

BioContinuum™ Seed Train Platform

Cellicon™ Perfusion Filter and Controller

A Superior Cell Retention Solution for N-1 Seed Train Intensification with Optimized Process Control

The benchtop Cellicon™ Perfusion Solution is designed to meet your perfused seed train challenges. It consists of a controller and a flat sheet cell retention filter with a single-use assembly running in tangential flow filtration mode. This easy-to-use solution increases perfusion process efficiency, and provides real-time monitoring and control for reliable and consistent performance.

Perfusion operations deliver high-density cell cultures that alleviate the burden of processing large production bioreactor volumes while increasing manufacturing flexibility. Introducing perfusion to your seed train makes it possible to inoculate a higher quantity of cells for one or more production bioreactors, thus increasing process efficiency.



Benefits

- High throughput and low fouling
- Predictable linear scale up from lab to manufacturing scale
- Reliable and reproducible performance
- Low crossflow and cell shear
- Comprehensive monitoring and precise control
- Ready to process in minutes

Applications

- Monoclonal antibodies
- Recombinant proteins

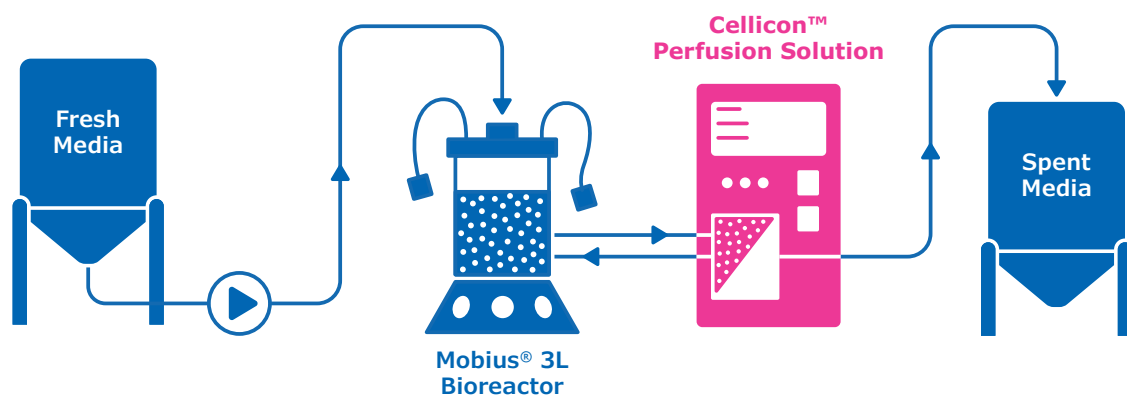


Figure 1: Perfusion set-up with Cellicon™ Perfusion Solution

High throughput and low fouling

While perfusion processes deliver high cell densities, most filters still experience premature fouling requiring change outs to achieve the required throughput. The Cellicon™ filter has been specifically designed to maximize throughput while effectively retaining cells (Figure 2).

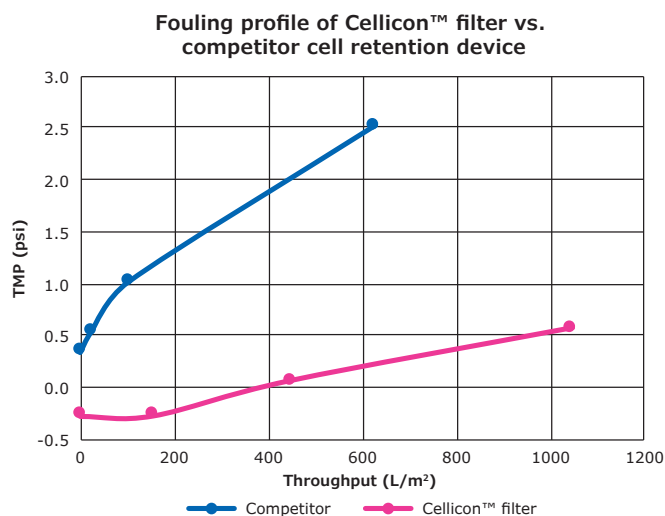


Figure 2: Fouling profiles of the Cellicon™ filter vs. a competitor filter

Predictable linear scale up from lab to manufacturing scale

All filters in the seed train Cellicon™ family have the same flow channel length and height, ensuring predictable linear scale up and scale down from the bench to production.

Trusted Durapore® Membrane

A trusted name in the industry, our Durapore® hydrophilic PVDF 5.0 µm microfiltration membrane is ideally suited for achieving maximum cell retention while minimizing fouling.

Durapore membranes are well-known for their exceptional combination of:

- Low extractables, low shedding, and broad chemical compatibility
- Low protein binding
- Tough and proven

Reliable and reproducible performance

The Cellicon™ controller's precise flow control feature helps maintain consistent crossflow, ensuring reproducible performance from run to run. Pressure sensors also allow real-time process monitoring, which enables improved process development capabilities and consistent performance.

The devices are manufactured in accordance with Good Manufacturing Practices (GMP). Our design and manufacturing process ensures repeatable performance from run to run (Figure 3).

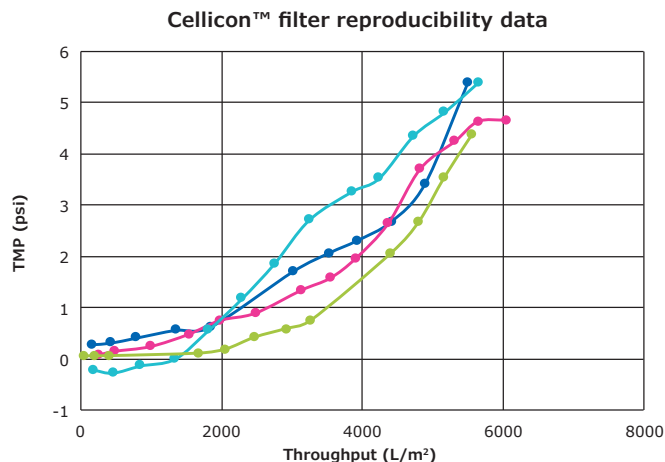


Figure 3: Data showing that the Cellicon™ filter produced reliable and reproducible data across four separate runs.

Low crossflow and gentle on cells

In a perfused seed train, high cell densities need to be achieved while preserving cell viability.

The filter allows you to run perfusion at crossflow rates ten times lower than traditional perfusion solutions, so a smaller pump is needed, which is especially beneficial at larger scales.

The low-shear levitating pump and unique filter design enable higher cell viability and reduced residence time of cells outside of the bioreactor, for optimal growth conditions. As a result, highly viable cell cultures of > 100 millions cells per mL can be reached (Figure 4).

N-1 process cell growth with Cellicon™ Perfusion Solution

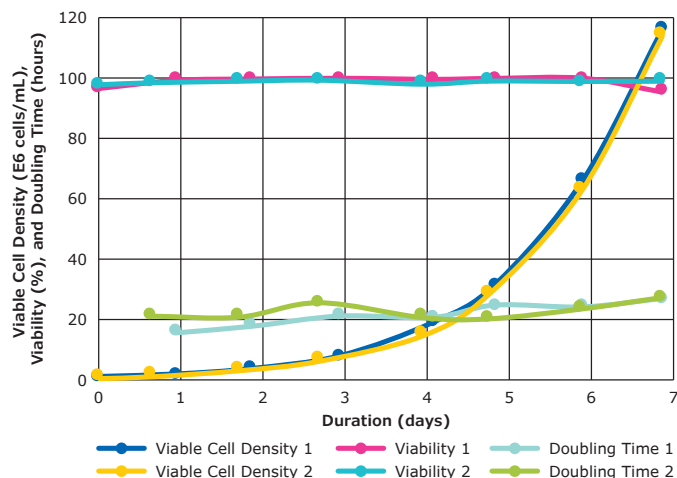


Figure 4: Viable cell density, viability and doubling time profiles of Cellicon™ filter

Comprehensive monitoring and precise control

The controller's touchscreen interface is easy to use. The P&ID screen monitors all active parameters, and the data display provides real-time processing at a glance (Figure 5).

Monitoring of feed, retentate and perfusate pressure allows users to quickly adjust conditions in real time. A consistent crossflow is maintained via a proportional-integral (PI) control loop, enabling high reproducibility from run to run. For individualized process control, visible and audible alarms can be enabled and configured to alert you to any changes in conditions.

The solution is easily integrated into your distributed control system (DCS) for remote monitoring.

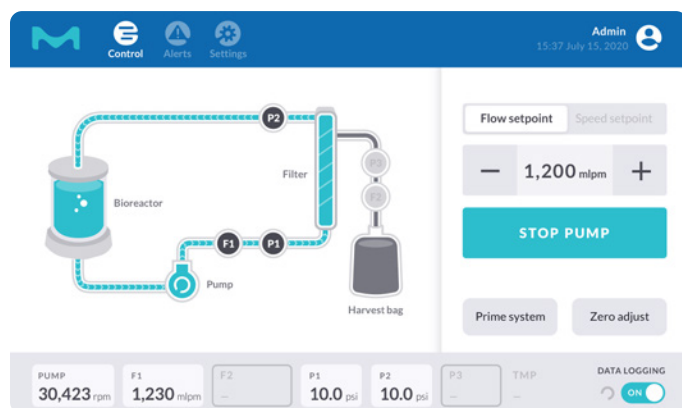


Figure 5: Main touchscreen of the Cellicon™ controller

Ready to process in minutes

This intuitive single-use system can be up and running in minutes. The filter assembly is supplied gamma-irradiated and dry (preservative-free), eliminating the need for flushing. Detailed assembly components are shown in Figure 6.

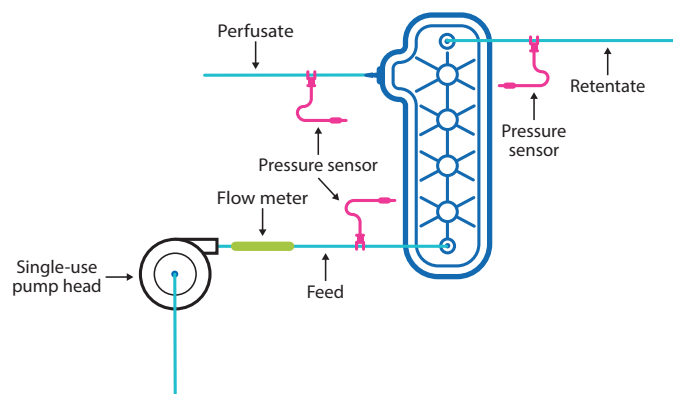


Figure 6: Diagram of Cellicon™ perfusion filter assembly with components labeled.

Simple tube welds connect the filter assembly to the bioreactor. The pressure sensors are easily plugged into the controller, and the non-fluid contact flow meter is clamped onto the assembly. After a quick priming step, you are ready to begin your perfusion process.

Part of the BioContinuum™ Seed Train Platform

Optimize your seed train intensification process with our range of perfusion products that will help you achieve optimum performance.

Our **Cellvento® 4CHO-X Expansion Medium** is specifically prepared to support seed train applications through N-1. It allows for optimal preparation of cells for production phases in perfusion while supporting high cell growth at low cell-specific perfusion rates (CSPR) to increase productivity at the N-stage.

Our **Mobius® 3L single-use bioreactor** combines the predictability of a stirred tank design with the flexibility of single-use, making it the ideal solution for bench-scale cell culture process development and N-1 perfusion.

For more information, please visit:
www.MerckMillipore.com/Seed-Train

The Emprove® Program - your fast track through regulatory challenges

Complementing our product portfolio, the Emprove® Program provides three types of dossiers to support different stages of development and manufacturing operations such as qualification, risk assessment and process optimization. The dossiers combine comprehensive product-specific testing data, quality statements and regulatory information in a readily available format to simplify your compliance needs.

For more information, please visit:
www.MerckMillipore.com/Emprove

BioContinuum™ Seed Train Platform



Specifications

| Cellicon™ Filter Assembly | | | | | |
|--|--|-----------|-----------|---|----------|
| Materials of Construction | | | | | |
| Filter | | | | | |
| Membrane | Polyvinylidene fluoride (Durapore® membrane, 5 µm) cast on non-woven support | | | | |
| Feed Screen | Polyethylene terephthalate (PET); Polyester | | | | |
| Housing/Housing Overmold | Polypropylene/Polypropylene (colored blue) | | | | |
| Assembly Components | | | | | |
| Tubing | AdvantaFlex® thermoplastic elastomer | | | | |
| Fittings | Polypropylene | | | | |
| Pressure Sensors | Polysulfone | | | | |
| Single-Use Pump Head | Polypropylene; magnet encapsulated in polypropylene (non-fluid contact) | | | | |
| Tubing Tie Wraps | Nylon (non-fluid contact) | | | | |
| Gamma Irradiation | | | | | |
| Each assembly is gamma irradiated | | | | | |
| Storage Conditions | | | | | |
| Temperature | 15 – 30 °C | | | | |
| Storage Solution | None; filtration device assembly is supplied dry | | | | |
| Maximum Operating Conditions | | | | | |
| Recommended Feed Crossflow Rate | 10 L/min/m² | | | | |
| Maximum Recommended Flux | 23 L/m²/hr | | | | |
| Maximum Feed (Inlet) Pressure | 5 psi (345 mbar) | | | | |
| Maximum Reverse Pressure | 1 psi (69 mbar) | | | | |
| Maximum Transmembrane Pressure (TMP) before ending run | 5 psi (345 mbar) | | | | |
| Operating pH Range | 4-8 | | | | |
| Nominal Dimensions and Hold-up Volume | | | | | |
| Membrane Area | 100 cm² | | | | |
| Length | 26 cm (10 in.) | | | | |
| Width | 7 cm (2.8 in.) | | | | |
| Feed to Retentate Fitting Distance | 22.5 cm (8.8 in.) | | | | |
| Feed Hold-up Volume (with tubing) | 3 ml (37 ml) | | | | |
| Perfusate Hold-up Volume (with tubing) | 11 ml (42 ml) | | | | |
| | | | | | |
| Tubing Dimensions | | | | | |
| Location | Material | Diameter | | Length In. (cm) | Quantity |
| | | Inner in. | Outer in. | | |
| Feed | AdvantaFlex® | 1/8" | 1/4" | 5 in. (12.7) pre-cut, 2 in. (5) nominal | 1 |
| | AdvantaFlex® | 1/8" | 1/4" | 5 in. (12.7) nominal | 1 |
| | Silicone | 1/4" | 7/16" | 6 in. (15.2) | 2 |
| | AdvantaFlex® | 1/8" | 1/4" | 24 in. (60.9) | 1 |
| Retentate | AdvantaFlex® | 1/8" | 1/4" | 2 in. (5) | 1 |
| | AdvantaFlex® | 1/8" | 1/4" | 24 in. (60.9) | 1 |
| Perfusate | AdvantaFlex® | 1/8" | 1/4" | 2 in. (5) | 1 |
| | AdvantaFlex® | 1/8" | 1/4" | 24 in. (60.9) | 1 |

*The filter is connected to the bioreactor via tube welding on the feed and retentate lines. The perfusate line is also tube welded to a sterile bag or collection vessel to collect the perfusate.

Manufacturing Release Criteria

| | |
|--|--|
| 100% Filter Integrity Tested | Each filter unit must pass an in-process integrity test using a visual inspection under magnification method. |
| 100% Filter Housing Pressure Test: | Each filter unit must pass a housing pressure decay test at an operating pressure above 5 psi. |
| Flow Rate and Pressure Drop | A statistically representative number of filter units from each lot must meet a pressure drop of less than or equal to 2 psi at 100 mL/min average feed flow of water. |
| 100% Assembly Leak Integrity Testing in Manufacturing | Each assembly unit is tested and must pass a leak integrity test using a pressure decay method. |

Regulatory Information

| | |
|-------------------------------------|---|
| Component Material Toxicity | All parts in the fluid path were tested pre-gamma irradiation and met the criteria of the USP <88>. Biological Reactivity Tests for Class VI Plastics and USP <87>, Cytotoxicity Testing. |
| Good Manufacturing Practices | This product is manufactured in a facility that adheres to current GMP. |
| ISO® 9001 Quality Standard | This product was manufactured in a facility with a Quality Management System approved by an accredited registering body to the appropriate ISO® 9001 Quality System Standard. |
| Validated Production Process | This product was fabricated using a validated manufacturing process. Principles of statistical process control and determinations of process capability have been applied to critical variables in the device fabrication process. In-process controls are used to assure stability of the process. |

Specifications

| | |
|----------------------------------|--|
| Cellicon™ Controller | |
| Pressure measurement | |
| Number of pressure sensors | 3 single-use sensors (feed, retentate, perfusate) |
| Pressure range | -7 to 15 psi |
| Pressure accuracy | +/- 0.25 psi @ 5 psi |
| Calibration required (Y/N) | No |
| Tare required (Y/N) | Yes |
| Flow measurement | |
| Technology | Ultrasonic |
| Flow range | 0.05 to 1 L/min (or 5-100 L/min/m ²) |
| Flow accuracy | Characterized at 100 mL/min |
| Tare required (Y/N) | Yes |
| Way of detection | Measurement out of fluid path |
| Pump motor | |
| Pump motor | Levitronix® Puralev i30 |
| Pump flow | capped at 7000 RPM |
| Max. Viscosity | 10 cP |
| Priming required (Y/N) | Yes |
| Console Interfaces | |
| PLC interface | 2X digital inputs, 2X digital outputs, 1 analog input 4-20 mA, 1 analog output 4-20 mA |
| Network interface | Modbus® TCP/IP control and access to setpoints, data registers, alarms, warnings and recipes |
| DC supply connector | 24 VDC with external AC/DC supply, software configurable, auto-resume function, 3-pin connector, global power supply |
| USB interface | USB port for data collection and software updates |
| Touch screen interface | 7 in. color multi touch |
| Controls | |
| Pump control | RPM (priming mode) or flow rate (perfusion mode) control possible, maximum pump RPM and RPM ramp rate both field adjustable |
| Language | English |
| PLC control | PLC control confirmed on touchscreen, disabling controls on console |
| Flow rate PID settings | P and I values are field settable |
| Pressure scaling and calibration | Via HMI |
| Software | |
| Definable user account levels | Yes |
| Alarm systems | Yes |
| Data logging | Yes, via USB |
| Start-up requirements | System has default settings |
| Back-up solution (Y/N) | Yes |
| Material of construction | |
| Pump head socket | Anodized aluminum |
| Integrated pump driver | Epoxy coated aluminum, polypropylene for bottom lid |
| Flow meter clamp on sensor | Anodized aluminum, 304 stainless steel |
| Filter holder | Zinc-aluminum alloy |
| Dimensions and weight | |
| Dimensions | D: 31 cm (12 in.) H: 21 cm (8.2 in.) W: 11 cm (4.4 in.) |
| Weight | 3.6 kg (8 lbs) |
| Regulatory Information | |
| Enclosure rating | IP54 |
| CE Mark | Controller is self-declared to meet the applicable European Directives. Please reference the product's Declaration of Conformity for more information. |
| User guide | Yes, online |

Ordering information

| Product Description | Catalog Number |
|--|----------------|
| Cellicon™ perfusion filter with 5 µm Durapore® membrane, filtration area 0.01 m ² | C5VP001A |
| Cellicon™ bench-scale controller (includes stand, flow meter, pump head socket, and controller power supply and cable) | CRS003L01 |
| Power Supply | |
| US, Canada, Taiwan, Thailand, Columbia, Peru | CRS00PW01 |
| Switzerland | CRS00PW02 |
| EU | CRS00PW03 |
| Japan | CRS00PW04 |
| UK, Hong Kong, Ireland, Singapore | CRS00PW05 |
| China, Australia, New Zealand, Argentina | CRS00PW06 |
| Korea | CRS00PW07 |
| India | CRS00PW08 |
| Replacement Parts | |
| Cellicon™ controller flow meter | CRS000SP01 |
| Cellicon™ controller pump head socket | CRS000SP02 |
| Cellicon™ controller Leviflow® connection cable | CRS000SP03 |
| Cellicon™ controller pressure sensor adaptor cable | CRS000SP04 |
| Cellicon™ controller holder spare parts kit | CRS000SP05 |

BioContinuum™ Platform

Converge, Intensify and Evolve. Together.

An expanding environment of advanced processing, software, automation and analytic technologies, unlocking the potential of Bioprocessing 4.0 and empowering biomanufacturers to achieve greater speed, flexibility and quality.



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For additional information, please visit
www.MerckMillipore.com/Cellicon

To place an order or receive technical assistance, please visit
www.MerckMillipore.com/contactPS

