WHITEPAPER

Making Quality Your Competitive Edge:

The Value of Advanced QC Microbiology Testing for CMOs/CDMOs

For contract manufacturers, the modernization of their QC microbiology labs represents a tremendous opportunity to improve operations and stand out from the competition.

Learn how automation and digitization in QC microbiology enable contract manufacturers to sell a “de-risked” pipeline to sponsors.

QC Microbiology Testing for CMOs/CDMOs

***In this whitepaper, we'll cover*:**

- Limitations and risks of traditional compendial microbial workflows
- Advantages of Rapid Microbial Methods (RMMs) in contract manufacturing settings
- Benefits of automation and digitization in QC microbiology labs
- The Importance of demonstrating mature quality systems to win contracts
- How optimized QC microbiology labs can be a selling point and not an internal bottleneck

CMO and CDMO Differentiation Through Advanced Quality Systems

The success of contract manufacturing organizations (CMOs) and contract development and manufacturing organizations (CDMOs) largely depends on the value and quantity of contracts they win. In a highly competitive field, emphasis is placed on capabilities, capacity, and availability. However, a CMO's/CDMO's reputation for quality and compliance management is particularly important—serving as a key point for differentiation.[i]

To increase quality and reduce patient risk, regulatory agencies continue to encourage drug manufacturers to incorporate advanced quality control (QC) methods and greater investment in modern automation and control systems.[ii,iii] Drug companies must know that their manufacturers have the utmost commitment to QC, in lock step with ever-increasing regulatory expectations.[iv] To meet the rising demands, contract manufacturers must plan for the future by investing in quality compliance.[v] That includes microbiological QC—an essential component of manufacturing quality systems.

Modernizing QC Microbiology Labs in Contract Manufacturing

Despite QC microbiology's importance, many CMOs/CDMOs still rely on more traditional workflows and methods that limit efficiency, accuracy, speed, and issue resolution.

To revamp the activity of QC microbiology labs, the "next gen" of CMOs/CDMOs are adopting rapid microbial methods (RMMs), particularly those that implement automated approaches.

By investing in automated RMMs, next gen CMOs and CDMOs can:

- Further de-risk their manufacturing efforts and avoid more regulatory challenges
- Avoid significant revenue losses and negative impact to their reputations
- Increase QC microbiology lab efficiency, testing accuracy, and data integrity
- Lower operational costs
- Showcase their investment and commitment to a mature quality system

With the introduction of modernized workflows that use automated RMMs, CMOs/CDMOs can distinguish themselves from other contract manufacturers. This whitepaper will discuss the limitations of traditional microbiology quality control in contract manufacturing and explore how modernizing QC microbiology labs with automated RMMs can improve your operations.

Limitations of Traditional QC Microbiology Workflows

Given that CMOs and CDMOs need to constantly manage high volume demands, tight timelines, and a low margin for error, inefficiencies can have massive downstream impacts. Unfortunately, for those depending on more traditional contamination detection workflows, the QC microbiology lab is often a major bottleneck and source of human error.

A lot goes into bioburden, environmental, and personnel monitoring – particularly when aseptic conditions are required. CMOs/CDMOs often need to collect, incubate, and analyze many samples to maintain tight control over processes. However, traditional compendial growth-based methods[vi,vii] are slow and highly manual, frequently causing bottlenecks.[viii,ix] This is particularly true when testing volumes are high. Congestion in the QC microbiological lab can delay contamination detection, investigation, and resolution. In turn, this can jeopardize product quality and regulatory compliance.

These workflows also rely on subjective visual colony detection and counting. While colony assessments must be inspected and verified by a second user, human error can still occur, especially when timeline pressures and work responsibilities mount.[x] As an added challenge, the human eye generally can't detect contamination until samples grow to larger cell populations (~5 x 10^6 bacterial cells). This means problems can persist for days before visual colonies appear, delaying resolution and increasing the risk of batch losses. By relying on human observation, contamination detection only occurs when actively monitored, which can further delay interventions.

In addition, traditional QC microbiology workflows are a source of human error that can diminish revenue, reduce margins, and damage a contract manufacturer's reputation. It is estimated that about 80% of pharmaceutical product quality issues occur due to human error, [XI] resulting in hundreds of hours of unnecessary investigation work and potentially millions of dollars in lost productivity. Regulatory deficiencies are even more difficult to resolve, with resolution times for 483s and warning letters ranging from six months to two years. [XII] And while the financial penalty of an unfavorable 483 can vary greatly depending on its severity, even a multi-million-dollar cost pales in comparison to the effect a regulatory warning letter can have on profitability. Case in point: the highly publicized loss of millions of doses of coronavirus vaccine in 2021 [XIII] after the U.S. Food and Drug Administration (FDA) closed a contract manufacturer's plant for failing to follow good manufacturing practices that could have been addressed with automation.

Maximizing QC Microbiology Operations Through Automation

To solve challenges and relieve bottlenecks, leading QC microbiology labs are adopting more automated processes to reduce manual steps and free up their teams for higher value work. A recent McKinsey report indicated that quality control labs incorporating more Industry 4.0 principles of automation, digital connectivity, and advanced analytics typically increase productivity by 50-100%. [XIV] In some cases, QC labs stand to boost productivity even more significantly, reaching up to 150-200%. Automation and digitization also facilitated better quality and compliance by eliminating manual errors and user variability. In some cases, these approaches reduce overall deviations by 65% and speed up closure times by over 90%. [XIV] Automated approaches and laboratory agility can also drop lead times by 60-70%. [XIV]

Given the central role of bioburden and environmental monitoring in QC micro lab activities, QC microbiologists can make use of automated RMMs to reduce manual activities, human error, and paper management. In doing so, automated RMMs increase user efficiency, testing throughput, and accelerate time-to-result.

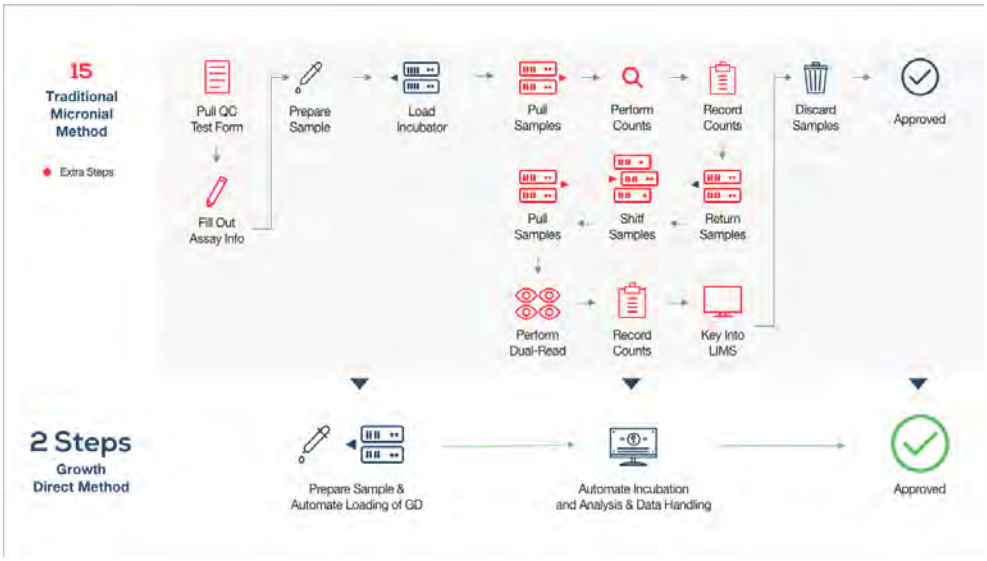

Figure 1: QC Microbiology Workflow Comparison: Traditional Method vs Growth Direct® System (an automated RMM)

The most efficient automated RMMs will track, load, incubate, count colonies, and analyze samples in a single system. In effect, this drastically cuts tedious, labor-intensive steps that currently consume the time and energy of your microbiology team (Figure 1).

Automated RMMs can lighten the load on your microbiology team, so they can spend their time executing higher-value work, like improving QC standard operating procedures (SOPs), identifying contaminations, performing investigations, and resolving issues. With more bandwidth to conduct important tasks more frequently, your QC micro team can elevate the maturity of your quality system and significantly lower manufacturing risks. This benefits both you and your client base. Furthermore, automated RMMs may help reduce user fatigue, burnout, and attrition by eliminating repetitive, error prone tasks like colony counting and manual sample/data entry. This may help retain your teams and their focus, further lowering the risk of user-error elsewhere in their work.

Rather than rely on detection by human eyes, RMMs detect contaminations sooner and make more objective measurements.[xv] For example, the Growth Direct® System effectively detects growing microbes using cellular autofluorescence—even colonies with as few as 120 bacterial cells or 12 eukaryotic cells.[xvi] In addition, the Growth Direct® System can deliver results up to four days sooner than traditional manual count methods (Figure 2).[xvii] This provides faster analysis of bioburden, personnel, and environmental monitoring data, without needing to dual-verify all plate count results.

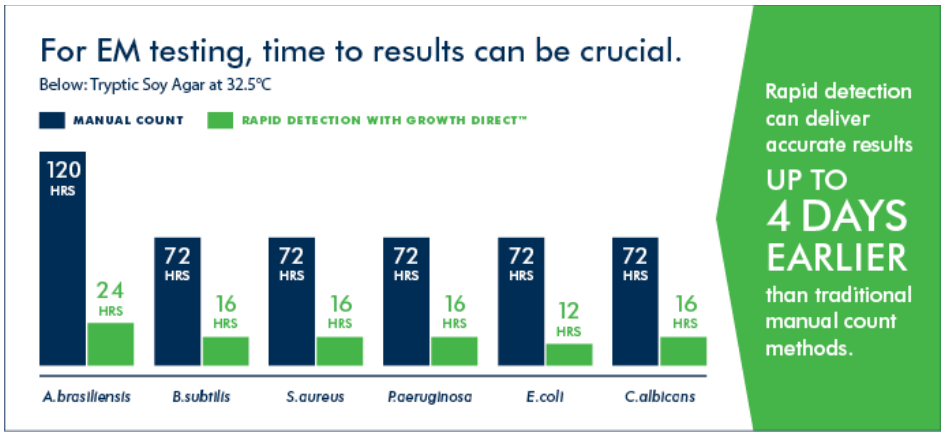

Figure 2: Rapid Detection Using the Growth Direct® System Automated RMM Enables Earlier Detection of Microbial Growth

The Value of LIMS-Integration

Automated RMMs are particularly valuable if they can be seamlessly integrated into laboratory information management systems (LIMS). Rather than rely on manual data transcription and dual-user verification, digital enablement through LIMS-integrated instrumentation vastly improves data integrity and transparency. For an average QC microbiology lab, digital enablement can decrease costs by 15-35%, driven in large part by a >80% reduction of manual documentation.[xiv] Furthermore, this integration also contributes to faster time-to-results and more immediate detection of contamination issues. If you offer clients connection to your LIMS system, LIMS-integrated automated RMMs can even directly and quickly transfer this critical information, all without any human input.

Since QC microbiology labs are often data silos, full LIMS integration means that your microbial testing data is carefully and accurately integrated into the broader system, providing a more holistic view of your operations. With data integrity being central to site compliance, regulatory bodies particularly appreciate how digitization of data collection can reduce patient risk.

Demonstrating Commitment to Quality Through Tactical Investment

The demand for reliable contract manufacturing continues to grow. The COVID-19 pandemic significantly elevated the importance of CMOs/CDMOs, especially as it relates to faster timelines, supply chains, and localized manufacturing. However, increased contract manufacturing investment[xv] and dependence[xvi] brings fiercer

competition between CMOs/CDMOs vying for partnerships and projects, compounded by the fragmented nature of the contract manufacturing market.[xvii]

To secure new business, a contract manufacturer must prove they are the right provider for the job. Given the risk-averse attitude of pharmaceutical companies, the quality of services and products often ranks as a top reason for favoring one CMO over another. In fact, in one recent survey, nearly a quarter of all respondents explicitly referenced quality as a critical selection criterion; it was the top CDMO attribute.[xviii] This underscores the need for CMOs/CDMOs to advertise their commitment to quality and the maturity of their quality management systems to secure a steady stream of new business.

The trouble is that every single contract organization will emphasize that quality control and quality assurance are essential. When everyone touts the same benefit, how does an individual organization demonstrate that their quality management offers advantages? What proof can be rapidly communicated to show that a QC microbiology program goes beyond the routine?

Discussing tangible investments in automated workflows and leading technologies goes a long way towards convincing potential clients. This may be especially true in QC microbiology labs, given that many CMOs/CDMOs still rely on highly-manual, traditional growth-based microbial methods. Advertising investments in automated RMMs represents an opportunity to *show* audiences how your quality systems play to *their* advantage.

For example, CMOs/CDMOs using an automated RMM, like the Growth Direct® System, can directly point to features like superior data integrity through full LIMS integration, the elimination of human colony counting errors, accelerated QC speed, faster contamination detection and resolution, and beyond. Even directly mentioning major instrument investments directly to potential clients can help demonstrate that quality is of the utmost importance. In effect, this also associates your efforts to well-trusted and well-established brands with reputations of enabling quality control excellence.

In the end, potential clients want to *know* your team is walking the walk—in addition to talking the talk. Promoting clear improvements in your QC micro lab provides that proof.

Final Remarks: Embracing the Risk-Averse Environment

Mounting regulatory attention and elevated standards have created a risk-averse environment, where pharmaceutical companies devote significant resources towards de-risking their drug pipeline to avoid costly setbacks.

While oversight responsibility lies with the sponsor pharma company, regulatory bodies (particularly, the FDA) have made it clear that both sponsor and contract manufacturer are jointly responsible for quality.[xxii,xxiii] Risk-aversion and regulatory scrutiny continue to raise expectations on CMOs and CDMOs. In essence, pharma companies want to know that they can rely on their contractors to deliver the highest standards of quality control and compliance.

Greater investment in QC microbiology labs provides you with a key mechanism to embrace the risk-aversion of your clients and regulators. Implementing an automated RMM technology to microbiological testing workflows—including plate enumeration, data management, and issue identification— provides a major step-up over many traditional QC micro labs and helps avoid regulatory missteps.

If you have additional questions about how to improve your QC microbiology lab's efficiency or want to speak with an expert about our Growth Direct® automated RMM system,
Contact Us Today!

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