Lonza

Building a Digitalized End-To-end Process for Environmental Monitoring

Growth Direct® System: the only fully automated non-destructive growth-based platform for QC microbiology testing.

The Challenges and Importance of Environmental Monitoring

Rigorous and comprehensive EM is crucial for good quality control in pharmaceutical manufacturing, helping to minimize the risk of microbial contamination, and to help ensure the highest levels of product quality and safety.

However, EM can be immensely challenging. Perhaps the biggest obstacle is that sample incubation and analysis for microbiological EM is labor-intensive; sampling is performed and EM contact plates are incubated, transferred, counted, read out and disposed of by hand, and data capture, review, and reporting for EM is largely manual, too. As a result, microbial testing can be time-consuming, tedious, and prone to error.

While there has long been demand for proven digital solutions to alleviate these challenges, industry-wide-pressure to improve operational efficiency has now created a valid business case for these solutions. This is especially the case in the cell and gene therapy (CGT) space, since processes here are long, complex, and costly, while patients have often exhausted other therapeutic options and need treatment quickly.

Moreover, the inherently unstable nature of fresh CGTs means that efficient release, shipment, and injection into the patient is paramount, necessitating a rapid TTR for EM, and expedited product batch release.

Lonza's Goal: To Optimize Lengthy, Manual EM Processes with Increased Digitalization

As part of its continuing digitalization journey, Lonza wanted fully automated and standardized EM for its Cell & Gene Manufacturing sites.

While Lonza executed EM data management at these sites in a paperless way using their MODA-EM® Module, Lonza grappled with the industry-wide challenge of other parts of the EM process (such as sample analysis) still being manual. For example, sampling processes required visual inspection and relied on subjective interpretation and validation procedures, which demanded significant input from laboratory personnel for enumeration, as well as repetitive analysis, interim read-outs, and manual record-keeping. As a result, the process was time-consuming, error-prone, and labor-intensive, with TTRs of up to 8 days.

Furthermore, EM processes exhibited significant variation across different sites. For example, some sites employed a single incubation method, while others utilized dual incubation. There were also differences in the choice of media, incubation temperatures, and sampling locations. This lack of standardization significantly increased the challenges associated with maintaining compliance and ensuring data integrity. This is especially the case in the cell and gene therapy (CGT) space, since processes here are long, complex, and costly, while
patients have often exhausted other therapeutic options and need treatment quickly.

The Solution: Integrating the MODA-EM® Module with the Growth Direct® System

Lonza's solution was to create a unique digitalized and automated E2E EM process that integrated two systems: Lonza's own MODA-EM® Module, a leading solution for paperless data collection and management for QC microbiology, and Rapid Micro Biosystems' Growth Direct® System for automated microbial testing.

At a Glance: The MODA-EM® Module
The MODA-EM® Module is a regulatory-compliant paperless solution that automates pharmaceutical QC processes. Users can easily manage and report on the full spectrum of EM and QC information, including surface, air, personnel, compressed gas, and product testing. The MODA-EM® Module also can seamlessly integrates with commonly used

Executive Summary

- Lonza wanted to achieve paperless quality control (QC) laboratories using automated digital systems.
- As part of this ambition, Lonza sought an end-to-end (E2E) automated solution to optimize environmental monitoring (EM) at four of its Cell & Gene Manufacturing sites across North America, Europe, and Asia.
- Lonza successfully integrated the MODA-EM® Module with Rapid Micro Biosystems' Growth Direct® System, combining paperless processes with automated microbial enumeration for pharmaceutical QC.
- To our knowledge, the project was the first industry implementation of an E2E automated incubation and read-out process for EM.
- Impact
- As a result of the integration, Lonza achieved:
- More accurate testing: Lonza reduced human error and improved data integrity.
- Faster processes: the E2E solution reduced time-to-detection and TTR to <72 hours (down from up to 8 days previously).
- Better compliance: Increased automation and standardization resulted in greater synergy across data management, aiding compliance and facilitating cost savings.

The project also provides a valuable blueprint for the industry to emulate.

instrumentation automation technologies and media found in manufacturing facilities, as well as with many laboratory information management systems (LIMS). With the module, organizations get timely, accurate QC monitoring through location-based scheduling, mobile data collection, and paperless lab processing.

Today the MODA-EM® Module remains the software of choice for EM, both for Lonza's manufacturing sites and for top 50 Pharma and Biotech organizations.

At a Glance: The Growth Direct® System
Rapid Micro Biosystems' Growth Direct® System provides automated microbial testing for pharmaceutical EM. The system features consumables designed to facilitate high-throughput automated handling with industry-standard growth media (instead of traditional agar contact plates), two automated incubators (with a 660-sample total capacity), advanced image analysis for colony detection and counting, and fully automated robotic sample handling.

By automating QC microbiology testing, the Growth Direct® System eliminates error-prone manual steps and dramatically reduces process steps and wait times.

The Growth Direct® System is the leading platform for automated microbial testing for top global Pharma Biotech and CDMO organizations within cGMP environments.

Lonza installed and integrated the Growth Direct® System with the existing MODA-EM® Modules at its four Cell & Gene Manufacturing sites: Portsmouth (NH) and Houston (TX), USA; Geleen, the Netherlands; and Tuas, Singapore. Lonza's Visp site in Switzerland (which focuses on biologics and small molecules) also integrated the two systems.

Behind the Scenes: Integrating the Two Systems

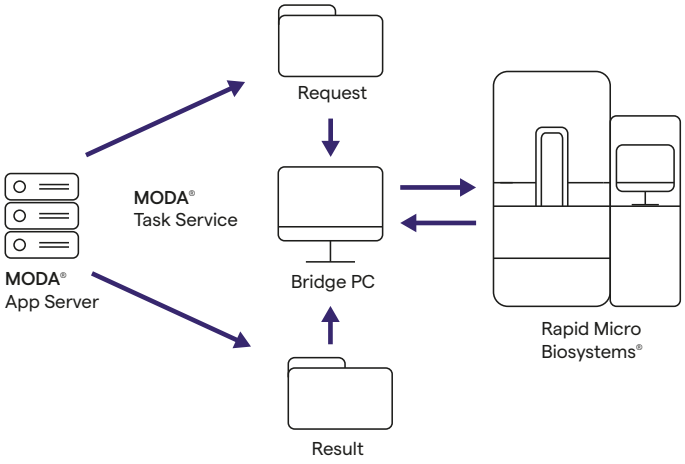
Integrating the two systems required collaboration between many expert teams — including Lonza's Information and Operational Technology (IT/OT) teams, the dedicated MODA-EM® team, QC and Quality Assurance (QA) teams, and external teams at Rapid Micro Biosystems — which were situated at multiple sites on three continents.

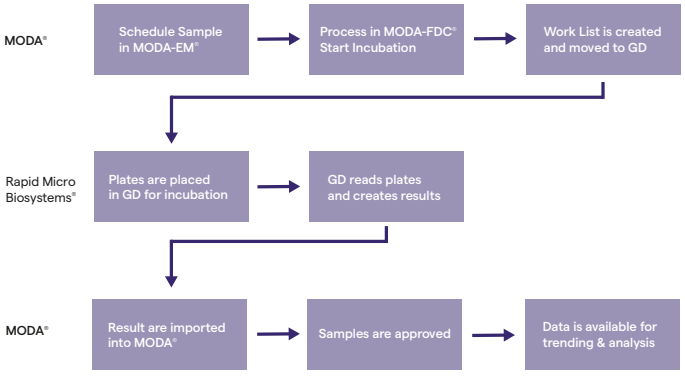
Several key objectives were critical to enabling the integration. The Lonza team, for example, had to update the MODA-EM® Module to a version that supported bi-directional communication and data transfer between the software application and the Growth Direct® System (the Growth Direct® System already comes with a LIMS key to enable data export).

The Lonza team also defined new robust communication pathways between the Growth Direct® System and the MODA-EM® Module to ensure that the right information was being transferred in the right way. Finally, Lonza had to carefully configure its existing IT/OT infrastructure and architecture to support information transfer without violating any security rules.

Additionally, as part of the deployment, the MODA-EM® Team and the Growth Direct® Team provided system operators with a full demonstration and comprehensive training to assure a smooth transition from manual to automated EM workflows.

As a result of this close and coordinated collaboration, the new integrated solution was fully up and running within 1.5 years.





Lonza's MODA-EM® Module v3.5 (and onwards) can now integrate with the Growth Direct® System, as well as other similar automated EM microbial testing systems. The v3.5 update is available for all MODA-EM® Module customers.

Lonza continually invests in the MODA-EM® Module to expand its capabilities and increase its value to QC teams, in line with Lonza's commitment to drive greater digitalization for its customers.

The Impacts:

Streamlined Testing to Get Critical Medicines to Patients Faster

An immediate benefit of the new E2E process was faster, 'walkaway' testing.

Being a paperless system, the MODA-EM® Module enabled Lonza's CGT laboratories to efficiently manage and report on the full spectrum of EM activity. For example, due to its automated abilities and removal of the need for labels, the MODA-EM® Module enabled progression from sample preparation to result approval in under 2 minutes (at least half, and up to one-sixth, of the time taken by other manual methods). The Growth Direct® System, on the other hand, automated microbial testing workflows and was able to count the same number of colonies in up to half the time of traditional methods (while also improving accuracy due to the system being more sensitive than the human eye).

By integrating the two systems, Lonza achieved further efficiency gains. Thanks to automated two-way communication between the systems — without the need for operator input — time delays and data transcription errors were eliminated, and QC teams were able to auto-approve no-growth cassettes automatically.

The significant time savings enabled a drastic reduction in both time-to-detection (TTD) and TTR. While TTR had previously been up to 8 days, the new integrated solution could deliver results in 72 hours or less. Such substantial time-savings are critical in CGT manufacturing, where it is especially important to get products to patients as swiftly as possible without compromising quality.

"CGT patients are often in a critical state and so need treatments urgently, but they can also be very sensitive to contaminated products," said Willem Dullaers, Associate Director, Quality Control, Geleen, Lonza. "It is therefore crucial that the products are delivered rapidly, while ensuring the manufacturing environment is clean and properly monitored. Faster EM results enabled by automated end-to-end EM processes are a key part of achieving that goal."

Fewer Errors and Better Data for Smoother Compliance

Alongside the time benefits, the new E2E digital EM process also improved EM accuracy and eased the path to compliance.

With the integrated E2E solution, consumables can be identified and traced via pre-printed QR codes, where labels are no longer needed, and results are then automatically transferred from the Growth Direct® System to the MODA-EM® Module. Throughout the entire EM incubation and read-out process, no paper is involved.

Overall, this has resulted in fewer errors due to the reduced manual workload and lack of person-to-person variability, greater data integrity and traceability, and easier reporting. Given that the entire process is compliant with 21 CFR Part 11 (the requirements for electronic records and signatures laid out by the U.S. Food and Drug Administration), ensuring regulatory compliance is also now much smoother.

Environmental monitoring cassettes ready for loading into the Growth Direct® System

A More Cost-Effective and Standardized Way Forward

By integrating the MODA-EM® Module with the Growth Direct® System, Lonza saw notable cost savings. For example, by automating many tasks that were previously done manually, the new E2E system enabled the laboratories to redistribute time, effort, and skill elsewhere — in a typical manufacturing environment, this could bring FTE-related cost savings of up to 20%, depending on the hourly costs at the site in question. These cost savings balanced out any new and higher system or consumable costs (e.g., new cassettes).

With greater automation and digitalization, the teams also saw greater indirect cost savings as a result of fewer deviations, faster product release, and achieving compliance with reduced effort.

Additionally, the E2E solution standardized how the four Cell & Gene Manufacturing sites worked; all sites swapped to single incubation and eliminated manual input. As a result, processes became more efficient and less prone to error.

Crucially, there is the possibility of expanding the E2E process to accommodate water and product bioburden testing in the future, and the nature of the integrated process also means that it is easy to scale and replicable across different laboratories and sites.

"The easy replicability and scalability of our new digital E2E EM process is greatly helping us to future-proof our QC testing operations at our manufacturing sites, whether CGT-focused or otherwise," said Willem Dullaers, Associate Director, Quality Control, Geleen, Lonza.

A Digitalized E2E Solution for Your Microbial Testing

Accurate and meticulous EM is a crucial but costly aspect of delivering medicines safely and efficiently to patients. However, traditional manual testing and reporting processes come with drawn out timelines and an increased risk of error, which can incur significant costs, delays, and other adverse consequences.

By deploying a digitalized E2E solution for the incubation, read-out, and reporting of EM samples, CGT and pharmaceutical manufacturers can begin to better address these risks and challenges, and drive faster delivery of medicines to patients.

Lonza implemented an industry-first example of such an E2E EM process, based on an integration of the MODA-EM® Module and the Growth Direct® System. As a result, Lonza has now reduced costs and errors and significantly shortened its EM timelines across several of its manufacturing sites.

Looking to reduce errors and shorten timelines with digital EM solutions?
Find out more about the MODA-EM® Module, and how the E2E process discussed in this case study can be reproduced in your lab, today.

The integration of the MODA-EM® Module and the Growth Direct® System discussed in this case study used MODA-EM® Module v3.5.

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