the identification of the most resistant microorganisms found in the facility as well as the most difficult-to-disinfect materials in the facility. This is also where the method for on-going evaluation of the sanitizers based on environmental monitoring data will be recorded. The choice of disinfection regimens should be reevaluated annually, and the contamination control plan should describe how this evaluation will occur.

Know the enemy

A successful contamination control program is geared to providing the most useful information on the microorganisms present while at the same time showing some fiscal responsibility. The FDA aseptic processing guidance document recommends genetic identification of all organisms isolated from the manufacturing environment on a regular basis. (FDA, 2004) This is a laudable goal, but few of us have anything near the required budget to accomplish this task, and in all honesty it is reasonable to wonder if it is really necessary. The numbers of CFU from validated sites (viable air and surface, non-viable) is sufficient to provide a measure of the state of control of the facility. However, periodic cataloging of the resident microflora will provide you with a good check on the continued effectiveness of the disinfectants in use. Shifts of bioburden to spore forming microorganisms will be strong evidence of the need for use of a sporicidal agent. Occasionally, this effort will also pick up shifts among non-spore-forming organisms – this is not due to "resistance" but rather ecological shifts towards species more naturally resistant to the disinfectant in use.

Control incoming bioburden

The first step in any control program is to control contamination at the very beginning of the process. This includes raw materials (excipients, API, water, etc) and the primary containers. All materials should be tested for incoming bioburden against documented acceptance criteria. Part of the incoming bioburden will also be any water used as an excipient to the process. A good guide for the water bioburden is the EMEA guidance on the subject (EMEA 2002).

Appropriate gowning

The gowning methods and materials are of critical importance to minimization of contamination. Although most attention is placed on aseptic gowning procedures, the appropriate use of gowning precautions will be a great boon to most non-sterile manufacturing facilities as well. All personnel should be well-trained in appropriate gowning practice and behavior. The contamination control plan should describe the rationale for the level of gowning chosen, the frequency of gown cleaning, behavior and the acceptable gown materials for the type of manufacturing process.

Training

Operator training is critical to contamination control. No supervisor can be present at all locations at all times. Each operator must be aware of his or her role in contamination control and how to minimize the risk to batch integrity. The PDA has published a technical report that speaks to some of these training requirements from the microbiological perspective (PDA 2001).

Controlled Environments

Control and monitoring of the environment is another critical element of the contamination control plan. Large portions of this can be addressed by the corporate Environmental Monitoring Master Plan (which provides rationale and consistency for a single EM philosophy

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Internet Address	Description
http://www.free-ed.net/free-ed/Science/Biology/microbiol01/default.asp	Free-Ed Microbiology: This free course of study is built around Prescott, Klein, and Harley, Microbiology, 5th edition; published by McGraw-Hill Higher Education.
http://student.ccbcmd.edu/~gkaiser/goshp.html	Dr. Kaiser's Microbiology Course - Excellent resource for basic microbiology information and graphics.
If you have found an Internet site that contains information of relevance to professional microbiology in the industrial sector, please let us know.	

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presumed failure appeared to be an isolated case. We kept the batch on hold pending our investigation.

The initial step of the investigation was to write an investigation protocol, based upon the criteria contained in the Aseptic Processing Guideline, in which we detailed exactly what we should do. Essentially there were seven specific areas that needed to be investigated:

1. Identification (speciation) of the organism in the sterility test
2. Record of laboratory tests and deviations
3. Monitoring of production area environment
4. Monitoring of personnel (laboratory and production)
5. Product pre-sterilization bioburden
6. Production record review
7. Manufacturing history (including media fills)

In addition we added four more areas to investigate, which placed the bulk of the investigation on the laboratory operation, aligning it with a MDD investigation:

8. API source
9. Excipients
10. Weighing facility (separate location)
11. Contract laboratory

We wrote the protocol and had it countersigned by senior management in my client's company, senior management in the contract filling plant and senior management in the contract laboratory. This was imperative because we would need the full cooperation of all parties in order to thoroughly conduct the investigation. Once we had this protocol in place we were ready to begin. Many of these activities were conducted concurrently and will be discussed with the omission of specific data to honor proprietary principles.

1. **Identification (speciation) of the organism in the sterility test**
   The organism was identified as *Proprionibacterium acnes*, indicating it was associated with human intervention.

2. **Record of laboratory tests and deviations** We reviewed the sterility test history of the contract laboratory for the past three years and found their sterility failure rate and false positive rate to be less than 0.1%. This organism had not been found in the past.

3. **Monitoring of production area environment** We reviewed the past three years of environmental monitoring data from the production area and found one instance of this organism eighteen months ago on an air sampling plate. It was not found in the sterile shrouded area and there were no associated sterility or environmental issues with this particular organism.

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4. **Monitoring of personnel (laboratory and production)** We did not find the organism on either the laboratory or production personnel in the past three years.

5. **Product pre-sterilization bioburden**
We reviewed the bioburden of the compounded product for the past three years and found one instance where it exceeded the limit of ≤10 CFU/100 mL; this organism was not isolated. The bioburden trend data indicated that there were bioburden counts within the specification only once or twice a year; each time the organism was a *Bacillus*. All the other times the bioburden was ≤10 CFU/100 mL. In the instance when the counts exceeded the limit (two years prior to this incident), the cause was traced to biofouling within the compounding tank, which was rectified by treatment with CIP 100 after each bi-annual media fill. Subsequently the problem vanished.

6. **Production record review**
Production records were reviewed for the past three years and there was no indication of any excursions that were not readily addressed during the runs. The current record was also reviewed and no excursions of any type were found.

7. **Manufacturing history (including media fills)**
There were no sterility, bioburden (other than the aforementioned) personnel or environmental OOS results during the past three years. The manufacturing area was pristine, the personnel were well trained and my client placed a man-in-the-plant for every batch that was run. Media fills (15,000 ampules each of TSB and FTM) were conducted twice a year and there was never a positive result.

8. **API source**
Microbial limit testing was performed on every batch of API by both the overseas manufacture and the US contract laboratory. The microbiological history was reviewed for the past three years and no instances of *Proprionibacterium acnes* were encountered by either facility. Occasionally *Bacillus* were found in levels below the specification ≤4 CFU/gm and appear infrequently in the pre-sterilization bioburden (addressed above).

9. **Excipients**
Microbial limit testing was performed on every batch of excipient by both the manufacture and the contract laboratory. The microbiological history was reviewed for the past three years and no instances of *Proprionibacterium acnes* were encountered by any facility. In addition, other than WFI the excipients were rather corrosive and not conducive supporting the growth of this organism.

10. **New Jersey weighing facility**
Every area of the NJ weighing facility that could have been in contact with the API and/or excipients was thoroughly scrutinized, including the receiving area, holding area, weighing room, transfer area, shipping area and even the analytical labs. This particular organism had not been found for the entire time the fa-

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cility was in operation (three years). Additionally the facility had been trending the microbial burden in the weighing room and the settling plate counts remained below 2 CFU per sample site.

11. **Contract laboratory**
    The contract laboratory was completely scrutinized, including the receiving area, staging area, anteroom, sterility suite, cleaning processes, HEPA filters, personnel, autoclave cycles, purchased media and sterility equipment, incubators, environmental isolates, and anything that was remotely associated with the product. This organism had not been isolated, dating back three years. The documentation was in order and provided complete cross referencing to media preparation, sterilization, growth promotion, organism maintenance, environmental monitoring, cleaning and (most importantly) training.

The bottom line was that although the operation was scattered across the world, it was so intensely monitored that we found only one other place (an air sampling plate in the production area) where the organism was observed, eighteen months prior to the presumed sterility test failure. Despite our findings the new senior management was exerting pressure to reject the batch, which I was not inclined to do because nothing made sense. Based upon the data we had collected, i.e. the type of organism (associated with the skin), the history of the weighing facility, production facility and laboratory, the validated process maintained its validated status and produced no sterility issues, excluding this one exception. The only certainty was that the weakest link in the process (as it is in most processes) was the sterility test. Unfortunately the investigation produced no clear cut answers and if we were to invalid the test results, we had to find a smoking gun. This was a major obstacle.

Under extreme pressure from upper management, we were able to buy some more time to continue the investigation. We went back to the laboratory and asked them if we could observe in real time the manner in which they handled the product from the time it entered the lab until after the final results were recorded. We performed a simulated study in which we shipped product to the lab for testing and I personally watched every step of the operation: receiving and logging the product into their system, storing the product, preparing it for testing, staging it and transferring it into the sterility suite. I even gowned up with the technicians and stood behind them while they performed the sterility test. Everything was perfect. I couldn't find the smoking gun and was resigned to the fact that we would have to reject the batch without any definitive root cause.

There was one glimmer of hope, however.

During the sterility test 20 ampules were pooled into a sterile container prior to filtration. The sterile containers were urine sample containers that were sterilized by gamma radiation. They were shipped to the lab in a large cardboard box containing a polyethylene bag filled with

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1000 containers. Before the sterility test the containers were staged in the set up room and transferred into the sterility suite. I asked why the containers were not individually wrapped and was told it was less expensive to buy them in bulk. The lab recently made the change from individually wrapped containers to the bulk package containers.

Somehow I had overlooked this fact during the initial investigation and after the simulated sterility test I asked the lab to sample the inside, outside and flaps of the cardboard box, and the polyethylene bag. As you may surmise, we found two samples that contained *Proprionibacterium acnes.*

The smoking gun! Residing right in the cardboard box that contained the sample containers used to pool the product before filtration. We were overjoyed (especially the contract lab). We had our evidence to invalidate the original test. Before retesting we asked the lab to purchase individually wrapped samples containers, then invalidated the original sterility test, performed the retest and released the product based upon the results of a successful test and the completion of the investigation by the client, contract manufacturer and contract laboratory.

How does my experience with the Aseptic Processing Guideline for sterility testing apply to an MDD or OOS you may encounter in your lab? There is always a reason for it. By carefully and methodically conducting your investigation, repeating parts of the investigation and scrutinizing the data like a hawk, you will begin to "sense" where the problem may reside. You will certainly be pressured to reject the batch, whether it is a sterility failure, microbial limit failure, assay failure or whatever. However, if it is a validated process and all the controls are within operating specifications, the most likely source of the problem will be human error (this is the "sense"). In order to figure out where the problem resides, it may be necessary to review all aspects of the process, from the raw materials to the weighing areas, to the production area and certainly the laboratory. It may be necessary to have an experienced third party sit with the technicians in each area and carefully observe the process from beginning to end. This close observation will help you discern a minor inconsistency which may lead to a major revelation.

Conducting a MDD is not an easy process and the pressure from management to reject the product may be intense. However, if you apply sound scientific principles and use them to find the source of the problem, not only will you be able to salvage the batch and save money (we saved $1MM in retail sales), but you will also verify that the validated process is fine, the suppliers are fine and the personnel are fine. Although the answer may be right in front of you it may take heroic efforts to find it.

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3. http://www.fda.gov/Cber/gdlns/ichactive.pdf ICH OOS
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Call for Abstracts

2007 PMF Fall Forum
October 11-12, 2007

The PMF Fall Forum has gained a reputation as the premier conference for presentation and *discussion* of current issues in industrial microbiology.

The format of the meeting is intimate, with participation and attendance restricted to encourage discussion and interaction among the registrants. This is the best chance all year to present on a topic of interest to you, and to get feedback and benchmarking information from those in the industry most interested in the development of science-based regulations for pharmaceutical, medical device and personal products microbiology.

Submit abstracts at
http://www.highpeaks.us/2007/fall.forum/abstracts.htm

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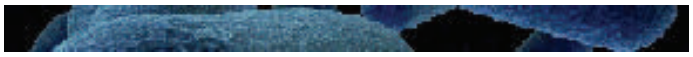

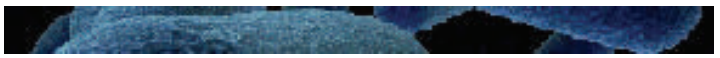

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across the different facilities of the corporation) or the site Environmental Master Plan (which provides consistency and detailed instruction for the various manufacturing buildings at a given site). However, the Contamination Control Plan should cite the relevant documents and their role in contamination control. Those interested in more on environmental monitoring should refer to the PDA's treatment of the subject for a good overview (PDA 2001).

The appropriate Environmental Monitoring (EM) plan for non-sterile manufactures and for API manufacturers is not well-defined from a regulatory sense. There are no strong recommendations such as those seen for the environmental monitoring of aseptic facilities; however the absence of regulatory guidance is not the same thing as the absence of need for the activity. EM is useful for determining the state of control of the facility (not so much, perhaps an indicator of the finished product quality) and so is an important part of the monitoring program for all manufacturers.

Well-defined and Understood Manufacturing Processes

The manufacturing process should be evaluated for its potential to limit or eliminate bioburden. The two common methods for performing this is either a HACCP-type (Jahnke and Kuhn 2003) or a FMEA approach. The use of organic solvents, heat, or other inhospitable activities can greatly reduce bioburden of a process. The contribution of compression (and associated shear), for example, should be evaluated for a potential reduction in risk of excessive microbial contamination (Blair 1991). The contribution of the finished product water activity should also contribute to this analysis (USP 2007).

Of particular importance in this evaluation for the potential for microbial contamination of the process are cleaning steps, equipment hold times, HVAC, control level of environments for critical tasks, open-system vs closed-system operations, and bioburden monitoring (among others specific to your process). As an example of the importance of the bioburden control point issue, there is a strong regulatory expectation in Europe that products sterilized by filtration should have a pre-filtration bioburden of not more than 10 CFU/100 mL immediately before the sterilizing filter.

Finally the Contamination Control Plan should cite the need clear SOPs on all aspects of manufacturing, monitoring and control. These SOPs are critical for training, documentation and batch release.

Minimization of Batch Residual Cross-over Contamination

The contamination control plan should also address the potential for a batch to be contaminated by material from the previous batch manufactured using that equipment. Obviously, the contamination control plan should describe the methods by which this likelihood is minimized.

The concern over batch residual cross-over is most relevant when there is more than one product manufactured at a site. This concern has little to do with the sterility of the finished product, and is relevant to sterile and non-sterile manufacture alike.

Minimization of Cleaning Material Residual Contamination

Validation of cleaning procedures is essential to demonstrate not only that the cleaning procedure effectively cleans and sanitizes the manufacturing equipment, but also that residual cleaning material is removed to prevent contamination of the next batch manufactured.

Conclusions

The Contamination Control Plan is an important document designed to formalize the rationale, methods and validation of contamination control procedures in a manufacturing facility. This plan is a valuable tool for pharmaceutical, medi-

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cal device and personal product manufactures and should be written to address all phases of the facilities life cycle. The Contamination Control Plan should specifically address:

- Minimizing the bioburden throughout the manufacturing processes
- Minimizing the level of batch residual cross-over contamination
- Minimizing the level of cleaning material residual contamination

The microbiologist, as SME, has a critical role to play in the first of these three primary goals, and this essay has therefore been directed at that first topic. Minimization of bioburden in the manufacturing process occurs through (but is not limited to):

- Minimizing bioburden in the process
- Control incoming bioburden
- Appropriate Gowning
- Controlled Environments
- Well-defined Standard Operating Procedures; and
- Well-defined and understood manufacturing processes.

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Upcoming Events

August

- 23rd - 24th **Training on Contamination Monitoring and Control**
  Location: Orlando, FL
  WebSite: http://www.microrite.com/

September

- 17th - 18th **PMF 2007 Cosmetic Microbiology Conference**
  Location: Newark, NJ
  WebSite: http://www.highpeaks.us/2007/cosmetic/
- 24th - 26th **PDA/FDA Joint Conference**
  Location: Washington, DC
  WebSite: www.pda.org
- 24th - 26th **USP Annual Scientific Meeting**
  Location: Tampa, FL
  WebSite: www.usp.org

October

- 11th - 12th **PMF 2007 Fall Forum**
  Location: Rochester, NY
  Contact: mary.ellen@highpeaks.us
- 29th - Nov. 2nd **PDA Conference on Pharmaceutical Microbiology**
  Location: Bethesda, MD
  Contact: www.pda.org

November

- 5th - 6th **2007 PMF Bacterial Endotoxin Summit**
  Location: Philadelphia, PA
  Contact: mary.ellen@highpeaks.us
- 14th **Biofilm in Pharmaceutical Manufacturing—The Fundamentals**
  Location: Campbell Univ., RTP Campus, RTP, NC
  Contact: Lucia Clontz +1 (919) 345-1522

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  http://www.highpeaks.us/in-house.htm
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  - GMP for the Microbiology Lab
  - Microbiology for Manufacturing
  - Microbiology for Management
  - Auditing the Microbiology Function
  - Investigating Microbiological Data Deviations
- USP
  Contact Steven Paul (stp@usp.org) for information on the course "Fundamentals of Microbiological Testing"

USP Corner

Any questions concerning USP documents should be sent to Radhakrishna (Radha) Tirumalai, Ph.D. You can reach Dr. Tirumalai at: (706) 353-4514, via mail at United States Pharmacopeia, 126 Twinbrook Parkway, Rockville, MD 20852 or via e-mail at RST@USP.org. You can write representing your company, or as an individual scientist.

Discussion List Update

PMFList:
Number of Subscribers: 2,402
Number of Countries: 64
Number of Messages Last Month: 290

PSDGList (Pharma Stability Discussion Group):
Number of Subscribers: 974
Number of Countries: 23

Membership is FREE. To **join the PMFList**, visit http://microbiol.org/pmflist.htm and register.

A sister Email is devoted to topics in the **stability testing** of pharmaceuticals, medical devices and personal products. To **join the PSDGList**, visit http://microbiol.org/psdglist.htm and register.

You can ask, answer, or read questions and comments from your colleagues. Archives of the lists are available at:

- http://lists.microbiol.org/archives/PMFLIST.html
- http://lists.microbiol.org/archives/PSDGLIST.html

The LAL User's Group is Back!

How do the principles described FDA's revised OOS Guidance apply to the Bacterial Endotoxin Test?
What do proposed revisions to the BET recently introduced in Pharmacopeial Forum mean to my laboratory?
How do I calculate endotoxin limits for non-compendial materials?
How do other users deal with "hot wells" in microtiter plates?

Good news for laboratories using the Bacterial Endotoxins Test! After a number of years away from the national scene, the LAL Users' Group has been reorganized under the PMF umbrella. We are grateful to the past members of the LAL User's Group organizing committee (Kevin Williams, Amy Karren, and Peter Lee) who have carried the organization for the past few years, and to Karen McCullough, one of the co-founders of the original Users' Group, who has agreed to lead the renewed organization.

"We are happy to be aligned with PMF. The new structure will provide us with greater visibility, more resources, and expanded opportunity for collaboration with those in other microbiology disciplines. Our goal is to provide as much useful information as we can to everyone who is responsible for performing or interpreting data from this test." said Karen.

The new organization will retain many of the attributes that made the LAL Users' Group unique and successful. The charter of the organization will still focus on dissemination of unbiased and useful scientific information to members. We still look to share problems, brainstorm solutions, help with interpretations of GMP and provide a User voice with regard to any new regulatory initiatives involving the LAL test.

As in the past, programming and publications will be directed by a Steering Committee, comprised of volunteers from industry. Manufacturers of lysate reagents, instruments and consumables will be invited to our meetings to share their latest technology, answer questions and provide updates. Guest speakers and FDA representatives will be invited to present on topics of interest to the Group.

Our first newsletter, with additional details about the Users' Group and information on our first meeting, will be published later this summer and distributed to all who are receiving this newsletter.

To subscribe to the newsletter, please contact Scott Sutton at scott.sutton@microbiol.org.