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â??Implementation of Rapid Microbiological Methods will play a vital role in contributing to the Global Health for drugsâ?•

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The inaugural BioLuminescence 2025 event by Merck took place in Ahmedabad on February 20, serving as a pivotal platform to enhance engagement with regulatory bodies, key opinion leaders, and stakeholders in the pharmaceutical industry. An internationally recognised microbiologist and subject matter expert in pharmaceutical microbiology, contamination control, Dr Michael Miller, President - Microbiology Consultants, LLC spoke about the Future of Pharma QC and how Rapid Microbiological Method (RMM) play a key role there.



What are some of the developments you have seen in quality control (QC) Microbiology from the past 10 years, some trends that stood out for you in this space?

There are a number of startups that have been pushing the envelope in microbial detection, quantification and identification and newer technologies that are miniaturised, such as lab-on-a-chip platforms, and real-time detection of microorganisms. I expect to see this trend continue in the foreseeable future.

What are the latest RMM technologies being developed to support pharmaceutical companies?

The science of biofluorescent particle counters (BFPC) has been around for a number of years. However, sterile pharma manufacturers are now validating these for routine use. They produce an autofluorescent unit (AFU) in real-time, allowing manufacturers to immediately react to excursions or out-of-trend findings for viable microorganisms, rather than retrospectively addressing these issues once incubation on standard plates have completed, which could be as long as a week since the batch was manufactured. And many of these systems are designed to capture the sampled air flow onto conventional media in the hopes of growing these for subsequent studies, such as microbial identification, which may help with investigations associated with the original contamination event. I also manage a catalogue of existing and next generation RMMs that is constantly changing as new technologies are introduced.

What are the key advantages and challenges associated with adopting RMM in the future of pharmaceutical QC?

The key advantage of using rapid methods, especially for newer cell and gene therapies, or advanced therapy medicinal products (ATMPs), is that these medicines can be tested and released much faster than conventional methods. This is important for short-shelf life products and those medicines that have an immediate medical need. And many RMM’s are more sensitive, accurate and precise than conventional methods, making them a better choice for microbiology testing, in terms of assessing product quality, which is directly linked with patient safety.

The perceived challenges with implementing RMMs have been associated with regulatory understanding and approval, which has been debunked for many years (i.e., regulators around the world have already approved multiple types of RMMs), and the supposed difficulty in validating these new methods for their intended use. The latter has been addressed by many regulatory

guidance documents and compendial chapters over the years, and will be specifically addressed with the 2025 revision to PDA Technical Report #33 (Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods), of which I am a co-chair.

How can the microbiological industry contribute to the development of collaborative strategies to address regulatory challenges in QC?

With respect to RMMs, the industry should continue to be educated to realise its benefits of implementation for a wide variety of applications, including finished product release for sterile and nonsterile medicines, in-process testing and environmental monitoring, to name a few. These are not necessarily regulatory challenges, as I have mentioned above, but more aligned with continuous improvement and better understanding of one's processes and products. The more the companies embrace and implement RMMs, the easier it will be for the industry as a whole moving forward.

What regulatory considerations should pharmaceutical companies be aware of when selecting an RMM system for their applications?

The selection of RMMs should be based on a firm's user requirements for microbiology testing, which may include the type of test, an intended time-to-detection, sample size and sample composition, data management and validation considerations. There are specific regulatory expectations for RMM validation, and these have already been published in a variety of guidance documents. The global pharmacopeias have also revised or added new chapters providing guidance on RMM and alternative method validation. And the upcoming revision to PDA TR#33 will specifically address regulatory expectations as well. For firms that are considering RMMs, I would encourage them to review the guidance currently available, participate in user groups, RMM conferences and training programmes, and engage in the support of consultants who may assist in developing their validation and implementation strategies.

How does the Parenteral Drug Association (PDA) support industries with their Scientific Publications and Forums?

The PDA provides global support for the pharma industry in many ways. I already mentioned the work we are doing with the revision to PDA TR#33, but there are numerous conferences the industry can participate in where RMMs are discussed. The PDA Journal of Pharmaceutical Science and Technology is another resource for RMM implementation strategies and validation research.

What are some of the aspects that can lead to a drastic change in Sterile Manufacturing?

It is a well known fact that people are the number one source of microbial contamination in sterile manufacturing. So, if we can eliminate the bugs and confirm we are operating in a state of control, we can significantly reduce the risk of producing a contaminated batch of product. I have been involved with the implementation of real-time BFPC systems in gloveless, robotic isolators for sterile manufacturing. The two go hand-in-hand, as microbial contamination from people is no longer a threat to sterile manufacturing, and real-time AFU data confirms the absence of microorganisms in these well-controlled environments. I will be a co-author on one such isolator system in which we have incorporated BFPCs for continuous, real-time monitoring of microorganisms. Look for these publications in the PDA Journal and other pharmaceutical trade journals.

What are some of the Future Technologies in the pipeline and QC requirements?

The recent revision to the EU GMP Annex 1 is a perfect example of how future technologies, such as RMMs, can play a role in the newest quality control requirements. Annex 1 now supports the use of rapid and alternative methods and continuous monitoring systems to increase the protection of the product from microorganisms and to assist in the rapid detection of potential contaminants in the environment and the product. Annex 1 will allow changing the current microbiological acceptance levels for environmental monitoring based on the new RMM signal instead of the CFU, as long as the RMM has been adequately validated. For these reasons, it makes sense for the industry to explore the implementation of RMMs to meet these new regulatory expectations.

How do you see the future of 'Made in India' drugs in terms of contribution to Global Health? How will it strengthen microbial QC help India's progress as a global drug manufacturer?

As many know, there have been critical issues associated with the manufacturer of drugs, especially from a microbial contamination control standpoint. Numerous firms, within India and around the world, have been forced to recall products or shut down facilities as a result of poor manufacturing practices but also the inability to generate meaningful microbiology data that supports a well-controlled manufacturing process and environment. RMMs will help bridge the gap between not knowing how well controlled a manufacturing process is with a more robust understanding that their contamination control strategies are actually working. Therefore, I see the implementation of RMMs playing a vital role in contributing to Global Health for drugs that are 'Made in India' as well as around the world.