charles river

MICROBIAL SOLUTIONS

Considerations When Choosing a Rapid Method

Pharmaceutical Industry

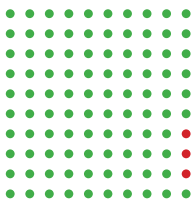
Decision Factors

- Critical information
- Range of application
- Lab efficiency
- Technical expertise

The key criteria in selecting a Rapid Microbial Method (RMM) share a common trait: a strong correlation to financial value. The quicker an RMM can help in making appropriate business decisions regarding the majority of a company's product samples, the greater the financial value that company will realize.

Consideration #1: Critical Information

Some have argued that a microbial test should always provide enumeration and identification of contaminants. This is not true in applications where microbial presence is an unexpected or rare event. Not surprisingly, it is within these same circumstances that the economic benefits of RMMs can be greatest. So, one should ask: "What results do I need to make a business decision quickly?"



Products test negative:
Rapid release
Reduced inventory and cost to manufacture

Products test positive:
Rapid response
Reduced contamination costs

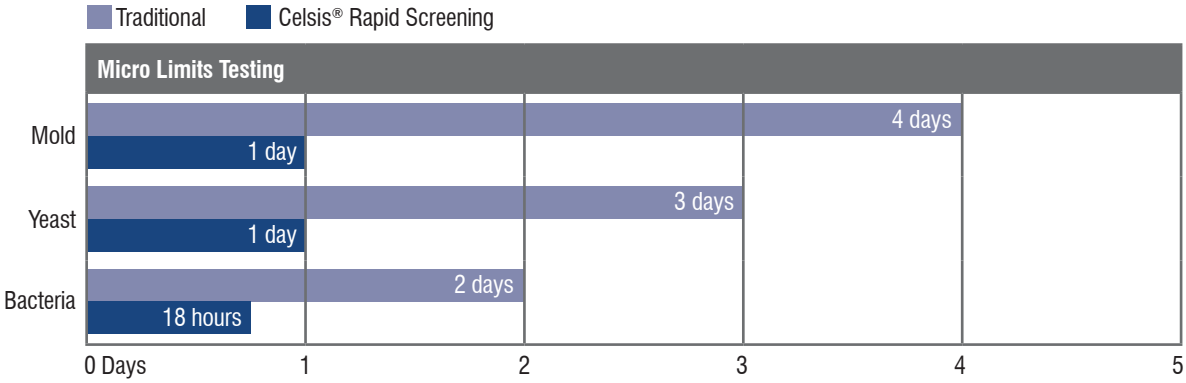
Most of the time, the product is safe for release. In the typical, controlled manufacturing facility, product passes the final microbial limits test more than 97% of the time. Therefore, a simple, rapid test that provides a positive or negative result is precisely what is needed need for the vast majority of production. The small percentage of product that presents positive in the initial screen can undergo further evaluation against release criteria. By taking that route, exceptions are managed while the majority of production is being released 2-6 days faster — quickly and cost effectively.

Look for a screening system that provides a "yes" or "no" answer.

This speaks directly to the criterion of critical information: What information is needed in order to make a business decision that allows more efficient management of production facilities? While the exact percentages of contamination may differ, utilizing time-consuming, resource-intensive methods to screen products is a significant waste when a rapid, presence/absence primary screen will indicate which products can be immediately moved out to distribution and which few products need a second look.

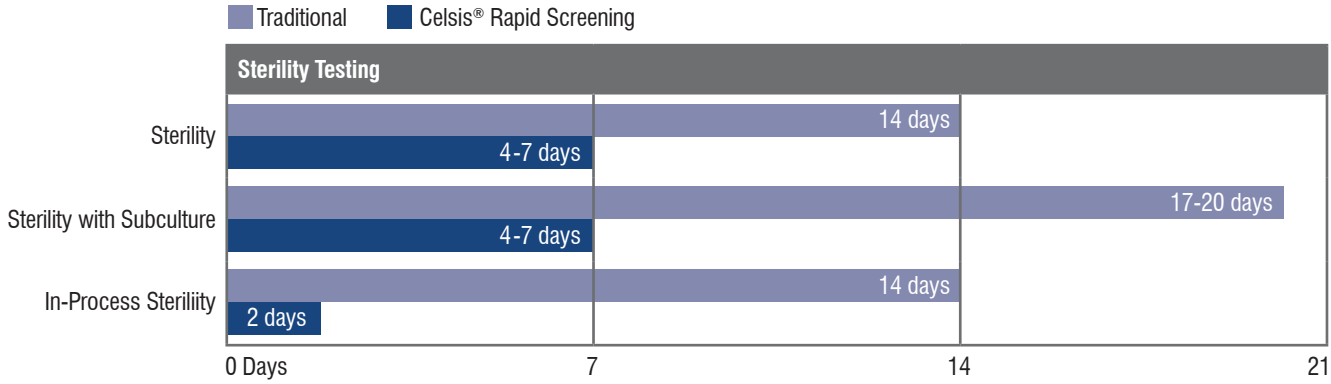
Micro limits testing

As a primary screening for Pharmacopeia Micro Limits Testing, a rapid screening system can provide results in 18-24 hours, depending on a company's requirements — typically, 24 hours for a full bacteria, yeast and mold assay. All products testing negative can be rapidly released with no additional testing necessary. Positives can be further evaluated against the company's release specification for enumeration and/or objectionable organism identification and, by selecting a non-destructive testing method, further identification work can be done using the enriched sample from the primary assay.



Sterility testing

Rapid screening for sterility testing offers even more dramatic results. A presence/absence test makes sense for sterility products and formulae, as they are either sterile or not. Used in lieu of the typical 14-day Pharmacopeia Sterility test, a rapid screening system can provide definitive results in half the time or less. A flexible, rapid system will eliminate additional delays caused by testing solid, non-filterable, colored and/or opaque products via traditional methods, which usually extends testing time to 17-21 days. For example, a major European pharmaceutical manufacturer recently adopted a rapid detection system to reduce its time to test and release sterile, in-process solutions from 14 days to only 2 days.



Consideration #2: Range of Application

The second consideration in choosing a rapid method is the range of raw materials, work-in-process and finished goods that can be tested with the system. The full economic benefits of RMMs cannot be realized if the method cannot be applied to the majority of a company's products. Therefore, one should ask, "Can the method be used across many of my products, or is it limited to a relatively small number of filterable solutions?"

Pharmaceuticals

- Oral drug suspensions
- Liquids, creams, syrups and ointments
- IV solutions
- Medicated wipes
- Ophthalmic solutions
- Oral care products
- Tablets and capsules
- Antacids
- Vaccines
- Nutritional drinks
- Raw and in-process materials

Consumer Products

- Shampoos and conditioners
- Soaps and scrubs
- Lotions and creams
- Wipes
- Gels and mousse
- Toothpaste
- Household cleaners
- Deodorant
- Cosmetics
- Condiments and juices
- Inks and dye

The "best" RMM has an approach to protocol development that takes into consideration the need to accommodate the wide range of product matrices commonly seen in product testing. So, if the method's sample preparation, for example, does not require filtration, the application will not be limited to filterable products only. Flexible sample preparation also allows for the effective neutralization of preservative systems or buffering of pH levels. Companies should not lose the flexibility they have with traditional methods to make standard product accommodations.

Further, the detection system itself should not be subject to interference by particulate matter or product pigmentation. A good choice is a system that will allow a company to assay the majority, if not all, of its products. The company will benefit from testing standardization and training, as well as from maximizing financial benefits through a broader application of rapid methods.

Consideration #3: Lab Efficiency

The "rapid" in rapid microbial methods refers to faster time to result, but an additional way to look at "rapid" is this third consideration: throughput and ease of use, or the ability of the rapid method to process samples efficiently with minimal input. Some rapid methods may require multiple extra steps to prepare samples, additional labor to deal with system complexity, or multiple systems to handle throughput requirements. The economic benefits of "rapid" may be negated if it takes an unreasonable amount of resources just to process the majority of samples with the rapid method. So, one should ask, "Can the rapid method process all of my samples without a major investment in space, people or additional instrumentation?"

Some RMMs offer the ability to process a large number of samples with minimal resource intensity — which refers to pure instrument throughput, the need for personnel to manage the system, and the sheer physical space necessary to accommodate it. Some systems will use a sample preparation technique that is as familiar as traditional agar plating methods so that additional labor is not required to run the system. In addition, look for a system that can minimize the potential for operator error or subjective readings, and one that is easy to use and to validate.

Look for an RMM that can test a wide variety of materials, including:

- Filterable/non-filterable
- Soluble/non-soluble
- High and low pH
- Preserved/non-preserved
- Clear, opaque and highly pigmented products

Finally, laboratory space is a major cost to consider. Some rapid methods, including the instrument itself and additional sample prep needed, require quite a bit of lab space. Some may require additional modules to accommodate testing volume. So, look for a system with a small footprint that can easily integrate into the existing bench space and can readily handle throughput requirements.

Consideration #4: Technical Expertise

The last, but not the least, important consideration in selecting an RMM is provider support. Choosing the right rapid method also means having an active relationship with a supplier who has the appropriate regulatory, validation, scientific and technical support. Without this, it is difficult to obtain maximum efficiencies from the investment, because the average user won't have the benefit of accumulated experience in and understanding of getting a system up and running. Finding a good team to work with will ensure a smooth implementation and a streamlined product release cycle that enables the company to realize the benefits of the rapid detection technology.

Important factors to consider when assessing an RMM provider

- What is the provider's experience with similar products or materials in my industry?
- Is there a straightforward process or tool for estimating ROI? Are the results reliable and beneficial?
- What services do they offer? In what regions of the world?
- Do they have experience assisting customers with regulatory compliance?
- Is on-site installation and training provided? What validation support is available?
- Do they have adequate validation guides and documentation?
- Has the system been accepted by the U.S. FDA and other global regulatory bodies?
- Is there a Drug Master File on record?

In summary, just as not all company micro lab needs are the same, not all RMMs are created equal. While rapid micro methods can provide significant value and savings quickly, the wrong system will cause frustration, delay and waste. Understanding the key criteria in selecting an RMM will facilitate choosing a system that will best provide rapid, relevant results while minimizing testing risk and optimizing resource allocation.

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