

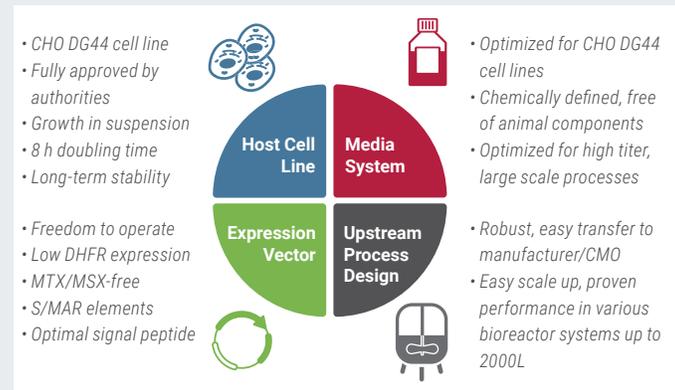
interpreting the huge amounts of process development data had become extremely labor intensive and time consuming. Most of the data was stored in Excel or Word files, which was a huge challenge for both in-project and cross-project analyses as massive amounts of data had to be manually integrated and correlated before the data could be utilized and interpreted.

To overcome this data bottleneck, Sartorius decided to invest into a new digital backbone that could connect all groups involved in cell line and process development. Sartorius started looking for a central workflow management solution that could handle their specific workflow requirements, including their proprietary CHO DG44 high-titer protein expression cell line platform, their cultivation processes using optimized media systems, and their fine-tuned process development procedures for high-titer large-scale processes of 2000 liters and more. Additional selection criteria included automating laboratory operations using barcoding and end-to-

end sample tracking. The envisioned solution should enable the transition to a fully paperless laboratory, make their R&D operations more efficient, and enhance scalability to support Sartorius' continued growth.

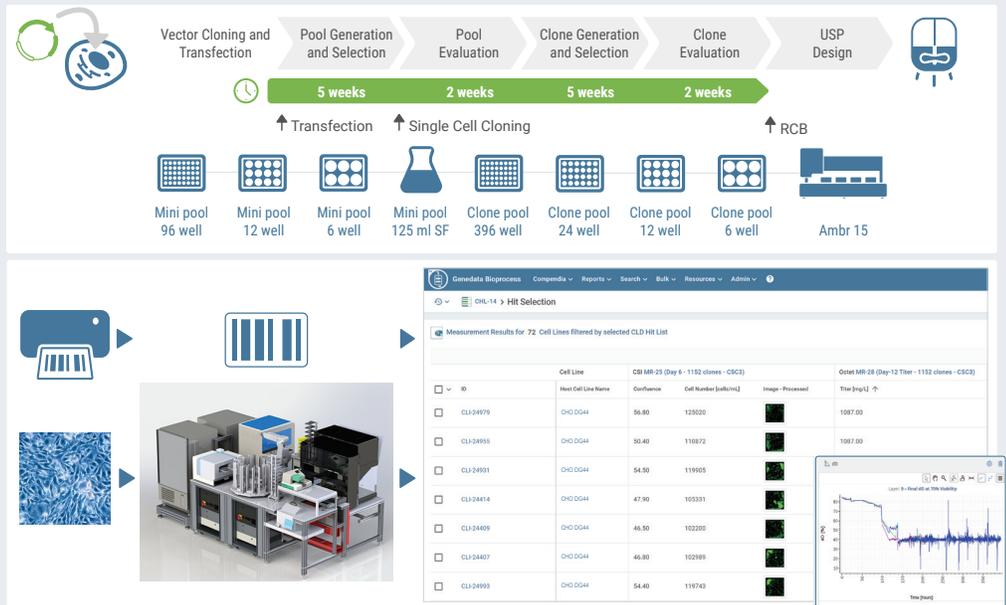
Solution

As Sartorius compared the available digitalization options, they immediately recognized that the Genedata Bioprocess® enterprise workflow platform not only checked all their boxes, but was also the only commercial-off-the-shelf (COTS) solution that included all required logic. "We aimed to extend automation and further enhance the efficiency of our cell line, upstream and bioanalytical development operations, and quickly realized that Genedata Bioprocess addresses our requirements off-the-shelf, eliminating the need for expensive customization," said Hugo de Wit. "What made Genedata unique is that they have developed a solution around what we do every day, the cell line generation, the transfections, the selection, and then bringing it forward into a process. That



Sartorius' Proprietary Cell Line and Process Development Process: Sartorius' CLD and USP platform is composed of a fully integrated workflow, consisting of Sartorius' proprietary mammalian host cell line CHO DG44, a tailored vector cloning process, and an optimized custom-media system for DG44. It provides an integrated upstream process design that enables robust scale up and easy transfer to manufacturing scale (in-house or CMO). The overall process from DNA to RCB is typically accomplished in only 14 weeks, starting with vector construction and nucleofection, followed by mini-pool generation under MTX-free conditions. Single cell clones are generated by FACS-based sorting of the top five pools and selected by titer. After clone expansion and selection based on batch titer and productivity, the top yielding clones are analyzed in fed-batch experiments in the amber15 and ambr250 scale-down bioreactors. Top clones are further evaluated and grown in UniVessel 5L and BioStat 50L, and optionally in larger bioreactors (up to 2000L) bioreactor systems. The media system consists of chemically defined media, free of animal components, proteins, or peptides, optimized for a robust production process to achieve reproducible and optimal product yield and quality, even in large scale manufacturing bioreactors. The process is 100% scalable and no media or process optimization is required.

Sartorius' Fully Automated and Digitalized Cell Line and Process Development Process, Based on Genedata Bioprocess: Genedata Bioprocess acts as Sartorius' data and workflow backbone, integrating and automating Sartorius' CLD and USP workflows. Genedata Bioprocess integrates all process steps, starting with initial vector design and cell transfection, to final RCB, scale-up and upstream process design, connecting, integrating and automating all sub-steps, including all laboratory instruments such as liquid-handling robots and analytics instruments (e.g., Octet, CellaVista, Vicell, FACS, HPLC) for titer, monoclonality and other CLD/USP measurements. Genedata Bioprocess provides a fully barcoded process, tracking all samples and aliquots, with Genedata orchestrating the interplay with all laboratory equipment including Sartorius' central automation station, which provides automated cell incubators, plate hotel, cell imagers, titer measurements, liquid handlers, a robotic arm on rails, and liquid dispensers. The deployment of Genedata Bioprocess has led to an immediate increase in throughput of CLD/USP projects by a factor of 3, substantially reducing the cost to develop bio-manufacturing processes and shortening timelines to BLA IND (for more details see main text).



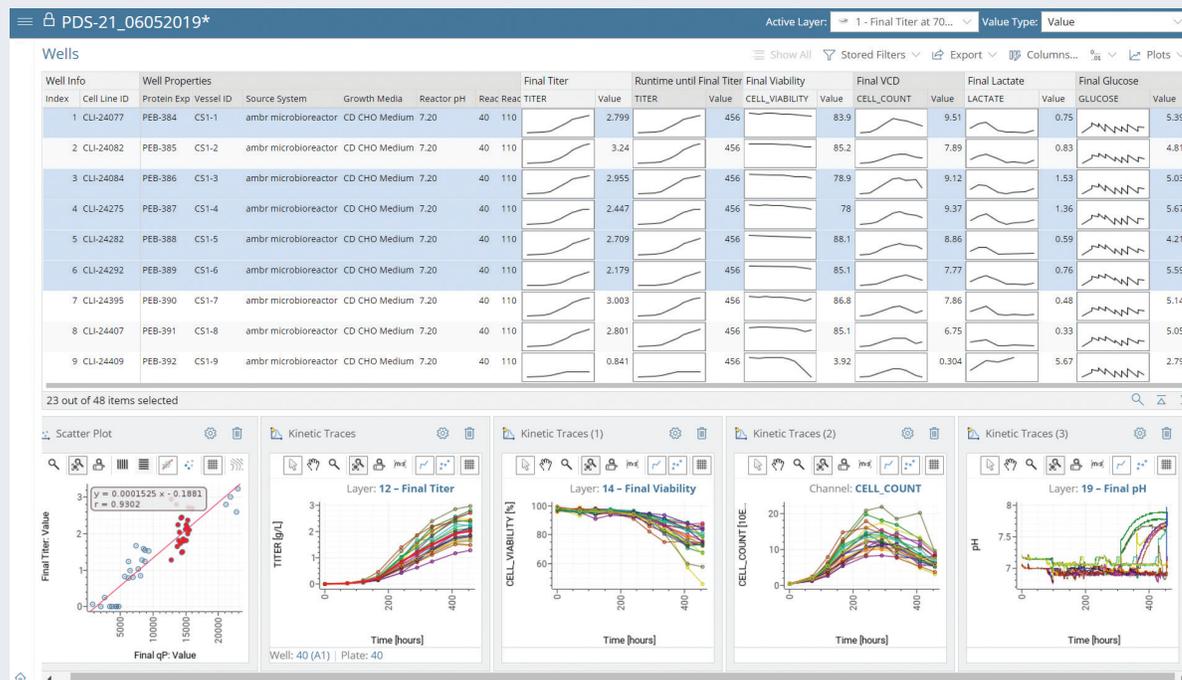
saves a lot of time because the Genedata platform was set up with it. The Genedata people that worked with us understood exactly what we were doing,” added de Wit.

Since Genedata Bioprocess is a COTS product, deployment at Sartorius was quick and efficient. Within just a few weeks, the platform was deployed and integrated with their many laboratory instruments and automation stations. The Genedata platform is aligned with industry best practices, so no major custom development was required, which made the roll-out very straightforward. In addition, the Genedata deployment team and Genedata scientific consultants ensured that communication, implementation, training, and user adoption was efficient across all of Sartorius’ R&D teams.

Sartorius was pleased at how easy it was to implement their fully automated laboratory workflows. “We were intrigued with the platform’s capability to be directly integrated into our wide array of laboratory equipment and with the way

this would facilitate seamless transfer of data and samples along the full development workflow,” stated Hugo de Wit. The Genedata platform seamlessly interacts with Sartorius’ screening robotics systems, bioreactors such as ambr15 and ambr250, BioStats, as well as analytics devices such as Octet. “Implementation of automation can be quite painful. Genedata helped solve this problem significantly because they bring already established workflows that are created by biologists for biologists. And that makes implementation much easier,” explained de Wit.

Today, Genedata Bioprocess is the digital workflow backbone of Sartorius’ quickly growing cell line and process development organization. It supports Sartorius’ unique and proprietary processes including CHO transfections, expression vectors, plasmid generation and optimization, media development, and tailored upstream process design workflows.



Identification of High-Performance Cell Lines, Scale Up and Upstream Process Design: The Genedata Bioprocess platform enables a high-throughput, parallel assessment of large numbers of cell line candidates, starting with top clones evaluated in ambr15 bioreactors (15 mL), and at ambr250 (250 mL) fermentation scales. Here, time course data from 48 parallel ambr15 (15 mL) fermentations are shown, which are used to analyze the performance of different stably expressing CHO cell lines. This is followed by an integrated upstream process design, including an upscaling from 15 mL to 250 mL to 5 L, 50L and in various stages up to 2000L. Genedata Bioprocess automatically collates and integrates all bioreactor online and offline data and analyses growth profiles (e.g., titer, confluence, pH, pO₂, VCD, qP, metabolites) across different clone candidates as well as different process parameters (e.g., different cell culture media). Integrated statistical tools enable a systematic assessment of cell lines and process parameters, e.g., by analyzing lactate concentrations which may result in lower product titers. Besides the automated data analysis capabilities, Genedata Bioprocess also allows the user to interactively analyze and visualize the data (see manual selections in the example above). All data are automatically queried from the bioreactor instruments as well as the assay and analytics instruments, and further processed. The platform generates various standard and custom reports, to facilitate corporate as well as regulatory documentation requirements.

Efficiency Gains & Cost Savings

With Genedata Bioprocess in place, Sartorius has significantly increased operational efficiency and reduced costs. The platform is used in the daily operations of all cell line and process development teams to monitor and assess key process and quality parameters such as confluence, titers, monoclonality, and viable cell density. In addition, by providing project progress tracking in real-time, Sartorius can now seamlessly and continuously monitor all resources across cell line and process development projects, enabling systematic resource planning and streamlining operations.

Across their development operations, Sartorius has benchmarked this increase in efficiency. “Thanks to Genedata, we have been able to triple our productivity. It’s fantastic to see that we can develop three times as many cell lines with the same amount of people. And Genedata has been a critical element to achieve that goal,” stated de Wit.

This gain in productivity is a direct result of the end-to-end digitalization of Sartorius’ process development workflows. Without losing the flexibility they had during their manual operations, Sartorius has significantly boosted their R&D throughput thanks to the automation of their workflows. Sartorius can now operate cell line screening and assessments almost continuously with a minimum of manual interaction and monitoring. Rather than spending hours on tedious and repetitive manual tasks, Sartorius’ R&D staff now have time to focus on more challenging and exciting tasks such as optimizing processes and experimental conditions, designing experiments, testing new protocols, or looking for patterns to further improve their laboratory processes.

On top of these efficiency gains, the Genedata platform has also increased process quality. By automating data transfer and documentation of critical data, Sartorius has minimized errors and ensured data integrity. “As much as we don’t want to admit it, every human being and organization in the end

is a potential risk factor for unintentional mistakes. And the more we automate our processes, the lower the risk of making these unintentional mistakes,” continued Hugo de Wit. However, benefits extend far beyond daily laboratory operations. As a globally operating organization, Sartorius is now able to document and access all business-critical information in real time without the need to send emails or dig through paper documents. A Sartorius-internal assessment showed that the time saved having central access to digital documentation is more than 30%. This digitalization has also been key for improving communication between collaborators, teams, companies, and divisions. “Paper doesn’t travel very easily, data does,” stated de Wit. Having all data centrally accessible greatly facilitates collaboration and data sharing both internally across different businesses and R&D teams as well as with Sartorius’ customers.

Outlook

Sartorius has just moved its cell line and process development division into a new 6,000-square-meter-R&D center to expand its operations and business. The Genedata platform has greatly helped with the upscaling of operations and will continue to be an integral component in supporting Sartorius’ future growth.

In addition, Sartorius is expanding their CDMO offering for cell and gene therapy (CGT) to support the development of innovative treatments for patients with cancer and genetic diseases. Next-generation R&D processes are being established, such as CAR-T, AAV, TIL, NK, lentivirus and other CGT modalities, and Genedata is working with Sartorius to expand the application range of the Genedata platform to support their new CGT processes.

Sartorius is very pleased with the extraordinary impact Genedata has had and continues to have on their operations. “If somebody would ask me, should I use Genedata? I would say you should start tomorrow,” concluded de Wit.

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GENEDATA SOLUTION



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