PMF NEWSLETTER

A PUBLICATION OF THE PHARMACEUTICAL MICROBIOLOGY FORUM
Distributed Internationally to 7,468 Subscribers in 83 Countries

Volume 13, Number 9 September, 2007

Water Sampling

The September newsletter contains an important essay on water sampling considerations from TC Soli, one of the leaders in water microbiology for the pharmaceutical industry. We are fortunate to have TC as a frequent contributer to the newsletter, and hope that everyone will find something of value in this thoughtful piece.

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

The PMFList sparked another train of thought for me this month. There was an ongoing discussion about method suitability studies, and whether 50% recovery or 70% recovery was a "better" criterion for these types of studies. As is normally the case, many opinions were expressed, some of them I thought were on target. This did get me to thinking about the question again, and I offer a version of these thoughts in this issue.

PMF exists to further the microbiologist in industry. To this end, PMF is presenting a series of conferences in 2008. A preliminary listing of these conferences is presented in this issue. Please let us know if there are other conferences we should be developing, or information that is not readily available that we might be able to provide.

The PMF is our organization - let's make sure it is focused on the topics of importance!

Scott Sutton scott.sutton@microbiol.org

THE IMPORTANCE OF WATER SAMPLING

T. C. Soli, Ph.D.
President, Soli Pharma Solutions

The routine maintenance and sanitization of a high purity water system to provide and distribute water of acceptable chemical and microbiological quality is undoubtedly the most important set of operations for a pharmaceutical water system. A close second is sampling. So, why is sampling so important? Anyone involved in testing those samples knows the answer. If the water sample is not reflective of the "true" water quality, "bad data" is the result. When decisions or further actions are based on "bad data", inappropriate or needless decisions, consequences, or actions are the result. Therefore, the message is simple: When collecting samples, collect them well.

Sampling can be done from sampling valves or usepoint valves. If sampling is done through usepoint valves used in manufacturing and you are part of an FDA-regulated industry, then you MUST sample the water exactly the same way that the water is used from that outlet – same hose, same outlet flushing procedure, same everything, nothing different. The rationale is simple: The water sample is usually intended to reflect the quality of water being used. Since the chemical and microbiological condition of the hose and the effectiveness of any flushing procedure have a great influence on most of the quality attributes, you have to mimic those flushing procedures and hose conditions to get a true picture of the quality of the water being used.

Sampling done from sampling valves is usually for a different purpose. These outlets are not manufacturing usepoints, and the samples collected from them are typically intended to reflect the quality of water inside the pipes. Therefore, anything that can be done to eliminate "external influences" that may degrade the water quality during its collection process is fully allowed. This includes using sterile hoses, inordinately long flushing procedures, extreme valve sanitization procedures, specially designed sampling valves, etc. After all, the purpose of this sampling is to get an accurate indication of the water quality inside the system at that location without the possible negative influences from the valve and hose (if used) or even the external environment as it leaves the system into your sampling container.

Sampling valves are also used for assessing the quality of water being delivered at a location within the water system where equipment is hard-piped to a usepoint valve in the system. Though a usepoint sample is needed, it may simply not be possible. In this case, a sampling valve can be used but it must be very near, preferably on or just downstream of the usepoint valve. However, such sampling valves should not be used when the outlet is not hard-piped or otherwise configured to preclude sampling from the outlet itself. Admittedly, such a sampling valve will not give a fully true picture of the water being used at a hard-piped usepoint, but it is better than collecting no sample at all or letting the next downstream valve sample

(Continued on page 6)

TC Soli - solipharmasol@earthlink.net
Soli Pharma Solutions - http://www.solipharmasol.com/

Microbial Recovery Studies – 50% or 70%?

Scott Sutton, Ph.D.
Vectech

Introduction

The PMFList is a source of great ideas for review and for further thought. One that keeps coming up on the list is the question of 70% recovery (as described in USP chapter <1227> Validation of Microbial Recovery from Pharmacopeial Articles) and 50% recovery as described in the harmonized chapter <61> Microbiological Examination Of Nonsterile Products: Microbial Enumeration Tests.

The questions and discussion seem to fall into two distinct groups – the first a discussion about when to apply 70% and when to apply 50% as your recovery criteria (with frequent complaints about the inferred lack of consistency in USP) and the second a discussion of what types of tests we are talking about. We will look at these issues separately.

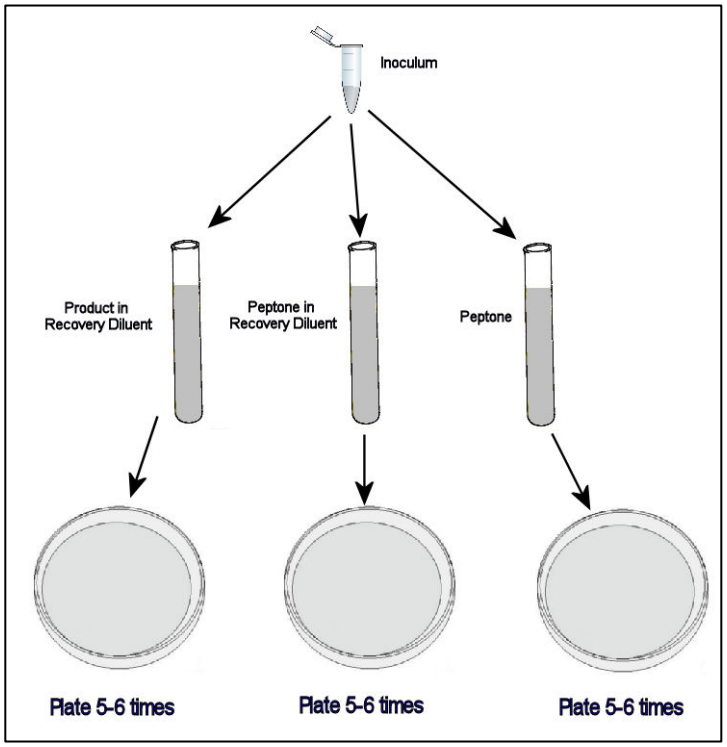
What are we talking about?

The first thing to do is to establish the scope of the discussion. For starters, let's begin by stating that the compendial chapters are, by definition, validated. This refers to those chapters in the USP that number under 1000. We therefore cannot really "validate" the test method, instead we are trying to demonstrate the suitability of the recovery method. This has been referred to as "verification" (Porter 2007) and in the harmonized Microbial Limits chapters as "method suitability."

The point of a method suitability study in microbiology is not to validate the assay, but rather to demonstrate that our specific test method is suitable; that the recovery scheme allows recovery of viable microorganisms. In other words, microorganisms are not prevented from growing in the experimental system by residual antimicrobial activity of the product

This demonstration is critical in accurate determination of disinfecting efficacy, bioburden, sterility or any test that requires determination of surviving microorganisms in a product containing antimicrobial properties. Failure to confirm adequate neutralization and recovery could result in underreporting of surviving microorganisms. This expectation of 70% recovery can also be applied to media growth promotion studies, where a new batch of media is compared to a previously qualified batch for its ability to support at least 70% of a standard inoculum.

A convenient method for this neutralization is through the use of recovery diluents designed to neutralize commonly used antimicrobials. A number of reagents are used in this regard (reviewed by Russell 1981; Furr & Rogers 1987). However, some of these compounds may be toxic to the test organisms (Reybrouck 1978) and so it is also important to determine the potential toxicity of the neutralizing medium (recovery diluent). These two activities, neutralizer efficacy and growth promotion (or neutralizer toxicity), are equally important in this consideration. A schematic of a design for this type of study is presented below, where a consistent inoculum is added to the product in the recovery diluent, peptone in the recovery diluent (use the same volume of peptone as that of the product), and into peptone. These are then plated 5-6 times to provide a good estimate of the number of organisms present (Wilson and Kullman 1931). The Neutralizer Efficacy is determined by comparing the recovery in the peptone suspension to that in the Product + Recovery Diluent suspension, Neutralizer Toxicity by comparing the Peptone suspension to the Peptone + Recovery Diluent (USP 2007).



Scott Sutton - scott.sutton@microbiol.org
Vectech - http://www.microbiol.org/consulting.htm

(Continued on page 5)

The PMF Fall Conference Schedule

http://www.microbiologyforum.org

2007 PMF Fall Forum

http://www.highpeaks.us/2007/fall.forum/index.htm
October 11-12, 2007
Rochester, NY

The purpose of this annual meeting is to provide the microbiology community presentations of recent work in the areas of validation and qualification of microbiological methods and analyses in support of manufacturing. Special emphasis this year will be on current research into questions of environmental monitoring.

This conference is your opportunity to interact with thought leaders in a small, personalized format while learning from the academic and industry leaders. The PMF Fall Forum has earned its reputation as the premier conference for in-depth presentation of microbiological research and discussion. This year will focus on environmental monitoring, with academic leaders presenting their research and industry science and regulatory experts their perspectives. The strength of the meeting is in analysis and discussion - bring your questions for this *intentionally intimate* meeting! However, as the meeting is kept small by design, places fill quickly.

- Overview of Environmental Monitoring for Aseptic Processing; Scott Sutton, Ph.D., *PMF*
- Group Discussion on Media Fill considerations
- Challenge Studies of the Blow-Fill-Seal Aseptic Packaging Process – The Effect of Heat Lethality on Product Contamination; Patrick Poisson *Cardinal Health, Inc*
- Microbiological Compliance and Risk in Aseptic Manufacturing; John Grazal, *AstraZeneca*
- A Risk-Based Approach for Investigating Environmental Monitoring Excursions; Robert Westney *Assoc. Dir, ImClone Systems, Inc*.
- Weak Rolling Adhesion Enhances Bacterial Surface Colonization; Albert Ding, Ph.D. *NIH Fellow.*
- Investigations into Sterility Failures; Frank Setterini
- Investigation of Cut-Off Sizes and Collection Efficiencies of Portable Microbial Samplers; Greg Mainelis, Ph.D. *Dept Environ Sci - Rutgers University*
- USP Perspectives; Radha Tirumalai, Ph.D. *USP*

2007 PMF Bacterial Endotoxin Summit

http://www.highpeaks.us/2007/BES/index.htm
November 8-9, 2007
New Brunswick, NJ

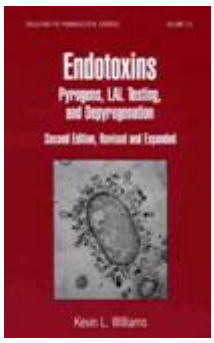
The FDA LAL Guideline is 20 years old! While the USP is clearly the most current and technically correct testing document, there are many GMP topics in the Guideline and beyond the Guideline that still need discussion.

Last year, the BES explored the basics of the LAL test. The focus of this year's meeting is to provide a forum for the sharing of questions, answers and information on GMP aspects of the Bacterial Endotoxin Test (BET).

This two-day interactive program includes case studies, problem solving and round table discussions. In addition, we'll have a mini exhibition, where vendors of BET testing reagents and equipment will all have their products on hand for viewing by participants.

Presentations

- The Big Moving Parts of Depyrogenation - Ron Berzofsky, Ph.D.
- How Much Testing is Enough? Determining Critical Control Points for Process Control - Karen McCullough
- Data Analysis: Setting Action and Alert Levels - Alan Baines
- Water System Failure - What's the Risk? - Mick Dawson, Ph.D.
- OOS and Investigation - Does the 2006 FDA OOS Guidance Apply to the BET? - John Dubczak
- BET Questions - CMC Submissions and 483 Concerns - Robert Mello, Ph.D. FDA
- What's New at Associates of Cape Cod? - Mick Dawson
- What's New at Charles River Endosafe? - John Dubczak
- What's New at Lonza? - Alan Baines



The book "Endotoxins: Pyrogens, LAL Testing, and Depyrogenation (Drugs and Pharmaceutical Science, Vol. 111)" by Kevin L. Williams (ed) Marcel Dekker Publ. (2001) will be provided to all registrants.


(Continued from page 3)

What is not part of this discussion?

It should be obvious from the previous discussion that the "method suitability" study is highly controlled. A standard inoculum is added to three tubes, and then replicate aliquots are removed and immediately plated. In a perfect world the numbers would be in agreement 100% of the time, but we work in microbiology. Even in such a simple design the opportunity for variability is enormous, and there are workers in the field who are vehement that no better than 50% should be expected between replicates of this type. One wonders if this is a limitation of the test system or of their laboratory training program. In any event, the discussion of 50% to 70% between the populations applies only to this design (and those closely related to it).

The recommendation in USP of 70% recovery was never meant to apply to studies of microbial recovery from solid surfaces. These studies are extremely complicated, and are confounded by issues of recovery efficacy of swabs, contact plates, and other methods (Buggy, *et al* 1983, Rose *et al* 2004, Whyte 1989). In addition, if vegetative cells are used for the study, there is the additional problem of die-off due to dessication (Potts 1994).

Recovery studies looking at bioburden of solid surfaces (facility, equipment, medical device or personnel) are not part of the 50% to 70% debate. They have their own set of issues and will be discussed in a later newsletter.

Is there any support for these numbers?

There are two studies which directly support the 70% recovery acceptance criterion.

Proud and Sutton (1992) describe the development of a "universal" diluting fluid for membrane filtration sterility testing using a modification of the design described above. The product was placed in a filtration apparatus containing 100 mL of the diluting fluid, and then passed through the membrane, followed by two additional 100 mL rinses. The membrane was then removed and placed on the surface of a nutrient agar plate for incubation and enumeration. Each treatment was performed at least three times. CFU were converted to their $\log_{10}$ values, and ANOVA analysis performed on the replicates. When all was said and done, a recovery of 75% of the inoculum count (raw CFU – untransformed) passed the ANOVA analysis.

Sutton, *et al*. (2002) conducted a large study on methods to recover microorganisms in the presence of surface disinfectants. "Neutralizer efficacy (NE) ratios were determined [in this study] by comparing the recovery of identical inocula from the neutralizing solution in the presence, or the absence, of a 1:10 dilution of the biocide. Neutralizer toxicity (NT) ratios were determined between recovery of viable microorganisms incubated for a short period in peptone, and in the neutralizing medium without the biocide. An effective and non-toxic neutralizer was initially identified by NE and NT ratios of ≥ 0.75.

(Continued on page 9)

(Continued from page 2)

represent it. In such situations, it is important to try to simulate usage of that hard-piped usepoint while collecting the sample through the sampling valve.

Valve design greatly influences the quality of a water sample. Ball valves are often used in water systems, especially in the pretreatment portions of the system. These valves have wet surfaces that encourage microbial biofilm growth that are isolated from the water flow until the valve is opened for sampling. As the water flows across these potentially biofilm colonized surfaces, the bacteria in the biofilm can be sloughed into the water stream. There may be no bacteria in the water system, but as the water flows through the valve, it picks up lots of bacteria in the valve. You might think that sufficient flushing would shear off all these valve-surface bacteria, but chances are it will not. The ball portion of the valve is colonized not only through the channel but also around the ball. O-ring seals on the ball are no match for a decent biofilm, and they slide effortlessly past them, so no matter how long you flush or how you "work the valve", bacteria will continue to be sheared off into what may have been otherwise sterile water as it exits the valve. Therefore, the chances of collecting a representative water sample from a ball valve are close to nil.

Needle valves are also usually big offenders, with a singular exception. Typically, needle valves have a large downstream surface within the valve that remains wet after the last sampling use, especially when oriented horizontally. That surface can grow biofilm like crazy. When a sample is collected, the water flows past this colonized surface as it exits the valve, picking up all manner of biofilm bacteria on the way out.

The exception I mentioned is the so-called sanitary sampling valve. It is intentionally mounted in a horizontal orientation so that its internal downstream surfaces can be bathed in a sanitizer such as alcohol or hydrogen peroxide after the valve is used in sampling to make those wetted surfaces hostile to microbial colonization. Furthermore, the upstream portion of the valve that is attached to the water system has the appearance of a very large hypodermic needle protruding into the middle of the fluid stream in the pipe. This design is intended to avoid sloughing off the pipe wall biofilm during sampling. Whether this

(Continued on page 7)

Would you like to sponsor the *PMF Newsletter*?

Opportunities to sponsor the operation of the *PMF Newsletter* are available.

Please contact the editor for details.

(Continued from page 6)

"hypodermic" design actually reduces microbial contamination of the sampled water or just creates additional surfaces for colonization is still questionable in my mind, but the hostility of the downstream surfaces of the valve DOES have a great advantage.

These days, it almost goes without saying that the sanitary valve of choice for a high purity water system is the diaphragm valve. The diaphragm valve works by having a flexible diaphragm inside the valve that is deformed as the control is turned, pushing the diaphragm against an opposing hard smooth surface to effectively pinch off the flow of water. Though it is not a perfect design for sealing or preventing biofilm development in the crevice created on the water-side of the pinch, it does allow, with proper downward orientation, for the surface downstream of the pinch to freely drain, and hopefully be allowed to completely dry so that biofilm does not develop on the downstream side of the valve between uses.

This free-draining valve orientation is essential to the success of diaphragm valves in minimizing the opportunities for biofilm development on the downstream surfaces and is conceptually related to the highly debated concept of using end caps on valves after use in order to prevent external valve contamination. There are legitimate reasons to cap some valves after use because of the gross chemical and microbial contamination possible in some environments where these valves could be located. However, most such valves are not located in grossly contaminated environments, so the level of potential contamination is minimal and the potential microbial contaminants are generally not the type found in water. So even if these contaminants are still present after valve flushing and able to find their way into a collected sample, their identities (and even colonial appearance) set them apart as aliens to the water system, allowing their contribution to the microbial count to be recognized as exogenous contaminants and potentially discountable as such. Nevertheless, the point of this discussion is that the use of end caps to prevent such exogenous contamination should be carefully considered because capping off the end of a usepoint valve while it is still wet could allow biofilm to develop in that portion of the valve away from any continuously sanitizing influences within the water system, except perhaps in a heated system where sanitizing temperatures may be conducted through stainless steel valve housings to the wet downstream parts of the valve. It should also be remembered that diaphragm valves have been known to develop leaks over time or when not completely closed, so capping off the valve might indeed contain such leaks, but would also fill the downstream valve compartment with water and promote biofilm development. In my opinion, it is better to have no end cap so you can detect a leak and fix it rather than to obscure its presence with an end cap and suffer the inevitable microbial consequences. In many situations, the protection of an

(Continued on page 8)

(Continued from page 7)

outlet from exogenous contamination can be gained with a simple open-weave Tyvek or paper "bonnet" around the outlet to allow air exchange and outlet drying, yet greatly reducing dust-borne external contamination.

The use of sanitary valves brings up an important point. Not all samples collected from a valve are for microbial testing. Other tests such as for endotoxin, TOC, conductivity, or even particulates could be performed on those samples in addition to microbial testing. Be absolutely certain that what you do to prepare the valve for microbial sample collection does not compromise ANY of the other test attributes that may also be assessed. For example, it is not wise to use alcohol in or on a sanitary valve if you plan to collect samples for TOC as well as microbial testing. If you have no choice, then the order of samples collected (e.g. TOC first, before valve sanitization, then microbial) is important. Also bear in mind that the chemical quality of the hose may also be important. A brand new flexible plastic or rubber hose may actually be chemically very dirty, not just from extraneous matter, but also from the plasticizers and other organics in and on the hose that contribute to its flexibility.

And now my final and perhaps most important point – flushing. Be vigorous, VERY vigorous. It is the RATE of flow across a surface that removes contaminants, including biofilm, not just the volume or duration of flow. So whenever you specify valve flushing as a mechanism to remove external contaminants or biofilm from hoses or valves prior to sampling, make certain the flow rate is somehow inferred. For instance, specifying that the valve be fully opened for X seconds or Y volume is far preferable to merely specifying flushing for X seconds or Y volume, which could be done with a trickle, accomplishing nothing. Also remember that if you then reduce the fully open flow to a rate suitable for sample collection, changes in the valve hydraulics may slough additional biofilm not removed in the fully opened flush. Therefore, you should continue to flush at that reduced flow rate for some period of time or volume (which you must also determine) before actually grabbing the sample. A frequently asked, but unanswerable question is how long or what volume should be flushed to give a "clean" sample. Every system is different with different pressures, valve sizes and designs, hose diameters and lengths, etc., so it is impossible to specify a universally acceptable flushing procedure. This is something that must be empirically determined by each user, knowing that different outlet configurations even within the same water system may require different flushing parameters. It may be possible to identify a worst case outlet configuration whose determined flushing procedure can be applied to all outlets.

Now, all of these precautions needed for good sample collection are all for naught if the procedures em-

(Continued on page 10)

(Continued from page 5)

Statistical evaluation of the data was performed by ANOVA, with Dunnett's test for multiple comparisons used to confirm failures. By this analysis, 239/244 identified failures were confirmed by ANOVA of 588 NT and NE comparisons (5 presumptive failures were not confirmed by statistical analysis). We therefore conclude that recovery of 75% is a suitable criterion (2% false negative rate) for neutralizer evaluations."

A side issue to this discussion is the occasional use of 70-130% recovery as the acceptance criteria. I have trouble with this one – would you really disqualify a method because it improves your recovery over expectations? In my opinion the acceptance criteria should be that the test treatment should recover at least 70%, with no consideration of recovery by the test in excess of the comparator treatment.

Which should you use?

I am of the opinion that 70% is easily attainable if the technicians are proficient and the recovery method works. This may require 5-6 replicates, rather than the usual duplicate plates per sample. However, this is a "verification" study or a "method suitability" study (or whatever we wish to call it) and so may be worth a bit more work.

So, how did they get different criteria in the USP? Chapter <1227> was developed to address a specific concern – that of providing information on microbial recovery studies (not limited to neutralizer efficacy) for use in the pharmaceutical industry. This work was well in progress by 1996 (USP 1996). The harmonization program discussed this point *much* later, and after negotiation the experts agreed to the 50% criterion so that agreement could occur. No data was presented to support the assertion that 50% was appropriate (by my records), it was, however, the number that could be accepted.

The harmonized USP chapter <61> (USP 2006) cites a 50% recovery frequency and so this is the official acceptance criteria *for this test*. If you wish to use 50% for the acceptance criteria for all method suitability studies (non-compendial bioburden tests, method suitability studies for disinfectancy tests, Antimicrobial Efficacy tests, media growth promotion, *etc*) I would strongly urge a solid rationale for failing to observe the recommendation of chapter <1227>. In addition, I would be prepared to answer questions of technician proficiency as the suspicion may be that your lab is not confident of reproducibility to 70% even between identical samples.

References

Buggy, B. *et al*. 1983. Comparison of Methods for Recovery of *Clostridium difficile* From an Environmental Surface. *J Clin Microbiol*. 18(2):348-352.

Furr, J .R. & DT Rogers. 1987. Preservation of Sterile Pharmaceutical Products. In Preservatives in the Food, Pharmaceutical and Environmental Industries pp. 211-230. Porter, DA. 2007. Qualification, Validation and Verification. *Pharm Technol* 31(4):146-154.

Potts, M. 1994. Dessication Tolerance of Prokaryotes. *Microbiol Rev*. 58(4):755-805.

Proud, DW and SVW Sutton. 1992. Development of a Universal Diluting Fluid for Membrane Filtration Sterility Testing. *Appl Environ Microbiol*. 58 (3):1035-38.

Reybouck, G. 1978. Bactericidal activity of 40 Potential Disinfectant Inactivators. *Zentralblatt fur Bakteriologie, Mikrobiologie und Hygiene Series B* 167**:**528-534.

Rose, L. *et al*. 2004. Swab Materials and Bacillus anthracis Spore Recovery from Nonporous Surfaces. *Emerg Infect Dis*. 10(6):1023-1029.

Russell, AD. 1981 Neutralization Procedures in the Evaluation of Bactericidal Activity. In Disinfectants: Their Use and Evaluation of Effectiveness. ed. Collins, C.H., Allwood, M.C., Bloomfield, S.F. & Fox, A. pp. 5-59.

Sutton, SVW, et al. 2002. Validation of Microbial Recovery From Disinfectants. *PDA J Pharm Sci Tech*. 56(5):255-266.

USP 2007. <1227> Validation of Microbial Recovery from Pharmacopeial Articles.

USP. 2006. <61> Microbial Examination of Nonsterile Products: Microbial Enumeration Tests. USP 29 Suppl 2. pp. 3757-3759.

USP. 1996. <1227> Validation of Microbial Recovery From Pharmacopeial Articles. *Pharm Forum*. 22 (6):3109-3115.

Whyte, W. 1989. Methods for Calculating the Efficiency of Bacterial Surface Sampling Techniques. *J Hosp Infect*. 13:33-41.

Wilson, PW and ED Kullman. 1931. A Statistical Inquiry Into Methods for Estimating Numbers of Rhizobia. *J Bacteriol*. 22:71-90.

(Continued from page 8)

ployed for water use from a given outlet and any related hose storage practices are atrocious. As mentioned earlier, FDA expects that water sampling MUST be conducted in exactly the same manner as water is used from that outlet – the very same hose used in manufacturing, the same outlet sanitization procedure (if any), and same outlet flushing procedure (if any), etc. To do otherwise, even knowing the microbial consequences, is a guaranteed 483 or worse. So the point here is that if it takes all these careful precautions I have discussed to avoid microbial contamination during sampling, it takes those same precautions to avoid contamination during use. If water use and hose storage procedures need to be improved to accommodate these precautions, then so be it – and before your next inspection!

So again, why is all this sampling stuff so important? You must get accurate test results to make accurate decisions. I dare say that in the pharmaceutical industry today, AT LEAST 50% (and probably closer to 90%) of all high or highly variable microbial test results are due to bad valve maintenance or inadequate or inconsistent flushing, none of which likely affect the quality of water within the water system. Don't let erroneously bad test results force you into bad decisions for needless system sanitization or cause you needless extra work with investigations and repeat sampling and testing. And if you find you need better valve maintenance or better hose storage or to just flush better to get good, consistent test results, then you definitely need those same changes for routine water use as well. Your water quality depends on it!

2008 PMF Calendar

February - Open Conference on Compendial Issues.
Baltimore, MD

March - Conference on Biotechnology
San Diego, CA

April - Validation Issues in Microbiology
Philadelphia, PA

May - GMP for the Microbiology Lab
Dallas/Ft. Worth, TX

June - Environmental Monitoring
Chicago, IL

September - Cosmetic Microbiology
Newark, NJ

October - 2008 PMF Fall Forum
Rochester, NY

November - Bacterial Endotoxin Summit
New Brunswick, NJ

The PMF Conferences are generally designed to provide an intimate atmosphere for discussion and comparison of ideas. This unique approach to conferences is appreciated both by the speakers and the participants as a degree of interaction is possible here that is available no where else.

Don't miss your opportunity in 2008 to come and share one of these unique experiences. If you have been to one of the PMF conferences in the past, you know how valuable this opportunity can be to developing your understanding of microbiology.

We look forward to seeing you in 2008!

Upcoming Events

2007 PMF Fall Forum
October 11-12, 2007
Rochester, NY

Implementation of Harmonized Compendial Tests
October 18-19, 2007
San Francisco, CA

2007 PMF Bacterial Endotoxin Summit
November 8-9, 2007
New Brunswick, NJ

Offering In-House Courses on Microbiology/Aseptic Processing:

- The Microbiology Network/High Peaks Associates
- http://www.highpeaks.us/in-house.htm
  Experienced in custom-designed courses for the lab or the manufacturing facility, including:
  - 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"

Don't miss the Fall Forum

October 11-12 in Rochester, NY

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: 2,588
Number of Countries: 64
Number of Messages Last Month: 292

PSDGList (Pharma Stability Discussion Group):
Number of Subscribers: 1023
Number of Countries: 26

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

JOBS

Science Careers: Mgr, QC Microbiology - Novartis Vaccines .
Title, Mgr, QC Microbiology. Location, Holly Springs, North Carolina. Job Description, Manager of the Sterility, Microbiology, PCR and Environmental
Manager of the Sterility, Microbiology, PCR and Environmental Monitoring Lab Areas (QC FCC / USA HS) Job Purpose Phase A (Start-up Phase/ Project Phase): Provide the technical knowledge and support for technology transfer from QC labs in Marburg, Germany to QC Holly Springs, USA. Novartis
http://aaas.sciencecareers.org/Mgr,+QC+Microbiology/46f207166d6650.html

Science Careers: Mgr, QC Microbiology - Novartis Vaccines
The Manager of Quality Control Microbiology is responsible for overseeing all aspects of Microbiology including Environmental Monitoring for products and the facility. The qualified individual will have a strong understanding of Manufacturing, Quality and GMP concepts and will ensure that the QC Microbiology functions are carried out accurately, efficiently and within budget to ensure successful and on- time release of product.
Vacaville, CA USA.
http://aaas.sciencecareers.org/texis/jobsearch/details.html?id=46f3593f6d6520&q=microbiology&pp=25&view=1&page=1

BAJobs.com: Bay Area jobs, San Francisco jobs, San Jose and more!
QC Microbiology Tech. Gilead Labs – San Dimas, CA USA
To support the operations of the Quality Control department by utilizing routine technologies and test methods. This person will support the daily operations of the laboratory by providing a focused level of support for the environmental monitoring function of the organization. This support will include scheduling and updating methods as specified, and other support to daily QC environmental monitoring operations.
http://www.bajobs.com/Details.aspx?ListingID=593ad7f6-773d-485a-b205-9ea37d15ca1b

DAVID LAWRENCE ASSOCIATES jobs, for QC Microbiology Manager ...
Job in Singapore, for QC Microbiology Manager. Headhunter Listing
http://jobs.monster.com.sg/details/4284068.html

Recent News

Right chemistry missing

The Australian - Sydney,Australia

A recent survey by the Pharmaceuticals Education Committee (PEC) found that the number one issue for pharmaceutical companies and biopharmaceutical is an educated workforce. Industry faces huge problems recruiting scientists, and it is a worldwide problem.

http://www.theaustralian.news.com.au/story/0,25197,22493613-5010800,00.html

FDA Act Brings Big Changes

Patent Baristas - Cincinnati,OH,USA

The act makes important changes to device user fees, originally established five years ago under the Medical Device User Fee and Modernization Act. President Bush has signed the FDA Amendments Act of 2007 into law. The Senate passed the bill, H.R. 3580, by unanimous consent on Sept. 20, a day after the House approved it in a 409-17 vote.

http://www.patentbaristas.com/archives/2007/09/28/fda-act-brings-big-changes/

More exemption to Indian pharma companies for R&D: Paswan

Economic Times - India

22 Sep, 2007, 1900 hrs IST, PTI MUMBAI: he government may give more exemptions to pharmaceutical companies to spur research and development, Union Chemicals and Fertiliser Minister Ram Vilas Paswan said on Saturday.

"Presently, the pharma industry enjoys 100 per cent margin for research and development, but I am prepared to give up to 150 per cent," Paswan told reporters here on the sidelines of the annual general meeting of the Organisation of Pharmaceutical Producers of India.

http://economictimes.indiatimes.com/News/Economy/More_exemption_to_pharma_companies_for_RD_Paswan/articleshow/2393530.cms

AstraZeneca to outsource manufacturing: not such a no-brainer

World Health Care Blog - Washington DC,DC,USA

by David Williams AstraZeneca has announced plans to outsource all pharmaceutical manufacturing over the next few years, according to The Times of London. David Smith, AstraZeneca's executive vice-president of operations, said that the company aimed to become a pure research, development and marketing organisation.

"Manufacturing for AstraZeneca is not a core activity," Mr Smith said. "AstraZeneca is about innovation and brand-building . . . There are lots of people and organisations that can manufacture better than we can."

http://www.worldhealthcareblog.org/2007/09/19/astrazeneca-to-outsource-manufacturing-not-such-a-no-brainer/