Encyclopedia of Rapid Microbiological Methods:  
*The Next Generation of Rapid Microbial Detection*

By: Michael J. Miller, Ph.D.

One of the greatest contributions to the field of microbiology came from the kitchen. In 1881, scientist Walter Hesse was searching for a solid medium that could be used to cultivate bacteria. Unlike gelatin, the growth medium of choice at that time, the material had to be stable at high temperatures, allow a variety of microorganisms to be separated easily, and resist digestion or liquefaction by certain microbial species. Fanny Angelina, Hesse’s wife and laboratory assistant, had the answer: Agar Agar, a gelling agent that she used in her jellies and puddings. This simple kitchen ingredient revolutionized the science of microbiology, allowing the separation and culturing of microbes to become a routine procedure. Now, almost 125 years later, microbiology agar is the most important and widely used microbial growth medium available today. Fanny would be proud... but should we be proud as well?

Although the growth of microbial cells on agar surfaces provides the laboratory with critical information about the amount and the type of organisms that may be present in a sample under evaluation, the time to result is usually longer than what is desired. Days and even weeks may elapse before microbial colonies are visually detected, and in most cases, confluent growth prevents individual organisms from being isolated, necessitating sub-culture onto additional agar media, delaying the time to result even further. Additionally, many laboratories are discovering that microorganisms, when stressed due to nutrient deprivation, or following exposure to sub-lethal concentrations of antimicrobial agents, such as preservatives, disinfectants, heat or decontaminating gases, may not replicate when cultured on artificial media, because the environment is not truly optimal for the resuscitation and subsequent proliferation of organisms that may be present. For these and many other technical and business reasons, the modern microbiological laboratory should look toward developing innovative approaches to the detection, quantification and identification of microorganisms. Fortunately, technology is now available, or close to being available, that will speed up microbiological analysis, and provide results in real-time, allowing pharmaceutical manufacturing to embrace the concepts of Process Analytical Technology (PAT) and the use of rapid microbiological methods (RMM).

The Encyclopedia of Rapid Microbiological Methods is a culmination of many years of research, development and implementation of new technologies by a number of industry sectors, including pharmaceuticals, medical device, cosmetic and personal care, health and clinical, food and beverage, and municipal water, as well as government agencies and their subsidiaries, including bio-defense laboratories, first responders and homeland security. Furthermore, support for novel ways in which to conduct microbiological
assays is becoming the norm for both regulatory agencies and pharmacopoeias, as demonstrated in recent initiatives and guidance documents provided by the FDA, EMEA, USP and Ph. Eur. The encyclopedia attempts to pull together the opinions of these organizations, suppliers of new microbiology platforms, and the laboratories and end-users of the technologies that will be discussed within its pages.

Volume 1 provides an overview of microbiological methods and opportunities for industry, regulatory and pharmacopoeial perspectives, and validation strategies. Topics include the history of microbiological methods, risk-based approaches to pharmaceutical microbiology, the realities and misconceptions of implementing rapid methods in the manufacturing environment, the use of rapid methods in bio-defense and the food industry, PAT, comparability protocols, 21 CFR Part 11 and practical guidance on RMM validation and implementation.

Volumes 2 and 3 explore specific rapid microbiological methods, technologies and associated instrumentation, from both a supplier and an end-user viewpoint. Volume 2 concentrates on growth-based and viability-based rapid microbiological technologies, including flow and solid phase cytometry, ATP bioluminescence, impedance microbiology, and a variety of microbial identification platforms relying on physiological responses.

Volume 3 concentrates on artifact-based and nucleic acid-based technologies, the detection of Mycoplasma, and the use of microarrays, biochips and biosensors. Some of the platforms that are discussed include fatty acid analysis, MALDI and SELDI-TOF mass spectrometry, portable endotoxin testing, 16S rRNA typing, DNA sequencing, PCR, advances in Micro-Electro-Mechanical Systems (MEMS) including Lab-On-A-Chip systems, and a novel instantaneous and real-time optical detection technique for airborne microorganisms.

These are very exciting times for the rapid detection, quantification and characterization of microorganisms. The information presented in the Encyclopedia of Rapid Microbiological Methods provides the reader with a comprehensive collection of technology reviews and validation strategies that will encourage today’s microbiologists to move away from centuries-old techniques and to embrace the next generation of novel, more-sensitive and rapid microbial detection platforms. I am optimistic that the material presented will provide a framework for all industry, clinical and government sectors required to evaluate the environment, products, processes and test samples for the presence of microorganisms to embrace the rapid methods that are available today, and what will be forthcoming in the years ahead. And yes, I am certain that Angelina would be proud!

Michael J. Miller, Ph.D. Biography

Dr. Michael J. Miller holds the position of Senior Research Fellow in the Manufacturing Science and Technology (MS&T) function of Eli Lilly and Company. In this role, he is responsible for providing technical leadership in microbiology and sterility assurance
within Manufacturing, Quality, Engineering, and Product Development. He is also accountable for leading Lilly’s corporate initiatives for Process Analytical Technology (PAT), barrier isolation technology and rapid microbiological methods. Prior to joining Eli Lilly, he held numerous business development, Quality and R&D leadership roles at Bausch & Lomb and Johnson & Johnson.

Dr. Miller has authored over 60 technical publications and presentations in the areas of rapid microbiological methods, PAT, ophthalmics, disinfection and sterilization, and has served as Chairperson for numerous rapid microbiological methods technical conferences in the United States and Europe. He was the Program Chairperson for the 2001 PDA Spring Meeting on Modern Pharmaceutical Microbiology, the Program Chairperson for the 2005 PDA Annual Meeting, and is currently serving on PDA’s strategic planning, program, and publication committees and advisory boards. He also serves as the Chairperson for USP Technical Committee 18, Working Group 6, which is responsible for developing a general chapter on rapid microbiological methods. While working at Bausch & Lomb, Dr. Miller was appointed as a United States delegate to ISO Technical Committee 172, Optics and Ophthalmics, and as a member of the American National Standards Institute (ANSI) Z80 committee. Dr. Miller holds a Ph.D. in Microbiology and Biochemistry from Georgia State University (GSU), a B.A. in Anthropology and Sociology from Hobart College, and has served as an adjunct professor at GSU and the University of Waterloo, School of Optometry.