

Articles of Interest to the Microbiologist

A Review of Microbiology-Related Research Published in Volume 60 (2006) of the *PDA Journal of Pharmaceutical Science and Technology*

Scott Sutton, PhD, Vectech Pharmaceutical Consultants

In keeping with this issue's theme of microbiology, I thought it might be interesting to go back over the past year of PDA Journals and review articles of specific interest to the field of microbiology that were published in volume 60 (2006). The scope of this review is limited to those articles on topics of immediate interest to the microbiology lab. For example, Part 11 issues are important, but not of immediate relevance, so not included. Issues of contamination in aseptic processing, on the other hand, although not specifically lab-related, are of microbiological concern and so appear below.

With that caveat, let me remind us all that the PDA Journal is a useful resource to the pharmaceutical QC microbiologist. In 2006 (volume 60) there were 12 articles and one technical report of direct relevance. These articles range from regulatory opinion, scientific review through to original research, and each are included in this review.

The summation below is arranged by issue number. Each individual citation includes the article title, author(s) and page number, followed by an uncritical description of the contents of each article (drawn heavily from the abstracts of each article). While specific passages from the abstracts are not enclosed with quotation marks, the author of this summation acknowledges the original authors and the fact that most of what appears below is, in fact, a reuse of their words.

Issue 1

Disinfection Using Ultraviolet Radiation as an Antimicrobial Agent: A Review and Synthesis of Mechanisms and Concerns. Piluso, LG *et al.* 1-16.

Piluso *et al* review the use of ultraviolet-based disinfection practices, the biological basis for them and some potential desensitization issues that may develop as well as suggesting some approaches to study and practically address these effects in this thorough review.

Issue 2

Viability-Based Rapid Microbiological Methods for Sterility Testing and the Need for Identification of Contamination. Moldenhauer, J. 81-88.

Dr. Moldenhauer reviews the science and regulatory issues surrounding the use of rapid microbiological methods (RMM) in sterility testing. She comprehensively reviewed currently available technologies against expectations. Particular weight was given to the need to have a preestablished strategy for evaluation of Sterility Test positives, as many of the rapid methods are destructive in nature. The current test, of course, allows identification of the contaminant as one of the first steps in this investigation. Dr. Moldenhauer also discussed the advantages and disadvantages of choosing a viability-based method of a non-growth-based method for this application.

Microbial Identification Strategies in the Pharmaceutical Industry.

Cundell, AM. 111-123.

Dr. Cundell discusses the overall strategies that may be successfully applied to microbial identification in support of microbial monitoring of utilities, pharmaceutical ingredients, the manufacturing environment and finished products. Emphasis is given to the justification of the microbial identification program, selection of identification methods and use of

speciation in successful product failure investigations.

The Expanded Application of Most Probable Number to the Quantitative Evaluation of Extremely Low Microbial Count. Sun, X *et al.* 124-134.

This paper is about the evaluation of the extremely low microbial counts from lab benches and cleanrooms by expanding the most probable number (MPN) methodology when the data follow Poisson distribution in order to achieve more accurate estimation with limited number of data. The MPN methodology was found to have a potential application for quality control in the extremely low level microbial counting environment in the cleanrooms levels ISO class 7 or above, and that further studies on the precision of this method and development of a sampling plan based on careful mathematical analysis will help to refine the approach.

Issue 3

Risk Assessment Paradigm: An Opportunity for Rationalizing the Choice of Biological Indicator During the Validation of Isolator Biodecontamination Cycles. Sansoe-Bourget, E. 156-163.

In this article the manufacture and control of biological indicators are analyzed using the hazard analysis and critical control point (HACCP) approach. The HACCP risk analysis, which must take into account the application of the isolator being qualified or requalified, is an efficient simplification tool for performing a decontamination cycle using either hydrogen peroxide gas or peracetic acid in a reliable, economical, and reproducible way. ►

Bacterial Adhesion to Surfaces: The Influence of Surface Roughness.

Riedewald, F. 164-171.

Riedewald reviews literature on bacterial adhesion to surfaces with an eye to reduction of biofilm in pipes and other smooth surfaces. This article discusses the current practice of using highly polished stainless steel surfaces, which is thought to minimize initial bacterial attachment and at the same time to maximize cleanability. It is suggested that this industrial practice is a misconception in that it provides no real benefit, and that far rougher surfaces could be used without increasing the rate of bacterial attachment or compromising cleanability.

Issue 4

Impact of Tubing Material on the Failure of Product-Specific Bubble Points of Sterilizing-Grade Filters.

Meyer, BK and D. Vargas. 248-253.

Meyer and Vargas investigated the effect of different preservatives commonly used in the biopharmaceutical industry on the product-specific bubble point of sterilizing-grade filters when used to filter product processed with different types of tubing. The preservatives tested were 0.25% phenol, m-cresol, and benzyl alcohol. The tubing tested was Sani-Pure® (platinum-cured silicone tubing), Versilic™ (peroxide-cured silicone tubing), C-Flex®, Pharmed®, and Cole-Parmer® (BioPharm silicone tubing). The results of their studies indicated that product-specific bubble point of a filter determined with only product may not reflect the true bubble point for preservative-containing products that are recirculated or contacted with certain tubing for 15 hours or greater. In addition, tubing material placed in contact with products containing preservatives should be evaluated for impact to the product-specific bubble point when being utilized with sterilizing-grade filters.

Current Practice in the Operation and Validation of Aseptic Blow-Fill-Seal Processes. Ljungqvist, B, *et al.* 254-258.

The authors summarize a worldwide survey performed by the BFS International Operators Association to illustrate current practice in aseptic blow-fill-seal (BFS) technology. The results are summarized and compared to the media fill data from the Product Quality and Research Institute (PQRI) survey reported in 2003. The survey highlights the differences and shows the robustness of the BFS technology. Compared to the results from the PQRI survey, the BFS survey shows a tenfold lower frequency of contaminated media fills.

Issue 5

Quantitative Risk Modeling In Aseptic Manufacture. Tidswell, EC and B McGarvey. 267-283.

Quantitative risk modeling augmented with Monte Carlo simulations represents a novel, innovative and more efficient means of risk assessment. This technique relies upon fewer assumptions and removes subjectivity to more swiftly generate an improved, more realistic, quantitative estimate of risk. The fundamental steps and requirements for an assessment of the risk of bioburden ingress into aseptically manufactured products are described. A case study exemplifies how quantitative risk modeling and Monte Carlo simulations achieve a more rapid and improved determination of the risk of bioburden ingress during the aseptic filling of a parenteral product in a technique that has promise in cleanroom management as well as the use of real-time data from RMM.

Challenges to a Blow/Fill/Seal Process with Airborne Microorganisms having Different Resistances to Dry Heat. Poisson, P, *et al.* 323-330.

Controlled challenges with air dispersed microorganisms having

widely different resistances to dry heat, carried out on 624 BFS machine processing growth medium, have shown that higher the heat resistance, the greater the extent of vial contamination. Differences in heat resistance affected also the extent of vial contamination when parison and vial formation were knowingly manipulated through changes made to each of three process variables, provision of ballooning air, mould vacuum delay and parison extrusion rate. The findings demonstrate that, in this investigational system, exposure of challenge microorganisms to heat inherent in the process has a controlling influence on vial contamination, an influence that could also control microbiological risk in production environments.

Issue 6

Active Air vs. Passive Air (Settle Plate) Monitoring in Routine Environmental Monitoring Programs. Andon, BM. 350-355.

Andon discusses the utility of active air versus passive air settle plate monitoring in a routine environmental monitoring program with an emphasis on the monitoring of the critical Grade A environments. While historical precedent and regulatory emphasis has encouraged the use of settle plates in the pharmaceutical industry, Andon argues that current active air sampling technology can be more advantageous and effective in assessing airborne viable contamination in cleanrooms than settle plate monitoring. Given that both methods are designed to assess viable airborne contamination, there may be no advantage in performing these two parallel methods, especially if doing so increases the number of interventions into critical areas, which may in turn increase the risk of contamination without providing any added benefit in terms of data collection and/or process control. Therefore, the best use of settle plate ►

monitoring may be as an optional test method for those applications where other, more efficient sampling methods may not be possible or may have limited applicability.

Microbiological Evaluation of Reused Catheter Guides in a Brazilian Hospital.

De Silva, MV *et al.* 356-365.

De Silva *et al* evaluated the controversial, but increasing, practice of reusing single-use medical devices. They analyzed 30 catheter guide units that were reused four times in patients at a public hospital. The catheter guides were sterilized after each use with a mixture of ethylene oxide/chlorofluorocarbons (12:88). Each unit cut into segments and the segments

analyzed for microbial counts (pour plate), direct inoculation sterility test, bacterial endotoxin, in vitro cytotoxicity, physical evaluation by scanning electron microscopy and/or microbial identification *via* biochemical assays. The results confirmed the presence of bacteria considered pathogenic to immunologically compromised patients with a maximum limit of 10^4 cfu/unit (catheter guide). Furthermore, bacterial endotoxins and significant modifications of the catheter guides' physical structure were also detected. Thus, the common practice of reusing single-use devices may increase patients' risk of infection or pyrogenic reactions, adding to the total period of hospitalization.

Supplement S-2

PDA Technical Report # 28 (Revised) Process Simulation Testing for Sterile Bulk Pharmaceutical Chemicals. PDA.

This revision to a popular PDA technical report outlines process simulation practices for sterile bulk pharmaceutical chemicals (sterile BPCs), utilizing concepts drawn from both bulk pharmaceutical chemical operations and sterile product manufacturing and adapted to fit the unique nature of these materials. It presents options for determining the adequacy of aseptic operations performed during large scale manufacturing while allowing for the committee's opinion of realistic acceptance criteria for such operations. 🍷

Pharmaceutical Filtration Book is a Must-Read

Jeanne Moldenhauer, Vectech Pharmaceutical Consultants

Recently, I finished reading *Pharmaceutical Filtration: the Management of Organism Removal* by **Ted Meltzer**, PhD, Capitola Consulting Company, and **Maik Jornitz**, Group VP, Global Product Management, Sartorius Group. When selecting the book, I made the assumption that this was another in-depth handbook on filtration, which would sit on the shelf until I needed to find resources to back up my beliefs in a report to support a client investigation. Boy was I wrong!

Most of the books previously written address the practical aspects of filtration, the "how and when to" perform different activities. This book, by contrast, explains the "why" to do

things and how changes in other areas affect the filtration process. In addition to the excellent resource on filtration, this book provides a wealth of information on other important topics.

Have you ever wondered how a biofilm forms? Perhaps you wanted to know how to prevent a biofilm in your facility. Others may want to know whether it is even possible to prevent biofilm. The chapter on biofilms presented a great deal of useful information in an organized way.

A great deal of engineering-type topics are also covered, like stainless steel and rouging, passivation and electropolishing, cartridge handling and so forth.

Some of the other topics included in the book are: Particles/Organisms, The Fluid Vehicle, The Operational Conditions, The Polymer Matrix, The Challenge Density, Organism Size Alterations, Grow-Through and Penetration, The Air Vent Filter, Multifilter Arrangements, Cartridge Type Constructions, Polymeric Constructions, Mechanism of Particle Retention, Mathematical Modeling of Filter Blockage, Adsorption Bonding, Electrical Double Layer, Hydrophobic Adsorptions and a great deal of Literature References.

Be sure to add this to your book must-have list! 🍷

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