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Welcome and Contents

While many biopharmaceutical companies are exploring paths toward continuous processing, many tools already exist for implementing process intensification. As the authors of this special report illustrate, hybrid continuous processes that benefit from single-use technologies along with continuing improvements in perfusion cell culture already now are enabling improvements in cost reduction and accelerating time to market. And novel high-throughput and automated small-scale systems are helping development scientists gather more information in less time than before, reduce their development footprints, and make more efficient use of capital equipment.

These novel tools enable critical decisions to be made early in development regarding a product candidate's manufacturability. The authors of this report describe ways in which process development engineers are learning much more about the specific behavior and characteristics of their biological products and processes under specific conditions at the earliest stages of development. Recognizing process challenges — and the ability to optimize processes efficiently — will allow development scientists and engineers to assess the big picture of their processes and further drive the success of the biopharmaceutical industry.

— S. Anne Montgomery
Editor in Chief
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On the cover:
State-of-the-art upstream processing with SSB's bioreactors ambr250 modular and Biostat STR

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Implementing Process Intensification in Commercial Manufacturing

Miriam Monge, Gerben Zijlstra, and Nick Hutchinson

Process intensification, including the use of continuous processes, is currently a hot topic within the biopharmaceutical industry. A significant number of companies are actively evaluating continuous or intensified bioprocessing technologies, and even more plan to test them in the future, especially in combination with single-use technologies. Where single-use technologies have enabled facilities to be built and commissioned in a fraction of the time and for a fraction of the investments of conventional facilities, so far they have been of limited use for commercial manufacturing because of their limited output. The process intensification trend within the industry is helping companies to mitigate this limitation and substantially improve the productivity of single-use manufacturing facilities, combining the best of both worlds in terms of speed, COGs and flexibility. In the face of increasing competition and market uncertainties, this provides biomanufacturers with more options. As surveys show, biomanufacturers expect suppliers to make introducing new intensified bioprocessing equipment and technologies their top development priority.

Applying the latest developments and manufacturing process intensification tools can help biomanufacturers reduce their final facility footprints and save significant time in process and facility development. Short intensified processes make much better use of capital equipment — e.g., facility outputs easily can be tripled. Longer continuous processing in a quasi-steady state could lead to higher quality and more consistent product. Yet the exact approach that companies take will depend on many factors.

Detlev Eisenkraetzer (Director of Fermentation Development, Roche Diagnostics) recently explained that an analysis performed within Roche failed to identify a benefit in switching to a long-term perfusion-based process. Roche compared a standard 14-day fed-batch process performed in 12,000-L stainless steel vessels to perfusion processes that ran for over 21 days with an intensified seed train using 2,000-L single-use bioreactors. They found that the product titers they were achieving in the perfusion process were insufficient for making the continuous setup advantageous economically. This analysis did, however, show significant benefit from running intensified fed-batch processes in single-use bioreactors over 14 days. Eisenkraetzer highlighted intensified bioprocessing as having huge potential, but enabling technologies used in commercial production must have the same level of robustness as those currently used in fed-batch processing, which achieve a success rate of over 95%.

Innovative single-use solutions enabling flexible and intensified bioprocessing

Planning for the Long Term: Gerben Zijlstra (Continuous Processing Platform Manager, Sartorius Stedim Biotech) believes that for most companies, fully integrated continuous processes are a long-term target, but that hybrid approaches are being evaluated or even implemented right now by a number of leading biotechnology companies, including Amgen, WuXi AppTec, and many others. Engineers need to obtain an understanding about which operations it makes sense to intensify for a specific process. They can use process-modeling software to focus on easy wins and reduce the burden on non-value–adding process development activities. “Firms can make more

educated decisions by performing a proper up-front analysis," said Priyanka Gupta (Global Process Modeling Manager, Sartorius Stedim Biotech). Her team is using the BioSolve software from Biopharm Services to help clients identify the best opportunities for intensification projects within their processes.

New Tools and Technologies: Sartorius Stedim Biotech (SSB) has invested in new technologies and solutions to support its customers with their bioprocess intensification efforts. It has demonstrated that its Cellca cell line can be grown in an intensified fed-batch mode with minimal adaptations and using combinations of commercially available media and feeds. Over 12 days, it delivers threefold higher productivity than a fed-batch process and even a fourfold higher productivity if allowed to run for 14 days (Figure 1). Furthermore, SSB has proven that cell culture scientists can grow this cell line to a concentration of over 100 million cells/mL by running a BIOSTAT RM single-use 2D bioreactor in perfusion mode with an integrated filter in the bottom of the bioreactor bag (Figure 2). This avoids the need for more expensive and difficult-to-operate external retention systems but enables customers to achieve high cell densities. Bioprocess engineers can use these cultures for banking at high cell densities or seed-train intensification as proposed by the BioPhorum Operations Group in its report, *A Technology Roadmap for the Biopharmaceutical Manufacturing Industry* (**1**).

In addition to this data from the rocking motion bioreactor, Patheon has previously presented its XD process (concentrated fed-batch) data generated in SSB's single-use stirred tank vessel, the BIOSTAT STR 500. The company used a TFF cell retention system and found that at 500-L scale it could reach a viable cell density of over 200 million cells/mL easily.

The Downstream Connection: To reap the productivity benefits of intensified upstream processing, downstream processing scientists need new solutions that can purify high-titer cell cultures. The kSep single-use centrifuge clarifies high cell density mammalian cell cultures and ensures full product recovery within a closed system. The shear forces generated by the system are low, thereby minimizing the release of DNA and host-cell proteins from lysing cells. The system needs no prerinse and requires only low wash volumes, leading to very limited dilution of the clarified harvest. That minimizes the liquid volumes that subsequent steps must handle.

Sanofi addressed the intensification of monoclonal antibody (mAb) purification processes

Figure 1: Running the Cellca cell line in intensified batch mode increases cumulative productivity by threefold over 12 days and fourfold over 15 days.

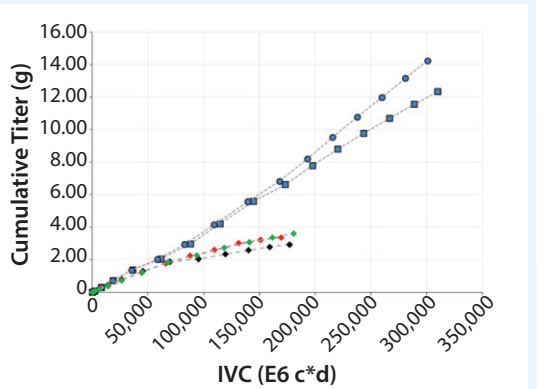
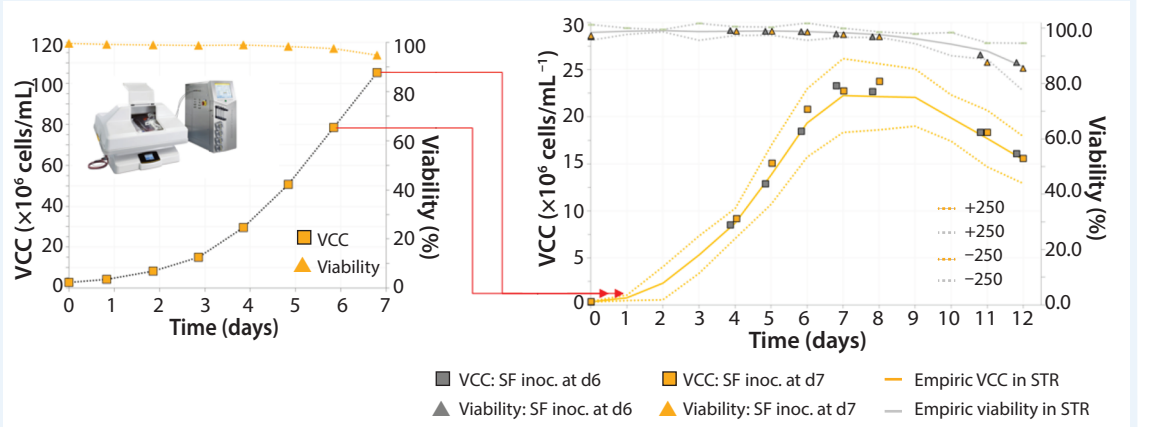


Figure 2: Sartorius Cellca cell line perfusion in 2D single-use rocking motion bioreactor



by taking advantage of the ability of Sartobind membrane adsorbers to allow very rapid cycling. Using 150-mL membranes, the company could purify 50 g of mAb in 2.5 hours with a yield of 90%. The productivity of this downstream process equated to 125 g/L/h without any compromise to the final product purity. It was 10-fold faster than a resin-based process and was much simpler because no packing or cleaning was required.

Raquel Orozco (Senior Bioprocess Engineer, Boehringer Ingelheim) is working on Boehringer Ingelheim's iSKID technology for process intensification. In her opinion, companies wishing to implement these types of technologies must focus on process automation and the way in which different unit operations "talk" to one another. Gerben Zijlstra believes that SSB can address this need through the company's Integrated Solutions team, which provides plant-wide automation through industrial SCADA systems or with its in-house MFCS solutions.

In the past, a shortage of suitable process development tools restricted the ability of engineers to develop the sophisticated control strategies needed for intensified bioprocesses. High-throughput and automated small-scale systems are helping development scientists gather more information in less time than before. SSB's ambr crossflow system is enabling scientists to assess the manufacturability of their biological products at the earliest stages in process development so that processing challenges such as product solubility and aggregation in different buffer systems can be identified and addressed sooner rather than later. Similarly, the ambr 250 high-throughput perfusion system allows a single scientist to run up to 24 perfusion bioreactors simultaneously. It uses membrane-based cell retention methods and can predict the performance of larger-scale perfusion cultures. Each bioreactor is single-use and can be set up in just a few minutes. At an even smaller scale, ambr 15 microbioreactors can be fitted with 3D-printed centrifuge adapters that allow them to mimic perfusion processes through the daily exchange of growth medium. That system provides more controlled conditions than shake flasks and allows clone selection, media blend screening, and feed and bleed rate optimization for improvement of product quality.

Handling Big Data: Using high-throughput screening tools with increasingly continuous bioprocesses potentially will create a Big Data problem. Raquel Orozco described how Boehringer Ingelheim is assessing software that will show all process data and allow process consistency to be measured using multivariate data analysis (MVDA). Detlev Eisenkraetzer says that from Roche's perspective, MVDA is a "must-have" for analyzing process data, and Anna Persson (Senior Principal Data Scientist, Sartorius Stedim Biotech) explained that biomanufacturers should use the Umetrics Suite of software to start training "Golden Batch" models of intensified processes from the very beginning of early process development data. The Umetrics Suite's integrated design of experiments (DoE) functionality can be combined with high-throughput screening tools such as the ambr systems to support rapid process development. Persson believes that tools such as the SIMCA multivariate analysis tool enable process engineers to convert data into useful applications by allowing easy, efficient historical data mining. She cites Shire as a customer that has gone one-step further and can prevent the loss of GMP batches using SIMCA-online as a process monitoring and early warning tool.

Creating the Flexible Facilities of the Future

Intensified bioprocessing techniques are allowing biologics manufacturers to achieve higher productivities from smaller production footprints in less time than before. In the near term, companies can make process improvements guided by process-cost–modeling tools to intensify their production trains. SSB can provide a range of innovations for intensified upstream and downstream processing and supports them with both novel high-throughput development tools and a suite of data analytics software. Armed with these tools, the industry will be able to make a smooth transition from current manufacturing paradigms to intensified and flexible biomanufacturing facilities of the future.

Reference

1 BioPhorum Operations Group Biomanufacturing Technology Roadmap (2017); www.biophorum.com/category/resources/technology-roadmapping-resources/introduction.

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Perfusion in Automated Single-Use Minibioreactors

Gerben Zijlstra, Melisa Carpio, and Nick Hutchinson

Biopharmaceutical companies are coming under pressure to reduce their costs to make biological drugs more affordable and increase access for a greater number of patients. The market is becoming increasingly competitive, not least due to the emerging biosimilar industry that is set to erode the revenues of companies with licensed innovator molecules. Peak drug sales are declining while the cost of developing biopharmaceuticals continues to increase. Scientists and engineers working for biotechnology companies must reduce development times to reach the clinic sooner and develop more productive bioprocesses that reduce cost of goods. However, they also must improve product quality in the face of increased regulatory scrutiny.

In response to these challenges, biomanufacturers are showing increasing interest in methods of intensifying their production processes or even making them fully continuous. Manufacturers of labile biologics adopted perfusion cell cultures many years ago, but increasingly, such cultures are being applied in production of nonlabile proteins such as monoclonal antibodies as a means of getting more product out of an equivalent-sized production asset. Alternatively, perfusion approaches allow biomanufacturers to reduce the size of their bioreactors and of the volumes that they must subsequently process, allowing the switch to single-use technologies and enabling flexible manufacturing facilities of the future.

In short, for a range of biopharmaceutical products, perfusion approaches are allowing higher viable cell densities and higher titers while reducing the need to move to larger bioreactor sizes. It has been reported by a leading biomanufacturer that when running a legacy fed-batch process in an intensified mode, the company was able to increase viable cell density by 10-fold and increase productivity by 100-fold.

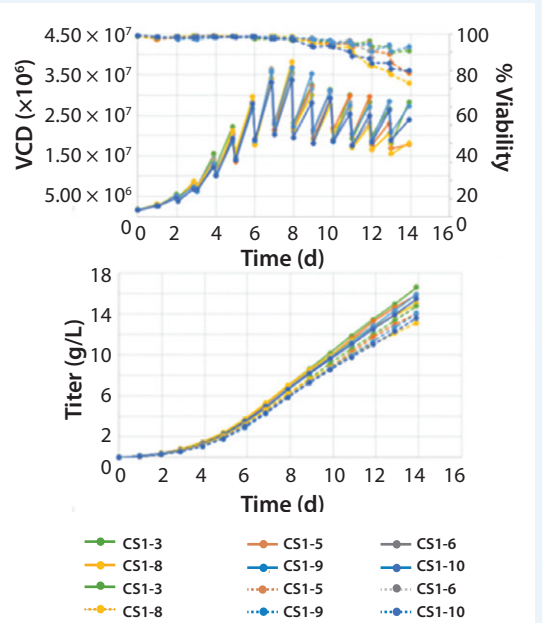
The problem facing cell culture scientists is the need for time, labor, and media requirements to develop perfusion-based processes, including $n-1$ perfusion and n-stage perfusion in the main

bioreactor with or without product retention, effectively. In the context of an industry in which many companies are trying to get molecules to the clinic as quickly as possible, it has been hard for researchers to justify the extra cost and labor needed to allow perfusion-based intensified processes to deliver the promised productivity gains. Some biopharmaceutical companies have reported that in their experiments, perfusion-based processes failed to deliver sufficiently high titers to compare favorably with large-scale fed-batch cultures. Those cell culture groups that can rapidly develop these more efficient processes have the potential to deliver competitive advantage over rivals that are stuck using traditional manufacturing paradigms.

The Rapid Development of Perfusion Processing with Automated Systems

Development scientists must find a way of screening perfusion culture conditions rapidly and efficiently. The ambr 15 and ambr 250 perfusion systems have successfully fulfilled this need for fed-batch cultures and are replacing standard glass bioreactors for process development and characterization studies. Initially, using either system for development of perfusion-based processes was challenging simply because it was not designed for such applications. However, recent advancements have allowed for perfusion mimics in the ambr 15 bioreactor and true perfusion in the ambr 250 system.

Figure 1: Intensified cell culture processing experiments performed in the ambr 15 bioreactor with custom centrifuge adapters; (TOP) viable cell density (VCD) and viability, (BOTTOM) cumulative titer



Mimicking Perfusion: The R&D team at Sartorius Stedim Biotech (SSB) has been conducting perfusion mimic experiments with

Figure 2: Overview of the ambr 250 bioreactor high throughput perfusion system

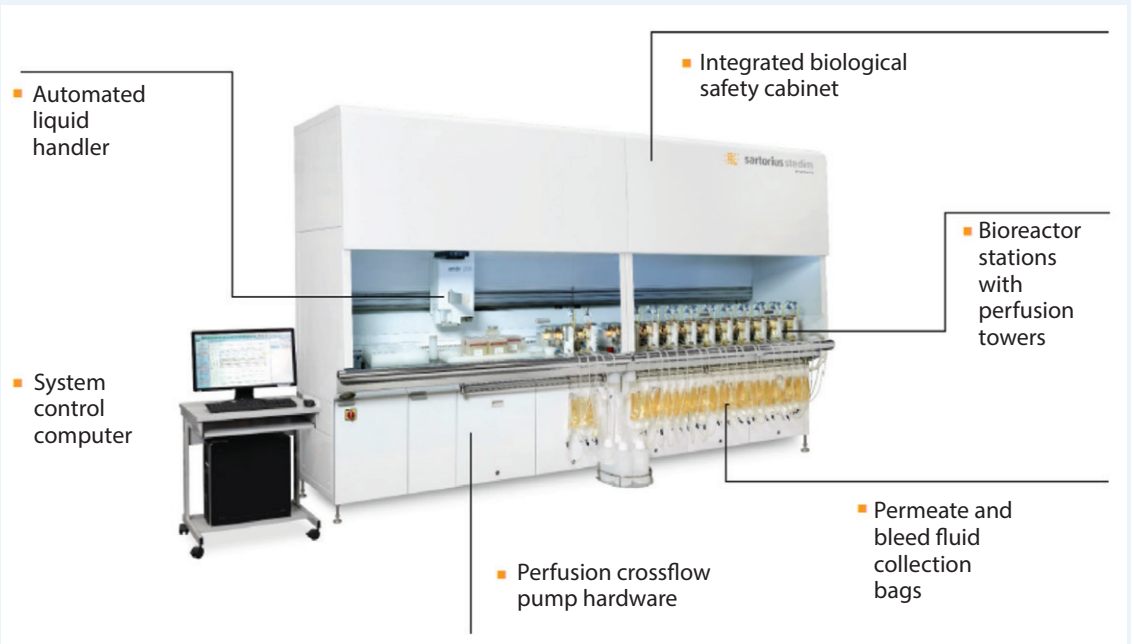
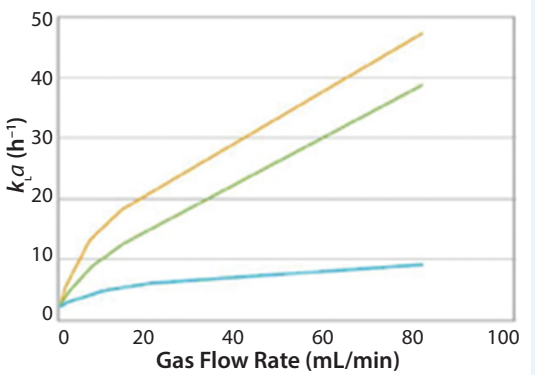
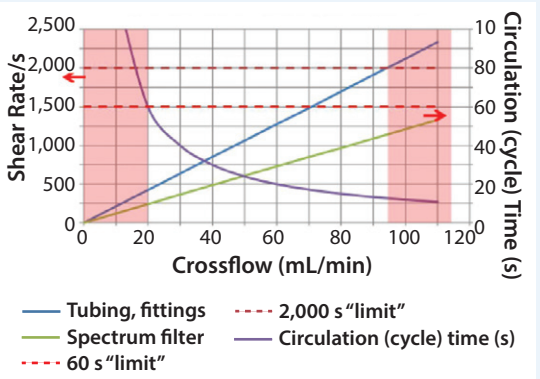


Figure 3: k_La data for the standard ambr 250 bioreactor open pipe sparger (BLUE), a high-efficiency sparger prototype (GREEN), and the ambr 250 bioreactor high throughput perfusion microsparger (ORANGE).



Sparger	6 x 0.15 mm Holes
k_La	21 h^{-1} @ 400 rpm, 40 mL/min air
	40 h^{-1} @ 500 rpm, 80 mL/min air

Figure 4: The effect of crossflow rate on both shear rate and circulation time in the ambr 250 bioreactor high-throughput perfusion system



Advice from industry experts indicated that the system must SUPPORT CELL DENSITIES of over 50 million, and ideally 100 to 150 million cells/mL.

CHO cells in the ambr 15 system. The company used custom designed 3D-printed centrifuge adapters that experimenters can fit to the ambr 15 vessels and has allowed a daily exchange of cell culture media equivalent to 1 vessel volume per day (VVD). SSB scientists ran six of these 10-mL cultures for 14 days, showing excellent consistency in growth and cumulative titer profiles. The cumulative titers were greater than 14 g/L, and the cell densities were in the region of 20 to 35 million cells/mL (Figure 1). Operating the ambr 15 vessels in this way provides more controlled conditions than when using shake flasks and allows media-blend screening, clone selection, and both feed and bleed rate optimization studies.

In addition to these developments for the ambr 15 system, SSB has launched a new perfusion option for ambr 250 high throughput (Figure 2). It combines the ambr 250 cell culture bioreactors with industry-standard hollow-fiber filters and single-use pump chambers to allow experiments to be performed in the laboratory that are scalable and predictive of large-scale perfusion cultures.

The system has been designed to fit into the existing footprint of a standard ambr 250 high-throughput system without reducing bioreactor capacity. Advice from industry experts indicated that the system must support cell densities of over 50 million, and ideally 100 to 150 million cells/mL. It needed to have a low impact on the health of cells, provide ongoing liquid level control, and have a bleed function to maintain the required cell density.

The ambr 250 high-throughput perfusion system can be run in either fed-batch or perfusion modes, allowing engineers to run both types of vessels side-by-side and determine which method will be most suitable for their particular cell line, or even to use some bioreactors for $n - 1$ perfusion seed generation for subsequent ambr 250 high inoculation fed-batch experiments. The system includes a high efficiency microsparger for enhanced oxygen transfer, which enables the achievement and sustainability of high cell densities. It can deliver media exchanges at a rate of between 0.5 and 4 VVD.

Figure 3 compares k_La data generated with the new sparger design, the standard ambr 250 open pipe sparger, and a development prototype. k_La values were determined using the gassing out method in 200 mL of phosphate-buffered saline (PBS). The selected design provided approximately five- to sixfold higher k_La values than the standard design.

SSB engineers recommend that the maximum range for the perfusion crossflow rate is 20 to 95 mL/minute with a typical working range of 50

Figure 5: The consistency of viable cell density data from ten cultures performed in the ambr 250 bioreactor high-throughput perfusion system

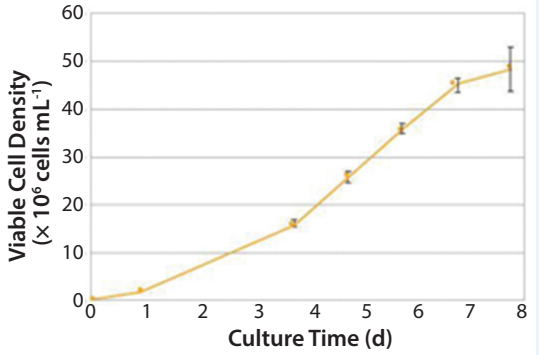
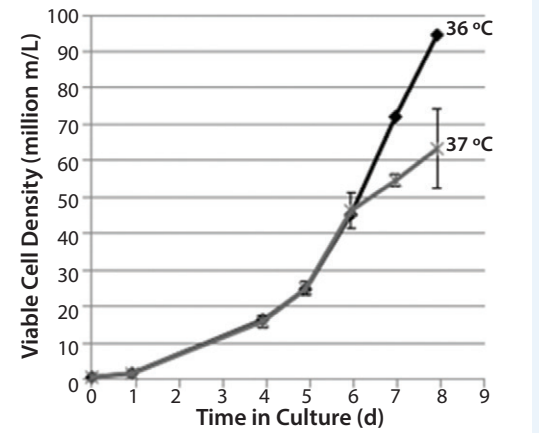


Figure 6: Viable cell densities of around 95 million cells/mL can be achieved in the ambr 250 bioreactor high-throughput perfusion system.



to 70 mL/minute. These recommendations are based on the data from Figure 4, which show the effect of increasing crossflow rate on both shear rate and circulation time. The recommended window of operation becomes apparent when the shear rate is restricted to a nominal limit of 2,000 s^{-1} and the circulation time limited to 60 seconds. The minimum internal diameter of the aperture of components in the recirculation loop is 2.0 mm.

Experiments performed with a thermocouple positioned within recirculation loop show that at a crossflow rate of 70 mL/min, a temperature drop of between 1 °C and 1.5 °C is observed. SSB does not anticipate that this small transient temperature drop will influence the cell culture significantly because of the quick circulation time back to the temperature controlled vessel.

To show the consistency of the ambr 250 high throughput perfusion, 10 CHO cultures were run over eight days. Average viable cell densities of around 50 million cells/mL were achieved by Day 8 of the cultures. The data are provided in Figure 5. The error bars on the graph represent the standard deviation between the replicates.

Higher cell densities, however, have been achieved. Four CHO processes were run at SSB laboratories at two different temperatures as part of internal staff training. Three runs were performed at 37 °C, and one was run at 36 °C. During the runs, the dilution rate was increased from 0.3 to 3.0 VVD. The results presented in Figure 6 show that viable cell densities of 95 million cells/mL were achieved in the system at a cell viability of over 99%. Good consistency is also demonstrated between the three runs performed at 37 °C. The deviations between the two temperatures at Day 6 were due to process changes done as part of the training run.

Client Experiences with the ambr 250 High-Throughput Perfusion System

Initial data to demonstrate the scalability of the ambr 250 high-throughput perfusion are being reported by companies that acted as test partners during system development. One test partner compared the performance of the new system to existing bench-scale, pilot, and commercial manufacturing processes. That company found that cell growth, viability, and product yield performance for the ambr 250 high-throughput perfusion system was comparable to equivalent data from commercial, pilot, and bench-scale processes. This shows that the ambr 250 perfusion was certainly no less predictive of the large-scale process than were the pilot or bench-scale bioreactors.

One of the test partners that evaluated the ambr 250 high-throughput system found that the automation allowed a 50% reduction in system hands-on time. The requirement for cell culture media was cut by 87%, thereby helping to reduce the cost of experiments. The partner also found that compared with its current setup, the single-use bioreactors significantly reduced downtime between experiments.

Another partner reported that it was able to run cultures for over 25 days and in some cases, at lower cell densities, for up to 60 days. The system supported growth to over 90 million cells/mL and was readily scalable to 10-L bioreactors. For in-house media development experiments, automation limited the potential for human errors

and ensured data of a high quality. That partner also described the benefit of having a significantly reduced requirement for growth media and noted that no other high-throughput technology was commercially available for the rapid and cost-effective development of perfusion processes.

One of the test partners found that the automated ambr 250 high-throughput system allowed a 50% REDUCTION in system hands-on time.

Intensifying Upstream Processes

Cell culture scientists working for biopharmaceutical companies need new high throughput tools for the development of perfusion-based intensified processes, including $n-1$ perfusion and n-stage perfusion bioreactors with or without product retention. Such tools will allow for development of more efficient bioprocesses, while delivering lower cost of goods. SSB has shown the use of a custom centrifuge adapter for its ambr 15 minibioreactor system that allows it to mimic large-scale perfusion performance during clone selection, media development, and process optimization studies. In addition, SSB has launched the ambr 250 perfusion option for automated, high-throughout development of intensified cell cultures. It uses industry-standard, single-use ambr 250 bioreactors vessels and is saving time, labor, and media in perfusion process development. Initial results are showing that the system can be used to generate high cell density cultures that represent large-scale perfusion culture performance. With these new tools, SSB is helping to revolutionize the development of intensified upstream processes.

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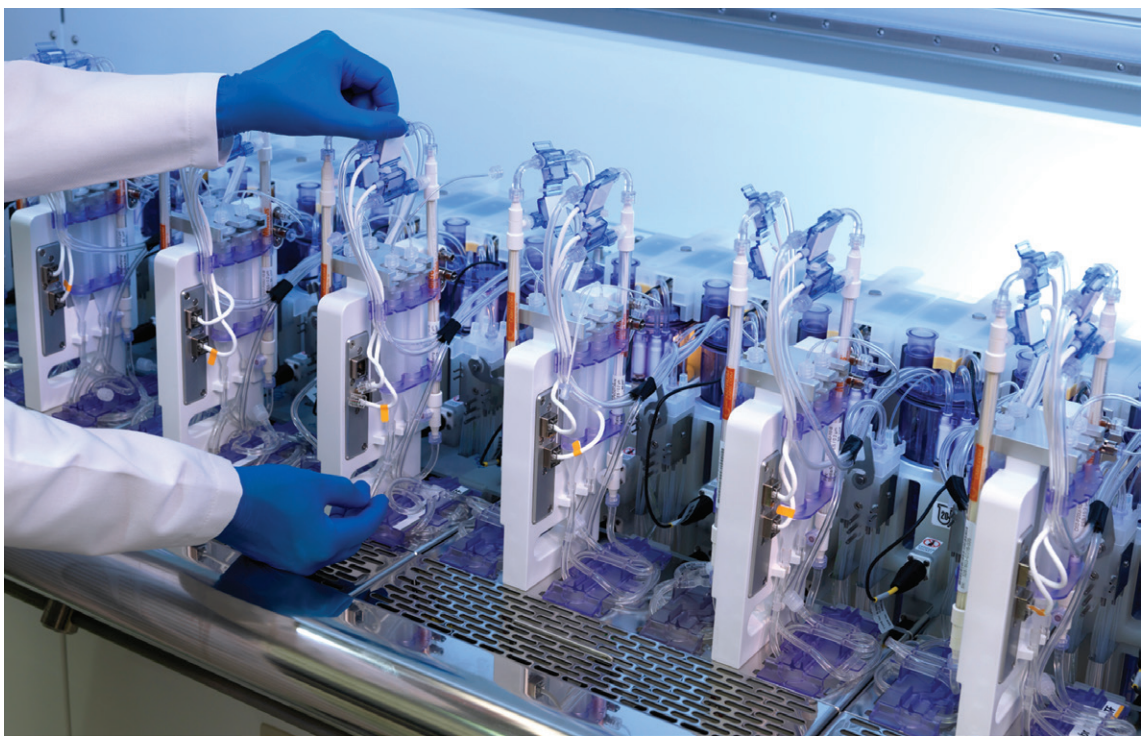
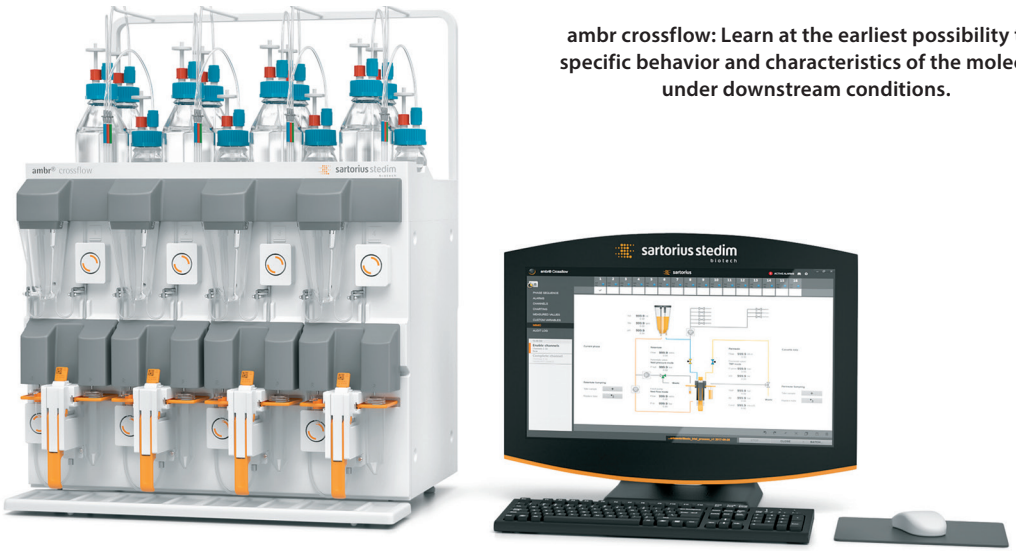


The ambr 250 high-throughout perfusion system is simple to set up and use. Its fully assembled and irradiated perfusion bioreactors include all the essential components.

Assessing Manufacturability During Candidate Selection

Marc Jenke and Nick Hutchinson



ambr crossflow: Learn at the earliest possibility the specific behavior and characteristics of the molecule under downstream conditions.

The biopharmaceutical industry is facing a number of challenges. In recent years, companies have experienced a decline in peak revenue sales from their newly launched products while the cost of developing a new biological drug continues to increase. The industry's pipeline of products is becoming increasingly diverse and requires production platforms that are more adaptable and flexible than ever before.

Scientists and engineers working in the early stages of product development have lacked the necessary tools that would enable them to improve the productivity of biopharmaceutical product development. Automated and high-throughput development technologies such as the ambr 15 cell culture and the ambr 250 high-throughput systems have alleviated this problem for upstream process development scientists. Equivalent systems have not been available to support downstream process development activities. This has prevented scientists from being able to assess the manufacturability of their products at the earliest stages of projects and thus identify processing, storage, and drug delivery problems from the outset of candidate development.

Consider, for example, ultra- and diafiltration operations. Increasingly, biopharmaceutical companies seek to increase the concentration of their final products to facilitate new methods of drug delivery. It is imperative that they understand the stability of those final products and how that can be influenced by different buffer solutions. Furthermore, manufacturers must establish the effect of product concentration on viscosity and the formation of product aggregates. Finally, they must accelerate the development of crossflow steps to reach the clinic quickly by gaining a preliminary knowledge of those processing conditions that will significantly affect the unit operation. In the past, this has been difficult for purification development and formulation scientists because of the large investment in time and resources needed to generate material for ultrafiltration studies and the lack of representative high-throughput screening technologies for scale-down studies.

A New Tool for Assessing Candidate Manufacturability

In response to this need, Sartorius Stedim Biotech (SSB) has developed the ambr crossflow automated high-throughput solution for parallel screening of crossflow conditions. The system works with ambr CF single-use filter cassettes that have a membrane area of 10 cm^2, offering a minimum recirculation volume of 5 mL. Users can expand the system to match their actual demand with four, eight, 12, or 16 channels allowing simultaneous performance of up to 16 crossflow trials. Figure 1 shows the specifications of the ambr crossflow bioreactor.

The HTS software used to run the system allows recipes to be created in phases using drag-and-drop functionality. All the channels are independent, and the recipes can be edited readily. The system has an automated set-up phase that includes system integrity testing, probe and pump calibration, and flux testing. The equivalent end-of-experiment phase allows product harvesting, rinsing, and cleaning-in-place (CIP) of the system, including associated liquid lines.

The ambr crossflow system is easy to set-up. Users require little training and support and can perform easily comparable parallel trials with variability from one channel to another. During development of the system, an experiment was performed in which a 2% BSA solution was loaded into four of the channels at a loading density of 0.2 g/cm^2. A 10 kDa Hydrosart membrane was used in each channel and the protein solution diafiltered at a concentration of 3.5 g/L with a fixed feed flow rate of 10 mL/min and a transmembrane pressure (TMP) of 1.5 bar. The coefficients of variance between the four channels for the prerun water flux test was less than 3% and for the final BSA concentration was less than 4%. The feed pressure, feed flow, and retentate weight profiles of the four runs overlaid one another perfectly. This shows that the

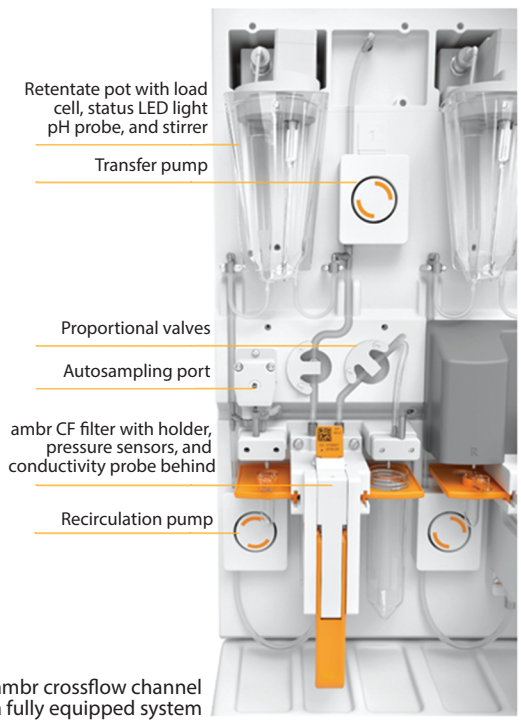
Performing an equivalent study on a standard benchtop crossflow system would have INCREASED the study time by 10-fold and required fivefold more material.

Figure 1: System specifications

ambr Crossflow Small-Scale Screening Device
10 cm^2 membrane area, 5 mL recirculation area

Filter area ambr CF filter	10 cm^2
Peristaltic pump (feed or load)	0–50 mL/min
Minimum recirculation volume	5 mL
Retentate vessel	100 mL
Load cell	0–150 g
Mixer	0–500 rpm
Pressure sensors	0–5 bar
Maximum inlet pressure	3.5 bar (50 psi)
pH probe operating range	4.0–9.0
Conductivity probe	1 to 60 nS/cm

- Dimensions (W × D × H), four-channel module 620 × 600 × 540 mm
- Weight, four-channel module 42 kg (93 lbs)



One ambr crossflow channel equals a fully equipped system

Figure 2: Characterization of a product concentration step with the ambr crossflow system

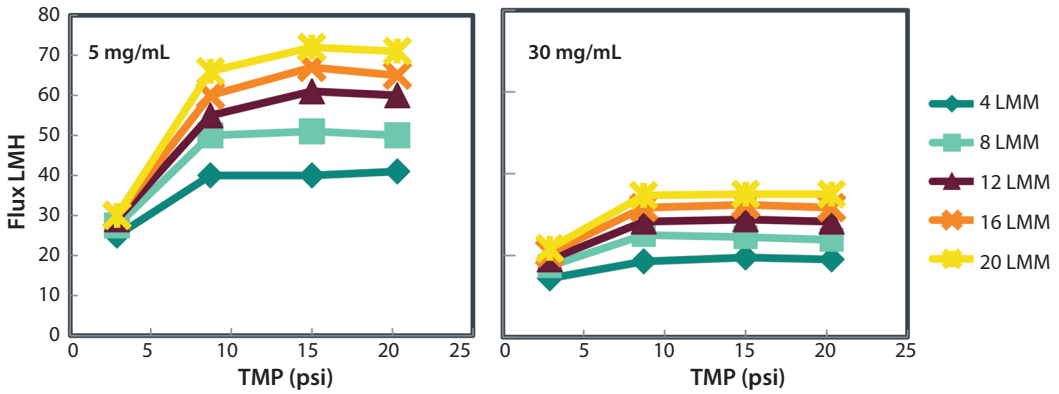
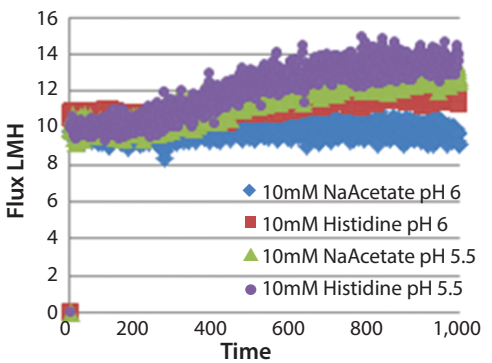


Figure 3: Diafiltration flux profiles generated by the ambr crossflow system



variability between the different channels is extremely low.

Working with a small-scale high throughput crossflow system will allow process development engineers to learn much more about the specific behavior and characteristics of their biological products under specific conditions at the earliest stages of development. They will be able to recognize product-specific processing challenges that will need to be overcome and enable the collection of critical information for optimization of downstream processes. Using very small quantities of product, scientists will be able to optimize buffer formulations, assess product stability under different conditions, establish upper concentration limits of formulations, and determine the ideal membranes and molecular weight cut-offs for their process.

Case Studies with the ambr Crossflow System

A flux characterization study was performed by the Biologics Process Development and Clinical Manufacturing team at MSD in Kenilworth, NJ, on a monoclonal antibody at three different feed concentrations, four different TMPs, and five cross flow rates. In total, 45 conditions were evaluated using a single preprogrammed experimental set-up. Only 0.21 g of product was required for the entire study because of the low hold-up volume of the system. Performing an equivalent study on a standard benchtop crossflow system would have increased the study time by 10-fold and required fivefold more material. Figure 2 shows results of the high- and low-concentration experiments. Although the absolute flux is lower than at large-scale, the trends in crossflow performance are fully scalable.

In conclusion, the ambr crossflow system is an automated high-throughput device that will help downstream processing engineering assess the manufacturability of their candidates at the earliest stages of product development. The material requirements are minimal, and the system is easy to use. Conducting automated crossflow experiments in parallel will help improve the productivity of biopharmaceutical development and support the launch of new drugs for unmet clinical needs.

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***Nick Hutchinson** was Technical Content Marketing Manager at the time of writing at Sartorius Stedim Biotech.*

Selected Resources for Process Intensification

Publications

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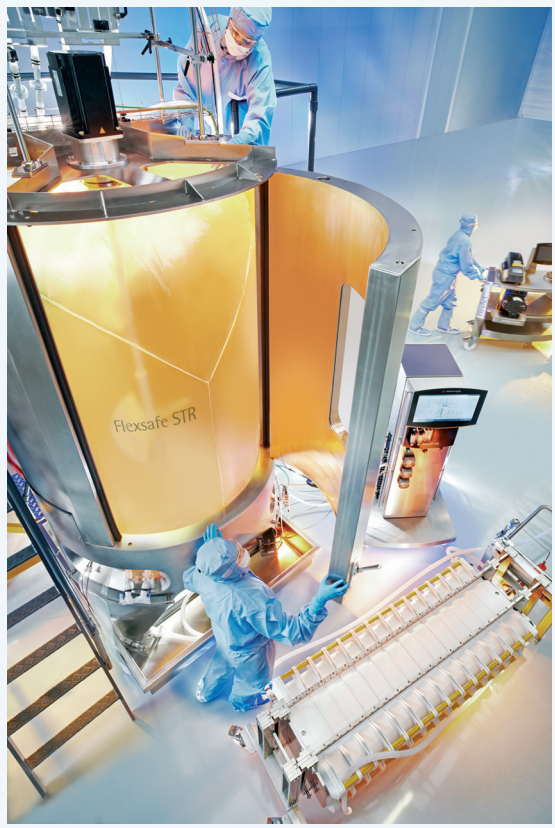
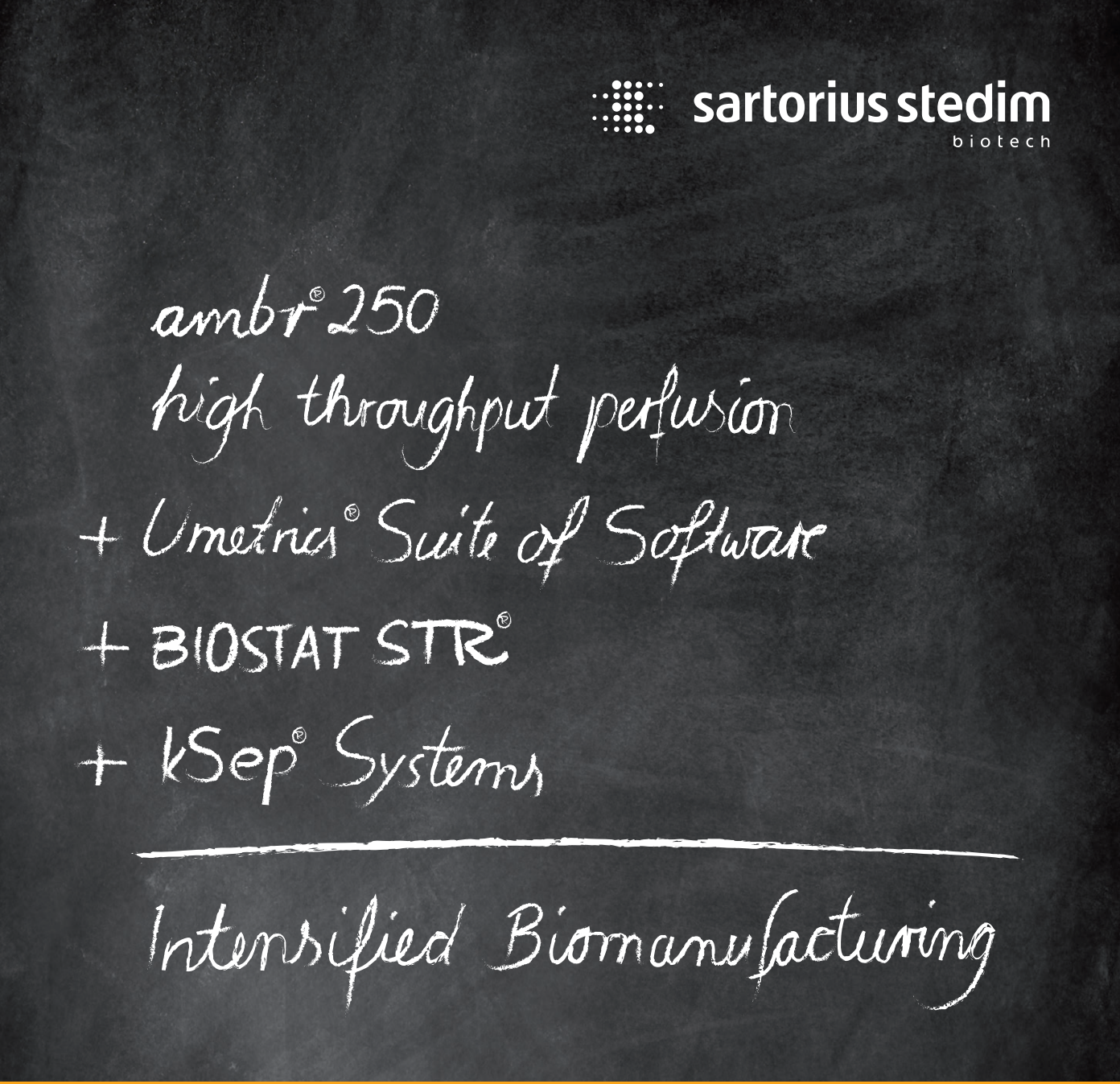
Continuous Manufacturing Reduces Costs for an Emerging Biosimilar Company, 6 September 2017; www.sartorius.com/sartorius/en/EUR/Integrated-Solutions/Resource-Library#AnchorVideos.

Development and Implementation of Continuous and Intensified Bioprocesses; An interview with Gerben Zijlstra from ESACT 2017; https://www.connect-upstream.com/en/intensified-biomanufacturing.

Continuous and Intensified Bioprocessing: A Practical Guide — Development, Implementation and Control of Intensified and Continuous Bioprocesses; May 2017; https://www.sartorius.com/sartorius/en/EUR/Integrated-Solutions/Resource-Library#AnchorVideos.





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