www.microbiologyforum.org

PMF NEWSLETTER

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Volume 12, Number 12 December, 2006

USP Revision Process

Every once in a while it is good to take a look at the regulatory revision process and its impact on the laboratory. This month we are fortunate to have an essay by David Porter on the USP revision process. This is of particular interest at the moment in the consideration of the harmonized microbial limits tests. Despite a three-year lead time, the industry was caught unaware of the changes. This is somewhat troubling as the quality of the USP chapters is directly based on industry input and review. Dr. Porter was, until recently, Director of General Chapters at USP and provides an insider's view of the working of the compendial revision process and the current harmonization efforts.

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 technique for single colony isolation is reviewed in the second article of this month's newsletter. This seems a very basic topic, but it is critical to proper identification of unknown microbial samples. As this step adds time and labor to the process of microbial identification, it is tempting to omit it from the process and identify microorganisms directly from the primary plate. This is a temptation that laboratories seem to be falling prey to with increased frequency. Unfortunately, it is a critical quality control step in the identification process and cannot be omitted. The editor describes proper streaking technique and the problems associated with failing to safeguard the identification process properly.

This issue also contains a listing of the articles that appeared over the course of the year. If you missed any past issues of the *PMF Newsletter* they can be downloaded from the archive at http://www.microbiologyforum.org/news.htm.

Finally, the 2007 Open Conference is rapidly approaching. Registration for this event is well underway, and attendance will be limited to ensure the opportunity for communication between the participants and the facilitators. Don't miss this opportunity provided by PMF to participate in standards setting, and industrial benchmarking of practices.

Scott Sutton, Ph.D. scott.sutton@microbiol.org

The Revision Process at the United States Pharmacopeia

David Porter, Ph.D.
Vectech Pharmaceutical Consultants, Inc.

Recently there have been a number of postponements to general chapters in the *United States Pharmacopeia*, and some substantial difficulties with others that have become official. The following pertaining to general chapter <467> may be found at the USP website, www.usp.org:

> "The Executive Committee of the Council of Experts has voted to delay the implementation date for the new requirements related to *USP* General Chapter <467> from January 1, 2007 to July 1, 2007. This decision affects two sections of the *USP–NF*: *General Notices* and the General Chapter. This decision, which is presented in the *4th IRA* in *Pharmacopeial Forum* 32(4), states: "The implementation date of the section on *Residual Solvents* in the *General Notices* and the change in the title of General Chapter <467> from *Organic Volatile Impurities* to *Residual Solvents* will be delayed from January 1, 2007 to July 1, 2007." Additionally, the section in <467> titled *Other Analytical Procedures*, originally slated to be deleted at the time when the title changes, will be kept in the chapter until the new implementation date. Users should also recall that references to "*Residual Solvents* <467>: meet the requirements" were retracted from *USP–NF* monographs according to the *Notice of Retraction* issued by USP on January 1, 2006. Specifications for *Organic Volatile Impurities* <467> in *USP–NF* monographs will remain official until July 1, 2007. After July 1, 2007, the change in the title of General Chapter <467> and the *General Notices* statement on Residual Solvents will be effective, and references to Organic Volatile Impurities will be deleted from monographs."

Another chapter that has run into difficulties is <231> *Heavy Metals*. A new version became official in *USP 29* that included three methods. It was Method II that was problematic. The following is also posted at the USP website:

> "In response to comments from industry, USP is reverting back to the *Heavy Metals* text that appeared in USP 28–NF 23 page 2300 for *Heavy Metals Method II*. The *USP 28–NF 23* test has been used in industry for some time. The search continues for a more robust and practical method. This change will appear in the *Third Interim Revision Announcement* to *USP 29–NF 24* which will be published in *Pharmacopeial Forum* 32(3) and will become official on June 1, 2006."

Posted at the USP website on November 14, 2006, is the following:

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"The implementation of the following harmonized microbiological quality *USP–NF* General Chapters has been postponed until May 1, 2009.

- <61> *Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests*
- <62> *Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms*

<1111> *Microbiological Examination of Nonsterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances For Pharmaceutical Use*

These *USP–NF* General Chapters were originally scheduled to be effective on August 1, 2007. These postponements are made in response to requests received from the user community to allow further time to implement the new methods, and to harmonize with the implementation schedules of the European and Japanese Pharmacopoeias.

The currently official *USP–NF* General Chapters <61> *Microbial Limit Tests* and <1111> *Microbiological Attributes of Nonsterile Pharmaceutical Products* will remain effective until May 1, 2009."

Based upon such substantive changes to implementation dates, or the appearance of portions of general chapters with methods apparently lacking high robustness, one might ask whether the revision process at USP is broken or in need of major repair.

Before considering this question, let's first review how the revision process is intended to function at USP . The public review and comment process is also delineated at the USP website, and is listed next, with my comments provided in "[ ]". Note that this process applies equally to monographs and general chapters.

1. Interested parties submit comments regarding compendial revisions ["Interested parties" indicates that anyone may contribute comments and/or suggestions that may lead to revision of currently official chapters, or result in the creation of new chapters.]
2. USP staff scientific liaison sends comments to appropriate USP Expert Committee for review/ approval. [Comments pertaining to microbiology chapters are sent to the Microbiology and Sterility Assurance Expert Committee. It is possible for more than one Expert Committee to be involved in chapter revision.]
3. The Expert Committee approves item for publication in *PF*. [*PF = Pharmacopeial Forum*]
4. USP scientific staff liaison and USP Executive Secretariat review item.
5. Item is published in *PF* for public review. [critical point]
6. Public comments received. [Comments arrive in various forms, including email, telephone calls, faxes, standard mail.]
7. Comments are provided to the Expert Committee by the scientific staff liaison, and committee, and in turn the committee responses to the comments are provided to the scientific staff liaison. [critical point]
8. The scientific staff liaison then compiles and analyzes received comments and committee responses.

If it is determined that further revision is necessary, then the process cycles back up to step 5. If not, the item is voted on for inclusion as an official article in the *USP* by the Expert Committee. Assuming the Expert Committee votes for approval, the article becomes official via publication in an *Interim Revision Announcement*, *USP–NF*, or *Supplement to USP–NF*.

With this review of the revision process at USP in mind, let's look for potential weak spots in the process. These spots are those in which the potential for publishing

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Internet Address	Description
http://www.accessexcellence.org/	A great place for biology science teachers/trainers. Contains current science news items, teachers exchange, hundreds of science labs and educational resources.
http://www.cellsalive.com/	Cells Alive! - Good general microbiology information, with images and videos.
If you have found an Internet site that contains information of relevance to professional microbiology in the industrial sector, please let us know.	

Streaking for Single Colonies
An Essential First Step in Microbial Identification

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

The computer programming guys have a useful acronym: GIGO (Garbage In, Garbage Out). This is useful in pretty much all aspects of life, and I am willing to defend that statement with pithy arguments at a later time. Right now, I want to take a brief look at how it applies to microbial identification.

From the outset, let's admit that the current state of microbial identification is a little confusing. We can ID by traditional biochemical tests (API Strips) or by elegant refinements of the traditional methods (for example, the Vitek 2 Compact). We can identify microorganisms by carbohydrate utilization (Biolog systems) or by the GC pattern of the cell's fatty acids (Sherlock System). If you want to go genotypic, then you currently have a choice between the Dupont RiboPrinter or Applied Biosystems MicroSeq systems. Your identification (genus and species) may well depend on which system you use as there is no objective standard, and each system is reliant on its proprietary database to assign an identification to the data.

Virtually all of these systems require a preliminary Gram stain to accurately identify the sample. The Gram stain requires a relatively fresh culture for best results (*PMF Newsletter*, Feb. 2006). This is the first reason to restreak for single colonies after isolation of a contaminant. However, each system also is dependent on the presentation of a monoclonal sample for accurate results. In fact, only one of these systems provides you with enough information to recognize if you have a contaminated (polyclonal) sample (no, I am not going to tell which one it is).

The basic fact is that acceptable microbiological practice (I am not even going to say "good lab practice" or "best lab practice" but "acceptable" or, if you prefer, "adequate") requires streaking for well-isolated, single colonies of good health for identification purposes. This is not difficult.

The best starting material is a relatively "clean-looking" colony on your primary plate. This colony should not show obvious signs of being multiple pin-prick colonies that merged into a single CFU. Using a sterile loop, sample from the center of the colony and begin a heavy streak onto a new plate of appropriate agar media. This is quadrant #1 (see accompanying figure). Streaking in quadrant #1 (and all subsequent streaking events) should be in the same direction, with the same part of the loop in contact with the agar. After the completion of the streaking in this quadrant, the loop should be resterilized (thoroughly flamed or discarded for a new, sterile disposable loop) and the plate streaked into quadrant #2 by drawing the fresh loop across two or three lines in quadrant #1. This should be done once or twice, then subsequent streaks performed without touching any of the previous line in the agar surface. The loop is resterilized, and the process is repeated in quadrants #3 and #4, each time the loop becoming contaminated by drawing it across a few lines in the previous quadrant. The idea is a successive dilu-

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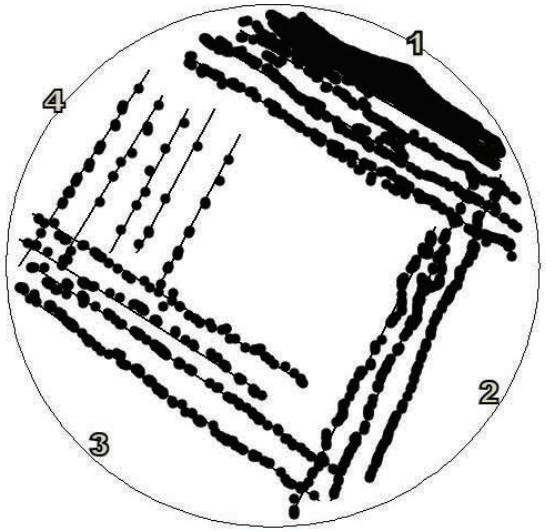
tion of the level of CFU in each quadrant, on each successive line after the initial inoculation in the prior quadrant. The plate is then incubated overnight for colony growth.

Single, well-isolated colonies should be evident in quadrant #4 or quadrant #3. Care should be taken not to accidentally contaminate the colony when harvesting.



One note of caution. This streaking for single colony isolates should be conducted a second time if the original plate was heavily contaminated, or if there are multiple colony morphologies evident on this initial streaked plate. The integrity of the microbial identification process requires a monoclonal colony (a colony that is from a single bacterial strain).

Remember – the *only* assurance you have of a correct identification is proper preparation of the monoclonal sample. To this concern, the final isolation plate should never be used as a storage device – the single well-isolated colony chosen should be re-streaked on a separate plate or agar-slant tube for storage.

This seems like a lot of work, and requires an additional day (at least) to the turn-around time for identification of a contaminant when compared to the time required if single-colony isolation is omitted from the process. However, if microbial identification is attempted directly from the colony on the primary test plate (environmental monitoring or bioburden plate) any resultant microbial identification must be suspect as there is no assurance that you are working with a pure culture. When auditing your microbiology lab (or your contract lab), check to see if an SOP is in place requiring this step, and also check the refrigerators and incubators to see if you can find evidence that this is, in fact, occurring. It is an unfortunately common practice to omit this essential step in microbial identification in an ill-advised attempt to save time and money. However, as there are few quality controls possible on the microbial identification process, you have to build the quality into the process to avoid the GIGO phenomenon.

We are in a period of high regulatory interest in environmental monitoring identifications (as part of aseptic production controls), and in the demonstration of absence of objectionable microorganisms in non-sterile finished drug products. This is not the time (if there ever was one) to save a few pennies by omitting a step necessary to the accurate and confident identification of a microbial colony.

Scott Sutton earned his Masters and Ph.D. in Microbiology from the Univ. Rochester (NY). With over 20 years of lab and leadership experience in the microbiology arena of the pharmaceutical and personal products industries, he now consults through Vectech Pharmaceutical Consultants, Inc. Clients have included start-ups, generics, established Fortune 500 companies, law firms and investment broker houses. Laboratory management, GMP, testing methodologies and microbiology-related project management of manufacturing processes are areas of special interest. He has worked with the USP Microbiology Committee of Experts since 1993, serving as vice-chair since 2000.

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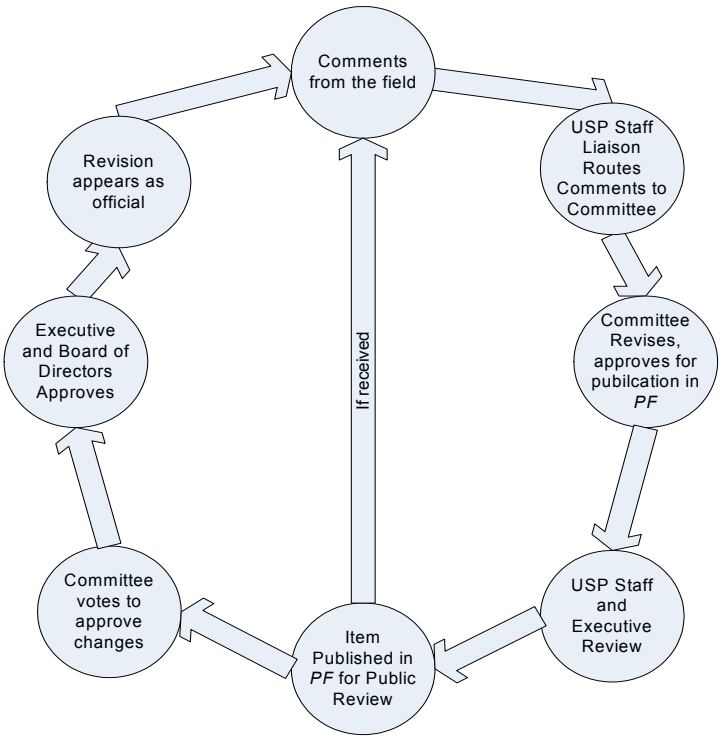
problematic general chapters as official increases.

The first step does not seem to be a likely candidate. The second step suggests a possibility that not all USP Expert Committees that should have at least some input into the revision process of a general chapter have indeed done so. For example, a general chapter with a portion pertaining to microbiological issues does not necessarily receive input from the Microbiology and Sterility Assurance expert committee.

The third step is potentially problematic. In this step, the expert committee approves an item for publication in *PF*, but in doing so it must make the assumption that it has sufficient information in hand to make the decision to publish. Where does this information come from?

The fourth step is also not likely to be problematic. It is at steps five through nine that, in my opinion, the greatest possibility of break down in the process occurs. In step four, the item is published *for public review*. As stated earlier, it is hoped that the expert committee has in hand much of the needed information prior to first publishing the item in *PF*. This is to minimize the number of times necessary to republish the item in *PF*. However, it is at steps five through nine that it becomes essential for there to be a thorough review of the item by potentially affected parties. An expectation of this process is that affected parties will read items that may impact them, evaluate the text and methods proposed to ensure that there aren't conditions/methods proposed in the items that would be impractical, unnecessarily burdensome or expensive, or which simply won't work. To a large degree, establishment of methods that are highly robust and rugged (important for a widely employed compendial method) requires input from potential users of the methods related to necessary conditions that must be present, or absent, for the method to work properly.



Consider *Method II* in chapter <231> *Heavy Metals*. The statement provided by the USP indicates that "…the search continues for a more robust and practical method." Implicit in this is the apparent lack of robustness in the method. The following statement from <1223> Validation of Alternative Microbiological Methods is indicative of the need for input from the reader of *PF*: "Robustness is a validation parameter best suited to determination by the supplier of the test method." The reason for this is that the supplier can use the method with many permutations of the method parameters, necessary to establish robustness. Extend this thinking to the importance of having readers of PF also try these proposed new methods using their test materials, personnel, equipment, etc. The more of such information that can be provided to USP and its Expert Committees, the greater the method robustness can be.

The delay in implementation dates for the new harmonized microbiology chapters is substantial, being almost two years. Among the reasons for this delay was apparent difficulties in obtaining commercially available media (for example, Rappaport Vassiliadis Salmonella Enrichment Broth) made with the compendial recipe. These chapters had been published in *PF* on several occasions, most recently as Stage 4 documents in the pharmacopeial harmonization process of the Pharmacopeial Discussion Group (PDG) in 2004. Given this length of time, why didn't the USP find out about this potential problem until the chapters were published in *USP 29 2S* and were planned to become official August 1, 2007?

Perhaps some of the answer to this question can

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come from a review of the PDG process . There are seven stages to the process, described below:

Stage 1: Identification. On the basis of an inquiry among its users, the PDG identifies subjects to be harmonized among PDG pharmacopeias and nominates a coordinating pharmacopeia for each subject.
Stage 2: Investigation. The coordinating pharmacopeia prepares a draft monograph or chapter, accompanied by a report giving the rationale for the proposal with validation data.
Stage 3: Proposal for Expert Committee Review. The three pharmacopeias forward the Stage 3 draft to their expert committee for comments.
Stage 4: Official Inquiry. The Stage 4 draft and the commentary are published in the revision document of each pharmacopeia in a section entitled International Harmonization.
Stage 5A: Consensus (Provisional). The Stage 5A draft is reviewed and commented on by the other two PDG pharmacopeias within 4 months of receipt. The three pharmacopeias shall do their utmost to reach full agreement at this stage to obtain a final **consensus document.**
Stage 5B: Consensus (Draft Sign-Off). When agreement is reached, the 5B draft is sent by the coordinating pharmacopeia to the other pharmacopeias no later than 4 weeks before a PDG meeting for final confirmation. The document is presented for sign-off at the PDG meeting.
Stage 6A: Regional Adoption. The document is submitted for adoption to the organization responsible for each pharmacopeia. Each pharmacopeia incorporates the harmonized draft according to its own procedures.
Stage 6B: Regional Implementation. The pharmacopeias will inform each other of the date of implementation in their particular region.
Stage 7: Inter-Regional Implementation. When a harmonized text has become official in all three pharmacopeias, EP and USP publish a statement indicating the harmonization status of the text; JP publishes a statement to the same effect at Stage 6B.

Of particular importance to this discussion is the fact that the proposed harmonized document is published in the pharmacopeial forums only at Stage 4. If agreement cannot be reached on a Stage 5 document, the item may be republished as a Stage 4 document. Once the Stage 5B document is signed off by the PDG, each individual pharmacopeia incorporates the harmonized draft according to its own procedures. This can result in differences in timing, additions of regional text, etc. What this means to the readers of *PF* is that they should pay attention to the Stage 4 documents, and evaluate the text and methods to ensure that they will not cause difficulties for their products.

At the end of the day, the answer to the questions above about where sufficient information comes from to assure the expert committee that it has all it needs, and why the USP didn't know about problems with various methods, comes down to communication. There were problems associated with the proposed changes to <467> that were not clearly understood prior to its planned appearance in *USP 29*. Method II in <231> *Heavy Metals* was not sufficiently robust, and this information was not known by USP prior to the chapter becoming official. The new harmonized microbiology chapters also apparently had underlying problems associated with them, again not known by USP prior to their appearance in *USP 29 2S*. It is essential that input be provided by the readers of PF in a timely manner related to proposed chapters and their revision. Without this timely information, the USP and its expert committees are faced with this question: Should we go ahead and publish the revision that was published in *PF* as an official article in the *USP*? If the USP and its Expert Committees are confronted with virtual silence in response to a *PF* proposal, the issue is whether there is silence because the readers are happy with the proposal, or because few if any potentially impacted people have read the proposal. In order for the revision process to not come to a screeching halt, the assumption must be the former.

Recent events suggest that the assumption made as to reader acceptance of proposed items has been in error, at least in some cases. Readers informing the USP of problems with proposed items after they have become official results in unnecessary complications for both the USP and its readers. In other words, the barn door is already open and the horses long gone. The USP revision process is open to the public, and in fact is highly dependent upon input from its readers to ensure that its methods are as good as they can be. As such, it is probably helpful for readers to think of the USP as **their** pharmacopeia, not just because it is mandated as such, but because they play a critical roll in its crea-

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tion and revision . If readers do so, then the answer to the question whether the revision process at USP is broken or in need of major repair is no.

David Porter, Ph.D. is a Pharma Consultant with an industrial/compendial background in microbiology, in vitro toxicology, and the application of statistics to experimental design, data analysis, and validation. While at the United States Pharmacopeia (USP), he served as a Scientist, Senior Scientist, Associate Director and Director, all within the area of general chapters. He also led the matrix team responsible for the development of a software package presenting an attractive graphical user interface with which to access the corporate revision-related database. His particular concentration while at USP pertained to general chapters pertaining to microbiology and biotechnology. His Ph.D. is in Zoology from the University of California at Berkeley .

He can be reached at dporter@vectech.com.

2007 Open Conference on Compendial Issues

February 19-21, 2007
Baltimore (Inner Harbor), MD, USA
Presented by the Pharmaceutical Microbiology Forum

This conference is your opportunity to interact with international regulators in frank and open discussion on issues of immediate relevance to the microbiology lab in a small, personalized format. It has been at least three years since this type of conference with this unique small, personalized format has been held.

The format and purpose of this meeting is somewhat unique. The compendia play a large role in the activities of the QC laboratory, and our input into their discussions is of enormous benefit to both their deliberations and the quality of the documents that result. The PMF is providing an opportunity for the membership to meet in small groups with representatives from international regulatory agencies to discuss issues relating to laboratory operations, GMP and the microbiological quality of finished products.
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Experts from international compendia and regulatory agencies will be in attendance to solicit your input on current issues. This is an unparalleled opportunity to benchmark your practices not only against current regulatory expectations, but also against other companies in the industry.

Details on this Interactive Conference

Upcoming Events

January 2007

- 21st - 23rd **RMUG Conference**
  Location: Arlington, VA, USA
  WebSite: RMUG Registration Forms

February

- 19th - 21st **PMF Open Conference on Compendial Issues**
  Location: Baltimore, MD, USA
  WebSite: www.highpeaks.us

March

- 5th - 6th **PMF Conference on Water Systems Microbiology**
  Location: Philadelphia, PA, USA
  WebSite: www.highpeaks.us

April

- April 1st - 4th **Annual Conference of the Association for General and Applied Microbiology (VAAM 2007)**
  Location: Osnabrück, Germany
  WebSite: www.conventus.de/vaam2007
- 16th - 17th **PMF Bacterial Endotoxin Summit**
  Location: Puerto Rico
  WebSite: www.highpeaks.us

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 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.

- USP
  Contact Steven Paul (stp@usp.org) for information on the course "Fundamentals of Microbiological Testing"

RMUG™ Meeting

The Rapid Micro Users Group ™ (**RMUG ™**) will host its 5th Annual Conference at the Hilton Crystal City in Arlington, VA January 21-23, 2007. "Crossing The Finish Line-Achieving Rapid Micro Approval" is this year's headline theme. The conference is a rewarding educational experience with new and comprehensive Technology Workshops, Exhibits and Seminars covering hot industry topics such as: Process Analytical Technology (PAT), Rapid Biological Indicators, Recovery of Organisms for Identification, New USP and EP Publications, Real-Time PCR and Real-Time Immuno-PCR. Every year RMUG ™ attracts about 120 attendees, including Laboratory Scientists, Microbiologists, QA and QC Managers, Biology and Scientific Regulatory Affairs Managers from both large and small corporations, as well as a strong FDA presence.

Your registration fees include a beautiful Monday night Gala dinner at the National Geographic Museum, Cocktail Reception, Two Day Conference, access to all Exhibits and Technology Workshops, Breakfast and Lunch during the conference and two or three night hotel accommodations.

If you would like more information or have any questions, please contact a RMUG ™ representative at (800)966-8832 or rmug@vectech.com.

Discussion List Update

PMFList:
Number of Subscribers: 1,861
Number of Countries: 63
Number of Messages Last Month: 224

PSDGList (Pharma Stability Discussion Group):
Number of Subscribers: 881
Number of Countries: 21

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

Q10 : Pharmaceutical Quality Systems

A new ICH Quality document has been proposed. The text of the proposal is below (from http://www.ich.org/cache/html/2726-616-1.html)

"It is proposed a new tripartite guideline be developed describing the modern quality systems needed to establish and maintain a state of control that can ensure the realization of a quality drug product and facilitate continual improvement over the life cycle of a drug product.

It is anticipated the guideline will augment existing GMPs with modern quality system elements for pharmaceutical manufacturing, providing the opportunity for robust processes, resulting in drug substances and drug products that consistently meet their intended attributes. There are several precedents of documents that define quality systems:

- ISO 9000: "Quality Management Systems"-- fundamentals and vocabulary
- ISO 9001: 2000: "Quality Management Systems"-- requirements
- ISO 9004: "Quality Management Systems" -- guidelines for performance improvements
- Eudralex Voleum 4: "Medicinal Product for Human and Veterinary Use: Good Manufacturing Practice"
- ICH Q7a: "Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients"
- US FDA: "Draft Guidance for Industry Concerning Quality Systems Approach to Pharmaceutical current Good Manufacturing Practice Regulations"
- ISO 13485: 2003 Medical devices -- Quality management systems; Requirements for regulatory purposes

Starting with the elements described in these documents, the proposed ICH Quality guideline would serve as a bridge between different regional regulations, thereby helping to achieve global harmonization of quality systems. It is also anticipated this proposed ICH guideline will focus on quality systems that facilitate implementation of ICH Q8 "Pharmaceutical Development" and ICH Q9 "Quality Risk Management," thus enabling the realization of the full benefits of the concepts contained within these two guidelines.

This guideline would apply to pharmaceutical drug substances and drug products throughout the product lifecycle, including process development, technology transfer and routine manufacturing."

The following was posted to the USP web site
(http://www.usp.org/USPNF/notices/postponementHarmonMicrobiology.html)

Revision Bulletin
NOTICE OF POSTPONEMENT
Harmonized Microbiology General Chapters
November 14, 2006

The implementation of the following harmonized microbiological quality USP–NF General Chapters has been postponed until May 1, 2009.

<61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests
<62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms
<1111> Microbiological Examination of Nonsterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances For Pharmaceutical Use

These USP–NF General Chapters were originally scheduled to be effective on August 1, 2007. These postponements are made in response to requests received from the user community to allow further time to implement the new methods, and to harmonize with the implementation schedules of the European and Japanese Pharmacopoeias.

The currently official USP–NF General Chapters <61> Microbial Limit Tests and <1111> Microbiological Attributes of Nonsterile Pharmaceutical Products will remain effective until May 1, 2009.

Questions should be directed to Dr. Radhakrishna Tirumalai, Senior Scientist (rst@usp.org).

2006 Article Listing

All past issues of the *PMF Newsletter* may be downloaded, free of charge or obligation, from http://www.microbiologyforum.org/news.htm

Volume 12, Number 1 - January

- Quality Control of Microbiological Media - Scott Sutton
- PAT and Real Time Release - Is This Proposal Workable? an essay by "Microbiologists for Common Sense and Reason" (MCSR)
- Book Review - Endotoxins by K.L. Williams

Volume 12, Number 2 - February

- Purified Water and WFI Alert and Action "Limits" - TC Soli
- The Gram Stain - Scott Sutton
- Mike Korczynski, a Gentleman, a Scholar, and a Friend - Roger Dabbah

Volume 12, Number 3 - March

- The Harmonization of the Microbial Limits Tests; Enumeration - Scott Sutton
- 483 Alerts - Richard Almond
- The Bacterial Endotoxin Summit
- Microrite's BactiSpell 2006 - Ziva Abraham
- 2005 Bibliography of Useful Articles

Volume 12, Number 4 - April

- The Harmonization of the Microbial Limits Tests; Absence of Specified Microorganisms - Scott Sutton
- The Importance of Data Analysis in DNA Fingerprinting - Jeff Little
- RMUG - Rapid Microbiology User's Group - Call for Subscribers
- Book Review - Quality Control Systems for the Microbiology Laboratory: The Key to Successful Inspections by Lucia Clontz (DHI Publications) 2001

Volume 12, Number 5 - May

- Follow-up to April's RiboPrinter Article - Little, Sherriff & Sutton
- DNA Fingerprinting: Basic Principles of Data Analysis - Grace Thornhill
- Biological Indicators and Third Party Verification - Russ Nyberg
- 483s from 2005 - Richard Almond
- Book Review: Pharmaceutical Filtration by T. Meltzer and M. Jornitz

Volume 12, Number 6 - June

- Review of The Parenteral Society and The Scottish Society for Contamination Control's Risk Management of Contamination (RMC) During Manufacturing Operations in Clean rooms (Technical Monograph No. 14) - Eric Strauss
- Microbial Limits Tests The Difference Between "Absence of Objectionable Microorganisms" and "Absence of Specified Microorganisms" - Scott Sutton
- Who is in Charge of the Micro Lab? - MCSR

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2006 Article Listing (cont)

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Volume 12, Number 6 - June (cont)

- Supplement 2 to USP 2006 Released
  - Harmonized Microbial Limits Chapters<61>, <62> and <1111>
  - <1072> Disinfectants and Antiseptics
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