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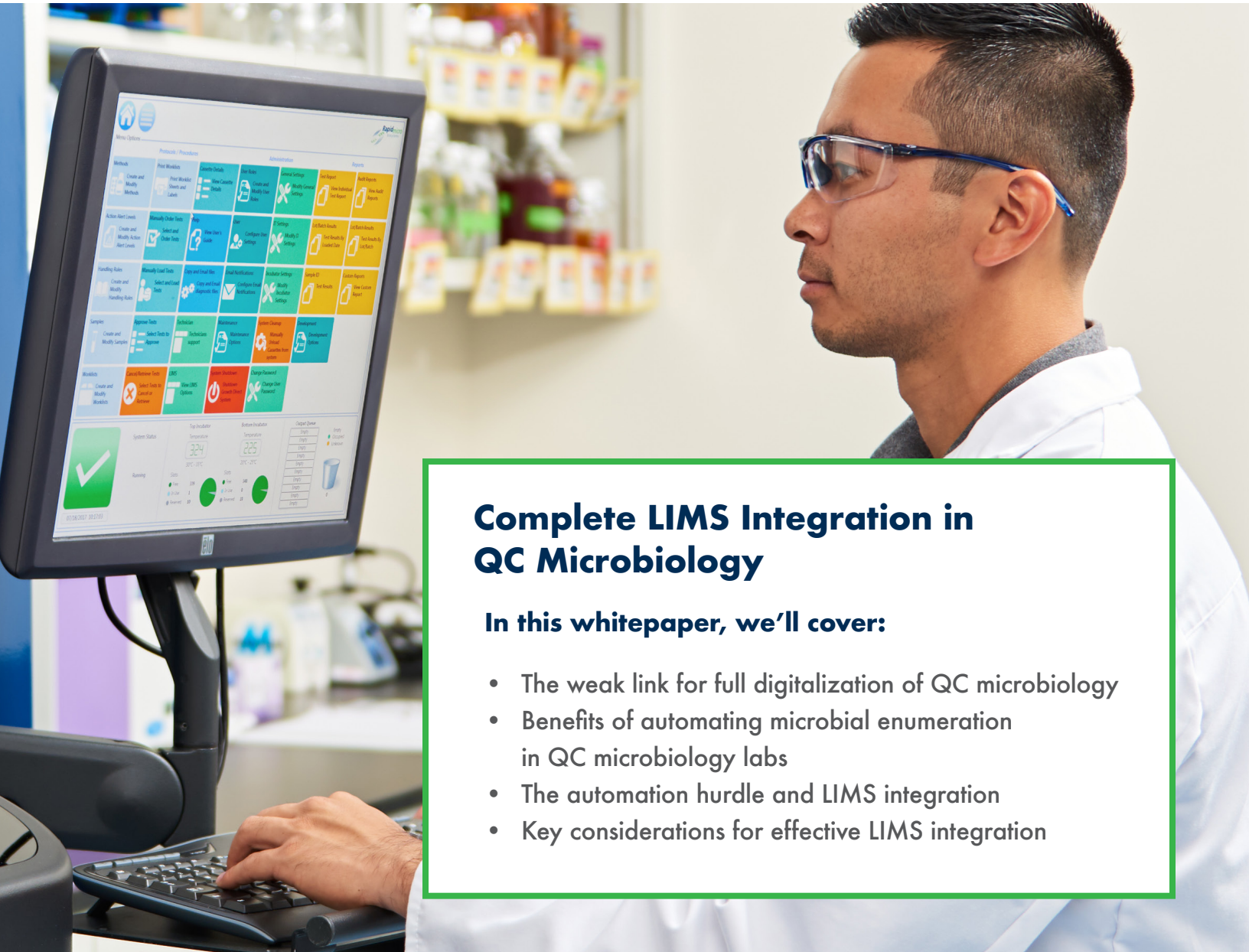
WHITEPAPER

LIMS Integration:

Overcoming the Hurdle of Microbial QC Digitalization

Many pharmaceutical manufacturers aspire to reach complete digitalization of their operations, given the clear benefits digital processes provide pharma companies, regulators, and patients. However, microbial enumeration in quality control (QC) workflows remains a manual process in most labs. Learn how automated microbial enumeration technologies can overcome this barrier to seamless integration of laboratory information management systems (LIMS), improving lab efficiency and tightening data integrity.



Complete LIMS Integration in QC Microbiology

In this whitepaper, we'll cover:

- The weak link for full digitalization of QC microbiology
- Benefits of automating microbial enumeration in QC microbiology labs
- The automation hurdle and LIMS integration
- Key considerations for effective LIMS integration

Though Pharma 4.0™ has been on the minds of industry leaders for years[1], organizations are accelerating efforts to digitalize pharmaceutical manufacturing. Central to this effort is the reliable integration of key automated workflows and instrumentation with laboratory information management systems (LIMS).

Despite tremendous strides, to fully capture the benefits promised by Pharma 4.0, all aspects of pharmaceutical manufacturing must be integrated. Otherwise, manufacturers will find themselves limited by the slowest, most manual, and least digitally connected workflow in their operation. Put another way, "a chain is only as strong as its weakest link."

One such weak link in pharmaceutical manufacturing lies within the QC microbiology lab, specifically microbial enumeration. Given that microbial enumeration is a central activity of QC microbiology labs for activities such as bioburden, personnel, and environmental monitoring, the use of traditional manual enumeration methods represents a key challenge toward complete digitalization. To strengthen this weak link, advanced QC microbiology labs are adopting automated rapid microbial methods (RMMs) that offer seamless LIMS integration.

By investing in LIMS-enabled automated RMMs, pharmaceutical manufacturers:

- Increase efficiency, accuracy, and consistency
- Instill greater institutional data access
- Enable a single data entry point and paperless operations
- Apply more rigorous control over data integrity
- Reduce risk and avoid regulatory issues

This whitepaper will discuss the automation and LIMS integration of microbial enumeration and its benefits.

Pharma 4.0: Achieving Connectivity from Lab to Line

Pharma 4.0, as commonly defined by the International Society for Pharmaceutical Engineering (ISPE) and its members,[1] is about building a "smart factory" by uniting advanced automation and real-time data analytics through interconnected systems. To achieve the complete connectivity envisioned by Pharma 4.0, pharma manufacturers must find ways to centralize all information collected in both labs and on the manufacturing floor.

A futuristic goal? Not necessarily. Rapid Micro Biosystems, Inc. has already seen a number of its customers bridge laboratory and manufacturing operations, after implementing the company's Growth Direct® System. Manufacturing execution systems (MES) have long been used to carefully track and document the production of goods from starting materials. Thus, many users opt to have their laboratory instruments interface with LIMS, which then ladder up to an organization's MES. Others opt to use their existing MES as a LIMS, if their system offers that functionality. While the latter option may reduce integration complexity, user experience can suffer. Separately, some manufacturers utilize multiple LIMS or MES systems, which can require even greater integration efforts.

As you consider your site's connectivity, it's important to recognize that some automated systems, most notably the Growth Direct® System, can integrate directly with both common LIMS and MES. In effect, these versatile technologies provide flexibility you can use to build highly connected systems that suit your needs.

Automated and digitalized microbiology labs can reduce costs by ~10-25% and improve productivity by an average of 50-100%.

Bringing Automation to Microbial Enumeration

Though automation adoption in QC microbiology has lagged behind due to stricter adherence to traditional methods[2] many organizations have already adopted technologies that automate key experimentation, like endotoxin testing and microbial identification. However, many QC labs still perform microbial enumeration with manual colony counting methods.

Automated and digitalized microbiology labs can reduce costs by ~10-25% and improve productivity by an average of 50-100%[3]. To capture these benefits, QC labs need to automate significant laborious tasks, including two-person review cycles, >80% of their manual documentation, >50% of their sample processing, and beyond. This means that labs aiming to digitalize in pursuit of Pharma 4.0 principles really can't afford to harbor any weak links, especially none as central and expansive as bioburden testing, personnel monitoring, and environmental monitoring. Traditional compendial growth-based methods[4 5] are prone

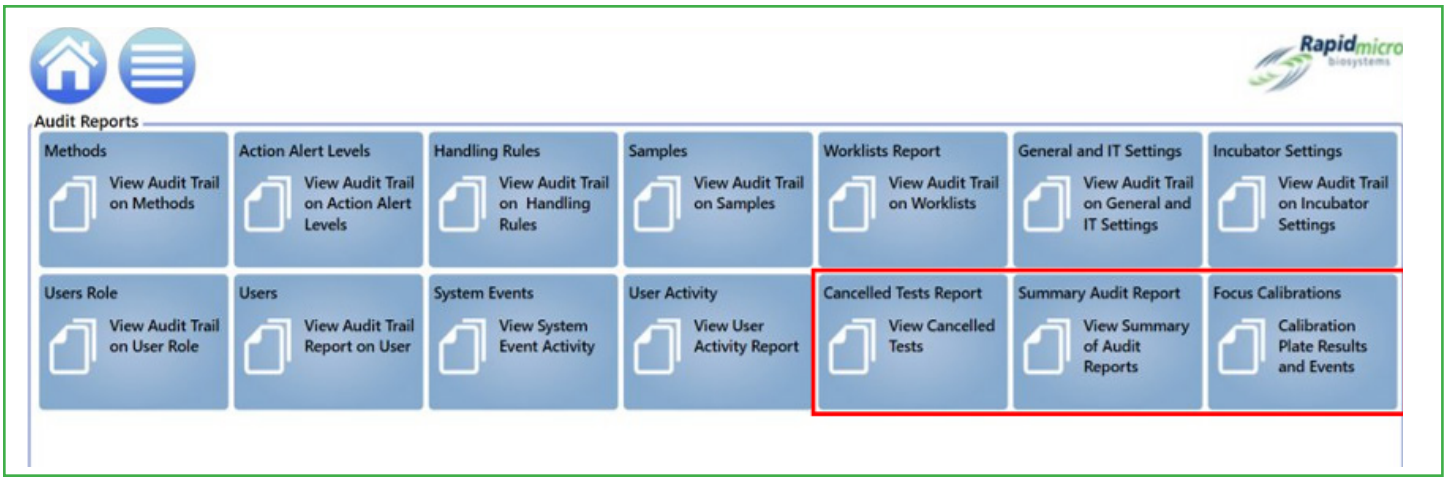


Figure 1: Audit reporting with the Growth Direct® System, including highlighted upgrades in version 4.0 software scheduled for 2022 release

to human error, limit time to result, require manual data management/entry, depend on paper workflows, and induce user fatigue[6]. This key digitalization bottleneck in QC microbiology labs can even delay contamination detection, investigation, and resolution[7 8]. Furthermore, since traditional enumeration methods rely on subjective visual colony counting[9], they require two independent reviews – otherwise known as the "four eyes" requirements. This especially manual stage prevents full automation and data integration from revolutionizing QC.

Making matters worse, manual enumeration represents a sizable gap for manufacturers trying to build more robust data trails for their own process monitoring and for regulator audits. In fact, it's one of the few areas in QC operations where sample collection, processing, data collection, and record keeping are done without reliable traceability. This means it can be very difficult to identify non-compliance and its root cause, increasing institutional risk and drawing the ire of regulators. Given that the number of data integrity observations is on the rise[10 11] – with data integrity issues present in as many as 70-90% of FDA Warning Letters from 2015 to 2018 – pharmaceutical manufacturers should resolve this key vulnerability in their QC processes and audit trails.

To avoid these manual tasks and their data integrity risks, advanced QC microbiology labs are adopting automated RMMs, such as the Growth Direct® System, to perform critical bioburden, environment, and personnel monitoring. The most advanced automated RMM systems will track, load, incubate, and analyze many samples simultaneously. In doing so, they eliminate a significant amount of tedious, low-value labor that otherwise drains the valuable time and energy of microbiologists. In particular, since the Growth Direct® System is an automated plate colony counting RMM, its output differs very little from traditional compendial methods. This means that its adoption does not change the approach microbiology teams are familiar with, only how efficiently they accomplish it. Additionally, to approve data sets, users must be able to review system logs and verify that no system issues occurred during the generation of that sample result. The Growth Direct® System has user-friendly audit trails that can facilitate that activity **(Figure 1)**.

With an automated RMM, microbiology labs can increase efficiency, reduce error rates, speed up time-to-result and issue detection[12 13] improve consistency, save time, lower staff fatigue, and strengthen audit trails.

The Automation Hurdle and LIMS Integration

It is essential to factor in LIMS use when making the decision to adopt new automated technologies, since the improvements they offer are often limited without also integrating that data into broader systems.

An ideal automated RMMs seamlessly integrates directly with your LIMS and helps to improve your data integrity by eliminating manual transcription and multi-point data entry, while collecting critical metadata (user info, timestamps, logs, etc.) and securing data access. This way RMM data is shared directly across your organization, helping your team stay connected, identify issues early, and increase overall transparency **(Figure 2).**

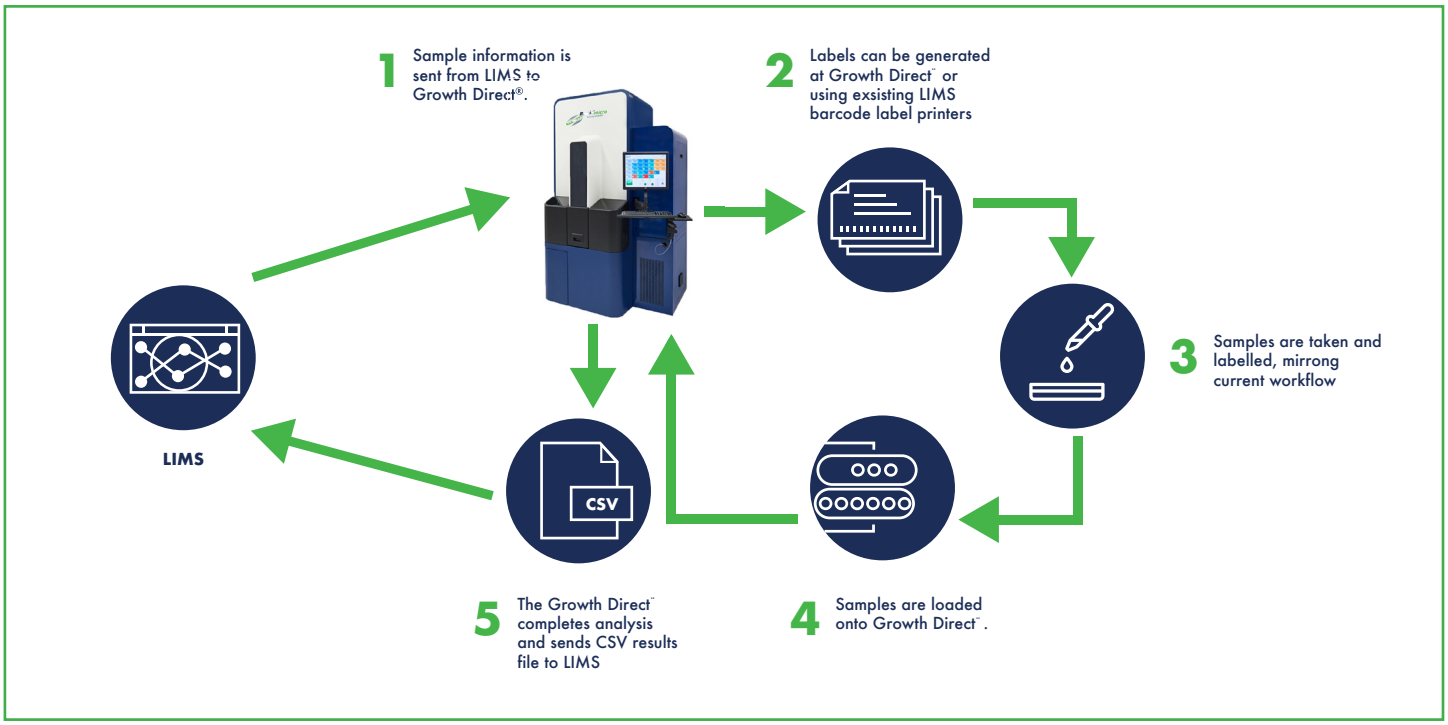


Figure 2: LIMS Integration with the Growth Direct® System, completing the digitalization of QC microbiology operations

Unfortunately, LIMS integration isn't trivial, often tripping up many of today's automation platforms. Some automated technologies provide excellent data collection and speed but struggle to reliably populate that data into LIMS systems. In effect, this means that the workflows would still require manual data transfer, which shifts the bottleneck instead of eliminating it. So, it is crucial to find an automated enumeration technology that you know works smoothly with your existing LIMS, or with the system you intend to put in place. Naturally, the more broadly compatible and versatile an automated RMM is with a broad range of LIMS, the easier it will be to find areliable match.

For example, the Growth Direct® System works with a wide range of LIMS, including LabVantage, LabWare, MODA, StarLIMS, SAP, Novatek, Sample Manager, and beyond **(Figure 3)**. Functionally speaking, this means the Growth Direct® System offers the widest implemented LIMS connectivity of any single automated colony counter platform. Automated RMMs built to cleanly interface with popular LIMS support a fully automated workflow that eliminates time-consuming manual and error prone steps, like data transcription. Specifically, the Growth Direct® System is designed to fully remove riskier human elements and obviate the need for dual data review cycles.

LIMS Used With The Growth Direct® System

Figure 3: Distribution of LIMS currently implemented with the Growth Direct® System worldwide

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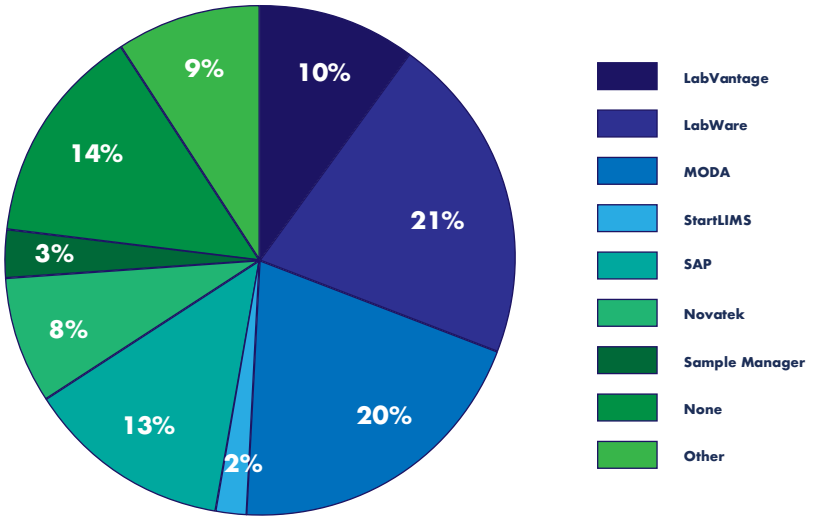

Key Considerations for Effective LIMS Integration: System Validation and Service

The decision to incorporate a LIMS-enabled automated RMM often focuses on the system's capabilities, benefits, and ease of use. Platform selection should also consider specific organizational requirements, which may include:

- Capacity
- Range of applications
- Broad, proven LIMS connectivity
- FDA and GMA regulatory acceptance

At the same time, the intricacies associated with installation, validation, and maintenance should not be overlooked. This is especially true for properly connecting an automated RMM to existing LIMS.

First and foremost, it's critical to remember that integrating any new sophisticated automated instrument into a LIMS system requires significant IT support. Automated RMMs are no exception.

To get the data integrity and efficiency benefits associated with automated workflows, manufacturers need to ensure data is correctly populating into the system in a timely and efficient fashion. The integration must also establish a secure and consistent connection between the instrument and the LIMS, which includes delivery confirmations and effective error tracking. Much of that work is well outside the skillsets of traditional QC teams. Thus, getting your IT team involved early can help them properly support the establishment of your new data flow **(Figure 4)** in a timely fashion.

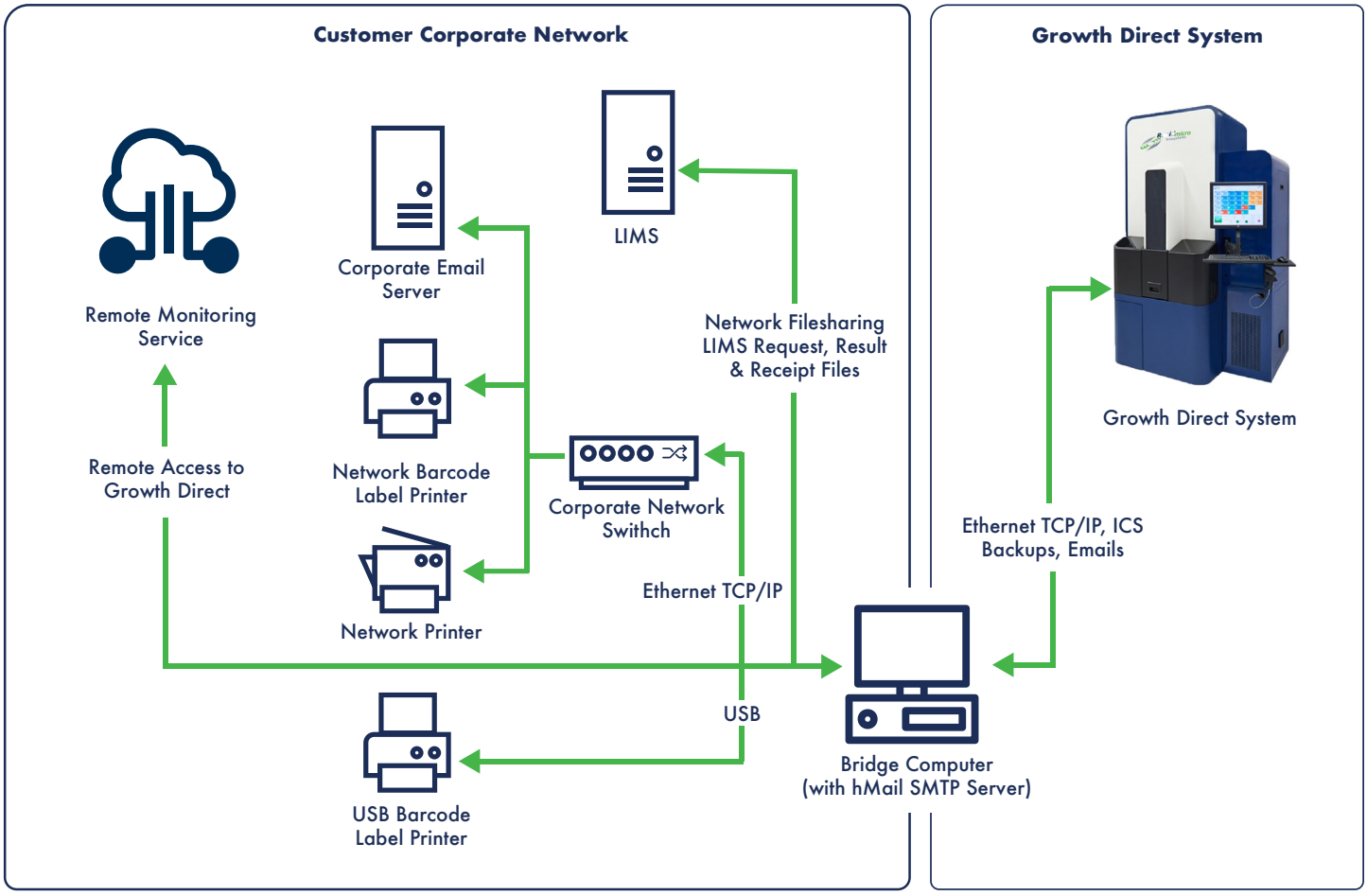

Figure 4: Example of data flow with the Growth Direct® System

According to Kham Nguyen, Director of Global Validation Services at Rapid Micro Biosystems, "one of the biggest challenges is getting all of the right people together, especially since it can seem like they're all speaking different languages." QC microbiologists and IT specialists typically have limited interactions with one another and have very different expertise, which means that working together can come with communication barriers.

Further complicating this is the fact that successful installation and validation often involve a dditional distantly associated stakeholders. In total, this work generally requires QC microbiologists, IT professionals, LIMS specialists, vendors, engineers, and others to work in unison – no easy task, especially if these teams have limited experience with LIMS.

"In the end, it's all about patient safety. For companies to provide that, they need accurate and complete information, as soon as it is available, especially when it pertains to potential contamination. This is the power of a fully connected QC microbiology lab."

-- Kham Nguyen,
Director of Global Validation Services,
Rapid Micro Biosystems

For this reason, it is critical for users to look for automated RMM providers that provide more than just a "box." A well-equipped and knowledgeable system validation and technical support staff can be a uniting force between your stakeholders. Additionally, leading RMM providers will also have dedicated project managers available to help facilitate meetings between appropriate staff, as well as organize and drive the implementation phase.

Rapid Micro Biosystems has long emphasized a commitment to helping partners install and validate the Growth Direct® System they purchase. A unique company strength is Rapid Micro's expert staff, highly experienced in helping to troubleshoot and rapidly correct issues. Given the many LIMS that work with the Growth Direct® System, the Rapid Micro team can draw on proven connectivity experience with a variety of systems used by pharmaceutical companies worldwide **(Figure 3)**. This experience in best practices needed to overcome automation hurdles can help you achieve full LIMS integration of your QC microbiology operations and realize all its benefits.

QC micro lab digitalization and automation requires a significant time and resource investment to install, validate, and maintain. Be sure to factor in the level of support a RMM provider can provide as part of your decision-making calculation.

Final Remarks: Integrated QC Creates Smarter Manufacturing

The highest levels of data integrity are increasingly essential to patient safety, regulatory compliance, and commercial success[14]. Thus, pharmaceutical manufacturers and quality experts should think seriously about securing their weakest link: microbial enumeration.

Rather than rely on error-prone manual data transcription and time-consuming dual-user verification, LIMS-integrated automated RMMs provide major improvements to data integrity, transparency, and productivity. In turn, automated RMMs help your QC team allocate more time to work that further matures your quality system and lowers manufacturing risk.

Collectively, automated RMMs help satisfy highly stringent data integrity standards that are increasingly prevalent in the pharmaceutical industry. Rather than fall behind the automation curve, you can enter the next generation of QC microbiology with the Growth Direct® System.

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If you have additional questions about QC microbiology data integrity and microbial enumeration, contact us today to speak with an expert about our Growth Direct® System.

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