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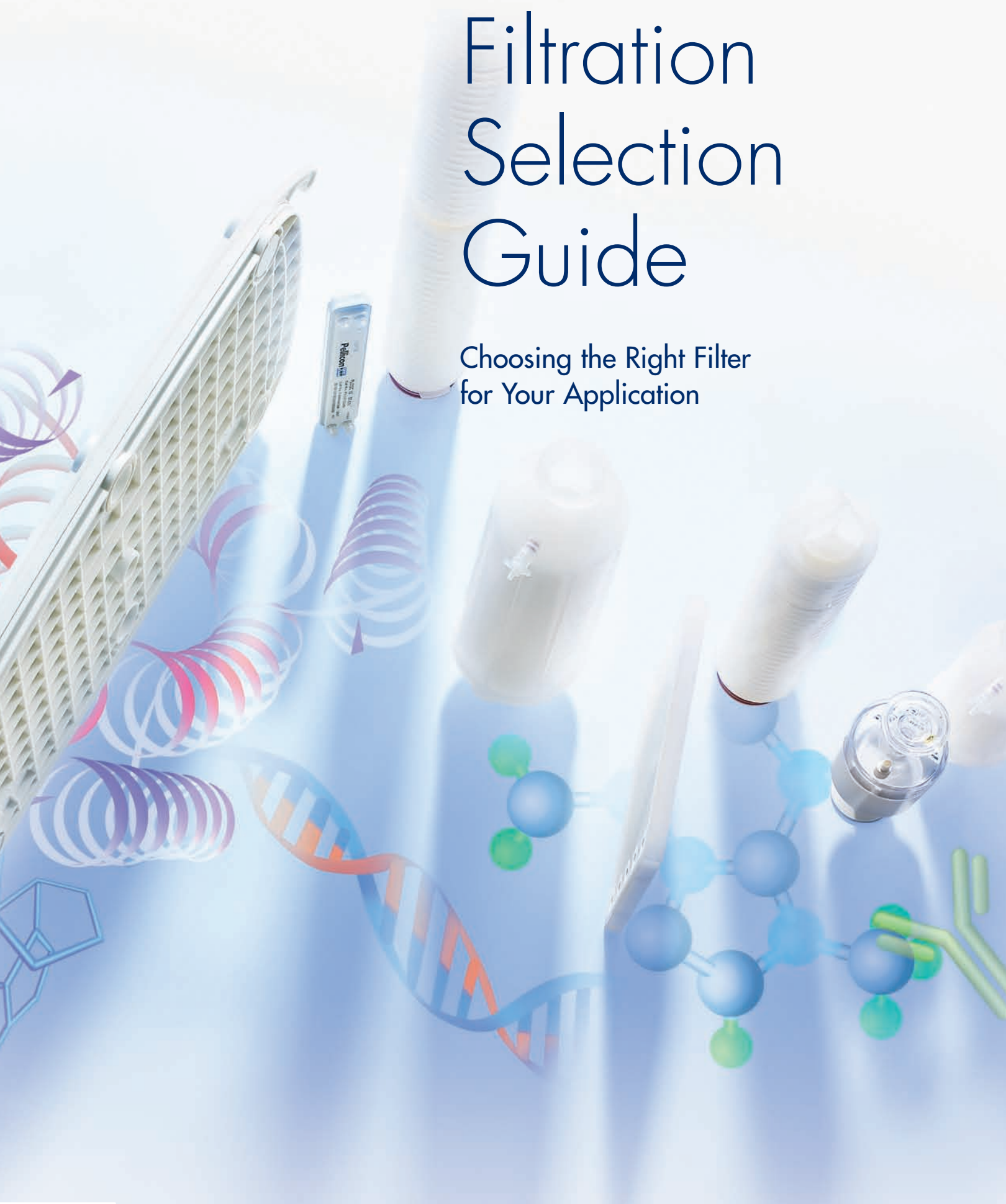
# Filtration Selection Guide

## Choosing the Right Filter for Your Application



From design and development through pilot to full scale manufacturing

# You get More with Millipore's choice of filtration solutions

The right choice in your filtration train will make a huge difference in yields, process economics and product viability. The right choice in your filtration partner can provide consistent product quality, reliable supply, easy scale-up, multiple product configurations and peace of mind.

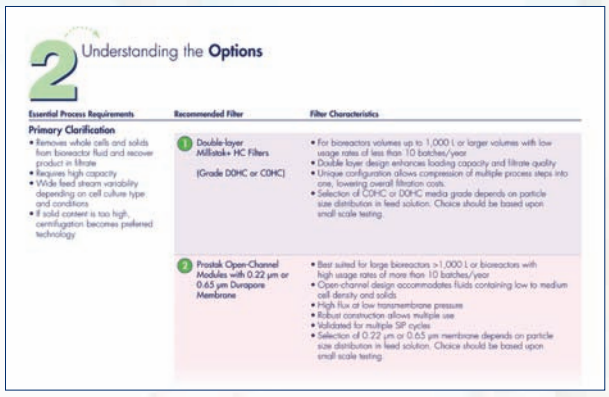
With 50 years experience in the biotech and pharmaceutical industry we understand your complex needs and processes. From design and development through clinical trial material, to pilot manufacturing and full-scale production, Millipore has the products, expertise and services to help you get to market faster with an economical filter train that will work for you today and tomorrow.

## Using this Guide is as Easy as 1, 2, 3

**1** A ***Typical Process Flow*** diagram.

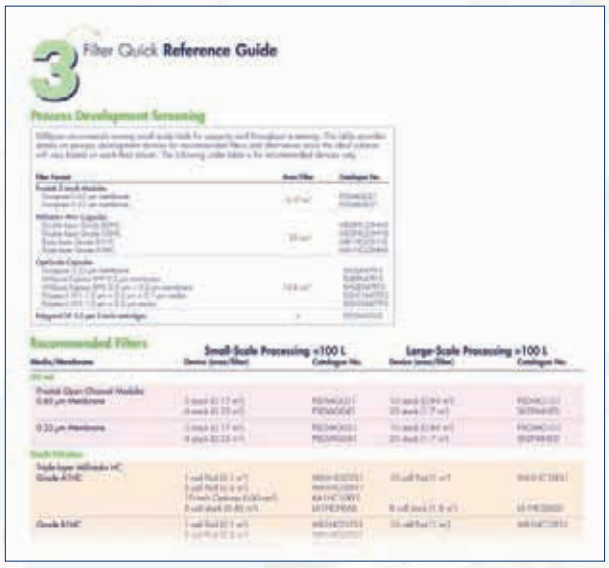
**2** Utilize ***Understanding the Options*** to review the essential requirements that any filtration solution should offer to be effective in that application.

Then review Millipore's product recommendations and the key characteristics of each filter that make it the ideal choice.




**3** Refer to the ***Filter Quick Reference Guide*** for product details such as surface area, volume, formats for various flow rates, and catalogue details.

Use the information in the ***Product Information Section*** for details on filter formats and connections, our disposable offering and comprehensive range of Access® Services.



# Filtration Selection Guide

## Product Information

Millipore offers every membrane and media in a wide range of formats and configurations that can be used from lab-scale to full-scale manufacturing. It is important to understand how each format can fit best in your application. The details in this section will give you basic knowledge of your choices.


Filter Format Quick Reference Guide
- Pleated and Wrapped Filters . . . 2
- Charged Depth Filters . . . 2
- Tangential Flow Filters . . . 3

Understanding the Options, A Filter Format Overview
- Quality Built Right In . . . 4
- Choosing the Proper Normal Flow Pleated Filter . . . 4
- Millistak+ Charged Depth Filters . . . 5
- A Wide Choice of Inlet/Outlet Connections . . . 6
- Tangential Flow Filtration . . . 7

Mobius™ Flexible Bioprocessing Solutions – Transforming Your Process with Disposable Manufacturing Technologies . . . 8

Access Services – When You Need Expert Resources . . . 12


## Application Guide

This tool is intended to give you an overview of key applications and the recommended Millipore filtration solutions. Understanding that every process stream is different, we recommend that scaling and optimization testing be conducted in-house or utilizing Millipore's Access Services team. Use this information as a starting point for development or optimization.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Facilities Water . . . 68

Tank Venting and Air Filtration . . . 70


No tool will replace the need to conduct process development and optimization experiments. The unique nature of every process stream combined with application and regulatory requirements play a part in determining the optimum filtration train. Use this filtration selection guide as a starting point for selecting and sizing the most appropriate Millipore filter.

No specific performance is guaranteed. Visit our on-line catalogue at **www.millipore.com** for individual product specifications and complete ordering information. For personal guidance on understanding the wide variety of options available please consult your local applications specialist or technical service.

# Filter Format Quick Reference Guide*

| Media/ Membrane | OptiScale® Capsule | Millipak® Units | Opticap XL1 Capsule | Opticap XL2 Capsule | Opticap XL3 Capsule | Opticap XL4 Capsule | Opticap XL5 Capsule | Opticap XL10 Capsule | Opticap XLT10 Capsule | Opticap XLT20 Capsule | Opticap XLT30 Capsule | Optiseal® Cartridge | 2-Inch Cartridge | 4-Inch Cartridge |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Opticap® Capsules | | | | | | | | | | | |
| **Clarification and Prefiltration** | | | | | | | | | | | | | | |
| Clarigard® | | | • | | | | • | • | | | | | • | |
| Milligard® | • | | | • | | • | • | • | • | • | • | | | • |
| Polysep™ II | • | | | • | | • | • | • | • | • | • | | | • |
| Polygard® CR | | | • | | | | • | • | | | | | • | |
| Polygard DF | | | | | | | | | | | | | • | |
| Durapore® 0.45 µm | •[4] | •[4] | | •[4] | | •[4] | •[4] | • | | | | • | | |
| **Final Filtration** | | | | | | | | | | | | | | |
| Durapore 0.1 µm | • | • | | • | | • | • | • | • | • | • | • | | |
| Durapore 0.22 µm | • | • | | • | | • | • | • | • | • | • | • | | |
| Multilayer Durapore | • | | | | | | | • | • | • | • | | | |
| Multimedia Durapore | • | | | | | | | • | | | | | | |
| Charged Durapore | | | | | | | | | | | | • | | |
| Durapore CBR | • | | | | | | | | | | | | | |
| Millipore Express® SHC | • | | | | • | | • | • | • | • | • | | | |
| Millipore Express SHF | • | | | | • | | • | • | • | • | • | | | |
| Millipore Express SHR | • | | | | • | | • | • | • | • | • | | | |
| **Viral Clearance** | | | | | | | | | | | | | | |
| Viresolve® NFP | •[1] | | | | | •[2] | | • | • | • | • | | | |
| Viresolve NFR | •[1] | | | | | •[2] | | • | • | • | • | | | |
| **Tank Venting and Air Filtration** | | | | | | | | | | | | | | |
| Aervent® | •[3] | | | • | | • | • | • | | | | | | |

[1] *Viresolve membranes are sold in the smaller OptiScale-25 Device format.* [2] *Available in original Opticap Capsules.*

## Charged Depth Filters

| | Mini Capsule | Pod | 10-Inch Opticap Capsule | Stacked Lenticular Disc Filters |
|---|---|---|---|---|
| Millistak®+ HC | | | | |
| Grade A1HC | • | • | • | • |
| Grade B1HC | • | • | • | • |
| Grade C0HC | • | • | • | • |
| Grade D0HC | • | • | • | • |
| Millistak+ DE | • | •[5] | • | • |
| Millistak+ CE | • | •[5] | • | • |
| Viresolve Prefilter | •[6] | •[5] | • | |

[5] *Coming in 2005* [6] *Viresolve prefilter available in OptiScale-40 device format.*


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** These tables only includes items mentioned in this selection guide. Visit our on-line catalogue at* www.millipore.com *for details on other filtration products. See connections on page 6.*

| | Cartridges | | | | | Gamma-compatible or Sterile Opticap XL or XLT Capsules | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 5-Inch Cartridge | 10-Inch Cartridge | 20-Inch Cartridge | 30-Inch Cartridge | 40-Inch Cartridge | Opticap XL3 Capsule | Opticap XL4 Capsule | Opticap XL5 Capsule | Opticap XL10 Capsule | Opticap XLT10 Capsule | Opticap XLT20 Capsule | Opticap XLT30 Capsule |
| | | | | | | | | | | | | |
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| | • | • | • | • | • | | | | | | | |

[3] *Aervent membrane is sold in the larger Aervent-50 Capsule format.* [4] *Single-layer filters only.*

## TFF Device Guide

| | Pellicon XL | Mini | Cassette | Maxi | 2-stack | 4-stack | 10-stack | 20-stack |
|---|---|---|---|---|---|---|---|---|
| Microfiltration (MF) | | | | | | | | |
| Prostak™ Modules | | | | | • | • | • | • |
| Pellicon® Cassettes | • | • | • | • | | | | |
| Ultrafiltration (UF) | | | | | | | | |
| Pellicon® Cassettes | • | • | • | • | | | | |

See *Understanding Your Filter Options* for an explanation of each filter format and available connections.

# Understanding Your Filter Options

From small-scale screening tools, disposable capsules and Pods, to cartridges, stacked disc filters and MF or UF cassettes, Millipore produces a wide range of device formats for use in process development, pilot and full-scale manufacturing. Filter formats vary depending on membrane/media type. See page 2 to match the filter membrane with its' available device formats. For complete product specifications please refer to the on-line catalogue at **www.millipore.com/products.**

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Charged Depth Filters . . . . . 5
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Tangential Flow Filtration . . . . . 7




## Quality Built Right In

Millipore's approach to quality is driven by our high standards of excellence and those of our customers. Our goal: to exceed customer expectations and ensure a sustained ability to provide a predicable, reliable supply of high-caliber products developed and produced in best-of-class environments.

Millipore membranes and devices are designed, developed and manufactured in accordance with a quality management system approved by an accredited registering body to an ISO® 9000 quality systems standard. Filters are subject to an array of quality control release tests, shipped with a certificate of quality and supported by a validation guide for compliance with regulatory agencies. For traceability, identification and easy document control, each device is clearly marked and labeled.

## Choosing the Proper Pleated Filter

Filtration media is available in a range of formats. The choice provides each user an opportunity to match the filtration solution to their needs and process scale. In making your decision, consideration should be given to batch size, validation effort, lead time, labor, sterilization philosophy, economics, interfaces with process equipment and facilities services. All of these play a role and should be evaluated.

### Single vs. Multi-layer Filters

When a process requires several filtration steps in series it is important to evaluate single vs. multi-layer options. Multiple stage single-layer filtration processes can be optimized by testing and adjusting each individual stage. This approach results in the most economical process possible. To ensure an optimized process single-layer filtration will require more small-scale testing, hardware, labor and validation.

Multiple layer filters are commonly used to compress multiple stages of single-layer filtration into a single element. Using filters with multiple layers shortens development time, and requires less hardware, floor-space and labor while assuring a robust and economical process.

### Cartridge Filters

Cartridge filters are commonly used for larger processes requiring more filtration area and/or lower unit operating cost. Cartridge filters are used in conjunction with stainless steel housings and can safely withstand multiple steam-in-place cycles. Millipore cartridge filters are robust, strong and reliable. A variety of connections (See pg. 6) are available to suit your application and housing needs.

### OptiScale Small-scale Disposable Capsules

OptiScale Disposable Capsule filters provide a convenient small-volume option for process development, screening and scaling. OptiScale capsule filters offer 13.8 $cm^2$ of filtration area, are faster and easier to set-up and use than conventional 47 mm discs with holders, and are completely disposable.

### OptiScale-25 Small Volume Disposable Capsule Filters

*Exclusively for the Viresolve Family of Filters*

OptiScale-25 capsules with Viresolve NFR or NFP membranes are used in small volume applications where feedstock requirements are minimal. Providing an active filtration area of 3.5 $cm^2$, these small devices are useful as an evaluation tool for impurity studies, protein passage studies, membrane area determination and virus validation. OptiScale-25 disposable capsule filters are sold as Evaluation Kits, each kit including 9 capsules: 3 devices each, of 3 different membrane lots.

**Opticap XL and XLT Disposable Capsule Filters**

Disposable capsule filters save you time and resources. They eliminate the need to sanitize between cycles and reduce the associated validation effort. Capsules are commonly used in processes where fast turnover between cycles is required and to minimize worker exposure to hazardous process fluids. Capsule filters, depending upon the materials of construction, are autoclavable or gamma-compatible. Capsule filters have the unique advantage of being able to be coupled with disposable biocontainers into process assemblies that can be irradiated prior to use, thus assuring sterility.

Opticap capsules are available in a wide range of sizes, filter medias and inlet/outlet connections (See pg. 6). They are proven performers in the industry. No matter what your application need Millipore has the right configuration.

### Sterile Options

Millipore Express and Durapore sterilizing-grade membranes are offered in 2 capsule options. Gamma-compatible capsules are designed to be sterilized by gamma irradiation prior to use and disposed of after use. Sterile Opticap XL or XLT capsules are gamma irradiated by Millipore and delivered sterile to your facility.

Opticap XL disposable capsule filters have a unique design to minimize hold-up volume and reduce production losses and are available in a range of sizes for easy scale-up.

Opticap XLT disposable T-line capsule filters are available with or without a pressure gauge port for ease in monitoring process conditions. The T-line design accommodates series or parallel filtration to match your application needs. A specially-designed stand enables quick and easy integration into your existing process.

**Millipak Disposable Filter Units**

Millipak sterilizing-grade units have a unique stacked filter design that allows minimal hold-up volume and no particle shedding, making Millipak filters ideally suited for high value-added applications such as sterile finish and fill. Millipak filters are available in a range of filtration areas from 100 $cm^2$ to 1,000 $cm^2$, and have adjustable upstream vents and drain valves with O-ring seal and several connections for easy process control (See pg. 6).

### Sterile Options

Millipak Gamma Gold units are available gamma-compatible and can be easily sterilized by gamma irradiation prior to use and disposed of after use.

## Charged Depth Filters

The ultimate in charged depth technology, Millistak+ filters utilize unique membranes and high quality materials. Choose any Millistak+ media type; HC, DE, CE or A and be confident that it will perform in a reliable manner .

**Millistak+ Mini Small-scale Disposable Capsules**

Millistak+ Mini capsules offer 23 $cm^2$ of effective surface area and are ideally suited for process development, screening and small-scale trials.

**Opticap Disposable Capsule Filters**

Original Opticap capsule filters with Millistak+ medias are ideal for pilot-scale and small-scale manufacturing.

**Stacked Lenticular Disc Filters**

Ideal for large-scale processing, stacked depth filters are available in 12- and 16-inch diameters and various surface areas to accommodate a range of process volumes.

**The Millistak+ Pod**

This new patented modular disposable filter format was designed for greater flexibility and productivity. Each Pod consists of one, five or ten 0.1 $m^2$ filter cells in a self-contained disposable enclosure. The Pods are lightweight and modular, and do not require housings. Multiple Pods can be configured up to 30 $m^2$ to match process volumes.

# A Choice of Inlet/Outlet Connections

## Opticap XL Capsules

Sanitary flange 38 mm
(1 ½ in.) inlet/outlet

Sanitary flange 19 mm
(¾ in.) inlet/outlet

Hose barb 14 mm
(9⁄16 in.) inlet/outlet

Sanitary flange 38 mm
(1 ½ in.) inlet and hose barb
14 mm (9⁄16 in.) outlet

Sanitary flange 19 mm
(¾ in.) inlet and hose barb
14 mm (9⁄16 in.) outlet

## Opticap XLT Capsules (Available with or without gauge port)

Sanitary flange 38 mm
(1 ½ in.) inlet/outlet

Sanitary flange 38 mm
(1 ½ in.) inlet and hose barb
16 mm (5⁄8 in.) outlet

Hose barb 16 mm
(5⁄8 in.) inlet/outlet

Hose barb 25 mm
(1 in.) inlet/outlet

Opticap XLT
full view

## Millipak Filter Units*

6 mm (¼ in.)
NPTM inlet/outlet

38 mm (1 ½ in.)
sanitary flange inlet/outlet

19 mm (¾ in.)
sanitary flange inlet/outlet

14 mm (9⁄16 in.)
hose barb inlet/outlet

6 mm (¼ in.) hose barb
inlet/outlet with filling bell

## OptiScale Capsules

19 mm (¾ in.) sanitary flange
inlet/6 mm (¼ in.) stepped
hose barb inlet/outlet

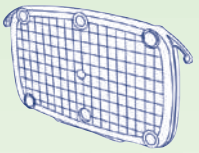
6 mm (¼ in.) stepped
hose barb inlet/outlet

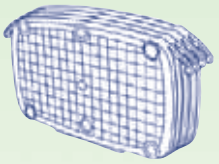
19 mm (¾ in.)
sanitary flange inlet/outlet

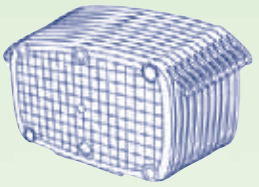
## Millistak+ Mini Capsules

14 mm (9⁄16 in.) stepped
hose barb inlet/outlet

## Charged Depth Filters


1-Cell Pod with 38 mm (1 ½ in.)
sanitary flange fittings


5-Cell Pod with 38 mm (1 ½ in.)
sanitary flange fittings


10-Cell Pod with 38 mm (1 ½ in.)
sanitary flange fittings

**Opticap Capsules**

19 mm (¾ in.)
sanitary flange inlet/outlet

14 mm (9⁄16 in.)
hose barb inlet/outlet

## Cartridge Configurations

Code 0 Style Cartridges
2-222 O-ring outlet

Code 7 Style Cartridges 2-226 O-ring
locking outlet with spear assembly

Code M Style Cartridges
2-118 O-ring

Optiseal Cartridges
2-123 O-ring

Code 5 Style Cartridges
2-222 O-ring outlet with spear assembly

Code N Style Cartridges
2-226 O-ring locking outlet

** Inlet and outlet connections can be configured to meet your needs. Some connections are size and media/membrane dependant. Contact Millipore for details.*

## Tangential Flow Filtration

Millipore offers a variety of scalable microfiltration (MF) and ultrafiltration (UF) devices that utilize our patented high-quality, void-free membranes offering you greater reliability, consistency and performance.

### The Pellicon Family of Devices

The Pellicon UF family of cassettes comes in a choice of feed channel screens. The A screen (tight screen) is optimized to operate Biomax® void-free membranes with maximum flux in low viscosity applications. C Screen (coarse screen) is optimized for PLC membranes with maximum flow and is ideal for low to intermediate viscosity applications. For concentration and diafiltration, the C Screen is optimized for use with Biomax 50 to 1,000 kD membranes. For viscous solutions or solutions with higher levels of suspended solids, V Screen is the ideal choice. Pellicon filters have a low minimum working volume — as low as 175 mL of retentate volume per square meter of membrane area — permitting high concentration factors to be reached with low starting volumes and maximizing the recovery of small sample volumes. No matter what Pellicon device you use, they all operate with the same pressure drop, flow velocity and concentration profile for true, rapid and simple scale-up.

#### Pellicon XL 50

Pellicon XL 50 cassettes incorporate Millipore's superior membranes in a small area (50 $cm^2$) device. These cassettes operate with the same pressure drop, flow velocity and concentration profile as the larger Pellicon cassettes.

#### Mini Cassettes

Mini filters (0.1 $m^2$) and holders are designed for laboratory filtration of 1 L to 10 L volumes, and scale-up linearly to Pellicon cassettes.

#### Standard Cassettes

Cassettes (0.5 $m^2$) are designed for pilot and small scale manufacturing of 5 L to 100 L and linearly scale to Pellicon Maxi cassettes.

#### Maxi Cassettes

Pellicon Maxi cassettes (2.5 $m^2$) are used in large scale manufacturing.

### Prostak Family of Devices

#### MF Modules

Designed for clarification applications, the Prostak MF module is a tangential flow stacked plate device with an open-channel configuration. These filters can be steamed and are available in 2-stack (0.17 $m^2$), 4-stack (0.33 $m^2$), 10-stack (0.84 $m^2$), and 20-stack (1.7 $m^2$) modules.

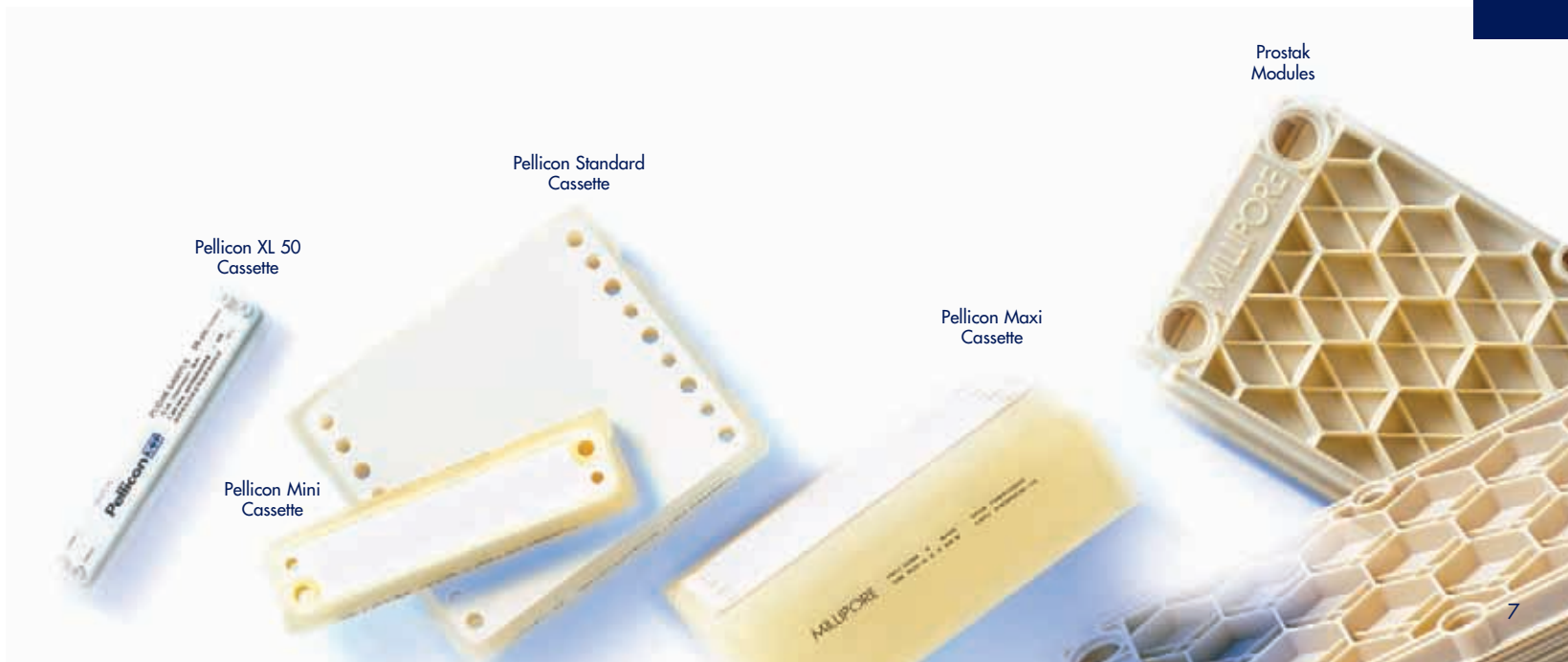
#### UF Modules

Designed for concentration and diafiltration applications that require broad solvent compatibility, Prostak UF modules are a tangential flow stacked plate device with screened channels. These filters are available in 4-stack (0.39 $m^2$), 10-stack (0.93 $m^2$), and 20-stack (1.9 $m^2$) modules.

## TFF Membrane Overview*

| Name | Pore Sizes/NMWL | Materials | pH Range Continuous | Protein Binding |
|---|---|---|---|---|
| Durapore Series | 0.1, 0.22, 0.45, 0.65 µm | Hydrophilic PVDF | 2 – 10 at 25 °C | Very low |
| Biomax Series | 5, 8, 10, 30, 50, 100, 300 500 and 1,000 kD | High flux hydrophilic polyethersulfone | 1 – 14 at 25 °C | Low |
| Ultracel® PLC Series | 5, 10, 30, 100, 300 and 1,000 kD | Composite regenerated cellulose | 2 – 12 at 25 °C | Very low |

* *This table includes only products mentioned in this selection guide.*
*Visit our on-line catalogue at* **www.millipore.com** *for details on other available TFF membranes.*



# Turnkey Solutions to Optimize Processing



## Mobius Flexible Bioprocessing Solutions

*We bring together unmatched expertise and disposable technologies to offer a complete, ready-to-process solution.*

- *Innovative separation and purification technologies*
- *The right connectology to link various steps in the process*
- *Quality container systems*
- *Custom design services*
- *Validation services and support*

mobius
flexible bioprocessing solutions

***No matter what your application, step or scale, Millipore's Mobius solutions can revolutionize your process.***

Turnkey disposable Mobius solutions can replace traditional stainless steel operations. Comprised of a suite of modular technologies and services that can be integrated into a ready-to-process solution, Mobius brings all the pieces together into a complete, validated system for your specific application needs.

*Mobius solutions can offer:*

- Reduced validation and cleaning efforts
- Quick turnaround times
- Flexibility in multi-product facilities
- Superior control over process consistency and security
- Reduced capital requirements

Millipore's Mobius technologies offer increased flexibility and easily integrate into existing processes, whether plastic-to-plastic or plastic-to-stainless.

## Filtration Devices

Millipore's high quality membrane filters are available in a wide range of self-contained, disposable configurations that don't require a stainless steel housing. Gamma-compatible and sterile options are available and are ideal for value-added applications. From small scale devices like Millipak filters to large volume Opticap XLT capsules, Millipore has a variety of filter technologies that are part of the suite of Mobius solutions.

For details on many disposable filter formats and inlet/outlet choices, see the Quick Reference Guide on page 2 and Understanding Your Filter Options beginning on page 4.

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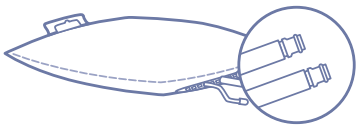
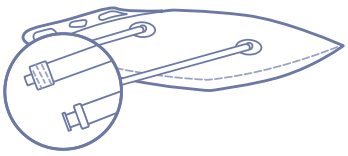
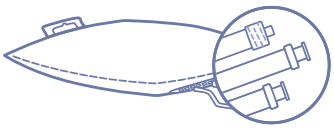
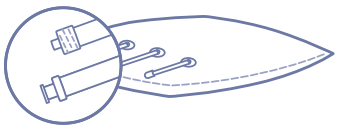
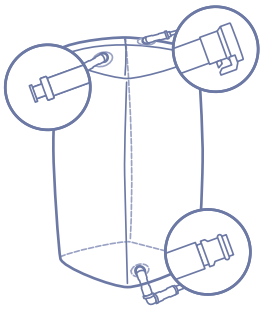
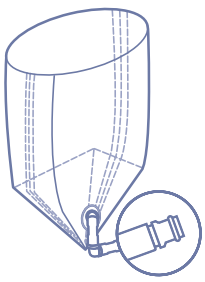
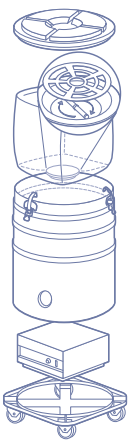
## Container Systems

Millipore offers HyClone HyQ® CX5-14 and CX3-9 BioProcess Container™ (BPC®) systems as a part of integrated Mobius assembly solutions. A wide range of flexible, scalable containers are available from small volume 2-D configurations starting at 50 mL to large volume 3-D configurations up to 1,500 L.

| Two-dimensional Systems* | | Applications | Size |
|---|---|---|---|
| **2-D Small Volume End-Ported Hanging Pillow** |  | Process development, QC sampling, bulk product storage, transfer and collection | 50, 100, 250, 500 mL; 1, 2 L |
| **2-D Small Volume Face-Ported** |  | Process development, QC sampling, bulk product storage, transfer and collection | 200, 500 mL; 1, 2 L |
| **2-D Hanging/Freezing** |  | Applications requiring freezing/thawing, heat inactivation and irradiation of product | 5, 10, 20 L |
| **2-D Large Volume Face-Ported** |  | Formulation and filling of sterile media, buffers and other process liquids; bioreactor and fermentation feed and harvest; waste collection; transportation and storage of bulk intermediate and final product | 5, 10, 20, 50, 100, 200, 300 L |

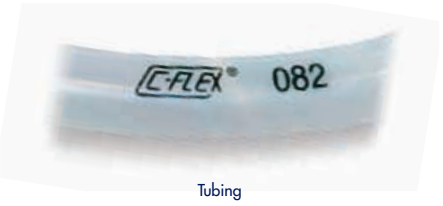
| Three-dimensional Systems* | | Applications | Size |
|---|---|---|---|
| **3-D Rectangular** |  | Formulation and filling of sterile media, buffers and other process liquids; bioreactor and fermentation feed and harvest; waste collection; transportation and storage of bulk intermediate product | 50, 100, 200, 500, 900, 1,000, 1,500 L |
| **Tank Liner** |  | Media hydration, non-sterile mixing, refiltration of process intermediates | 50, 100, 200, 300, 500, 1,000, 1,500 L |
| **Mixtainer™ Mixing System** |  | Stirring, suspending, holding and storing sterile fluids | 50, 100, 200 L |

** Bioprocessing containers are only available as an integrated part of Mobius assemblies. Containers are not sold individually. Other container systems, configurations and accessories are available. Contact your Millipore Application Specialist.*

## Connectology

Disposable Lynx® connectors, clamps and valves provide the critical link between disposable fluid paths and the various steps in your process. The easy to use and reliable Lynx connectors enable fluid transfer while maintaining sterility. Tubing and manifolds are also available in a range of sizes and materials to fit your application.

Lynx Connectors

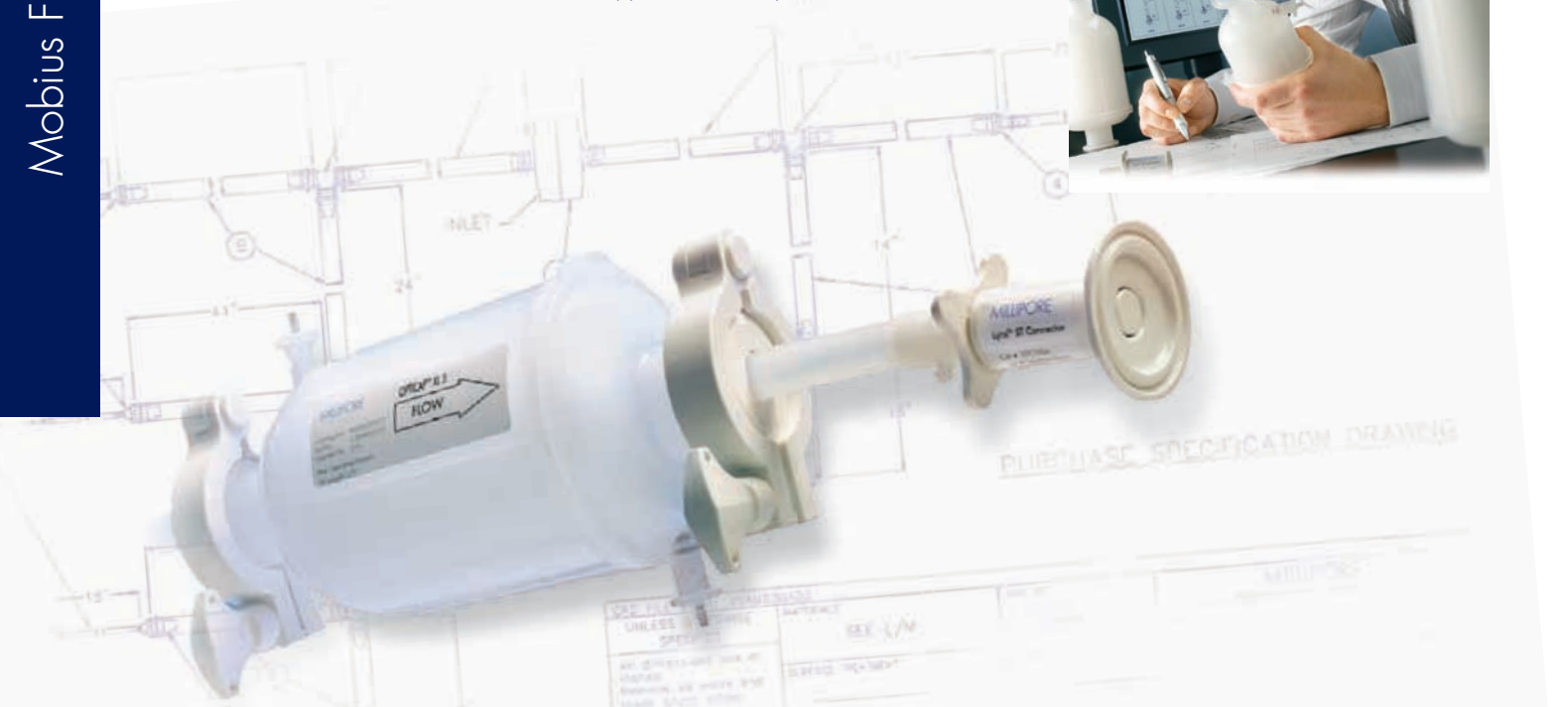



Tubing

| Product | Type | Size | Cat No. |
|---|---|---|---|
| Lynx ST | Steam To | ¾ in. TC x ¼ in. hose barb<br>1 ½ in. TC x ½ in. hose barb | STC11FHN01<br>STC2T12N01 |
| Lynx S2S | Sterile To Sterile | ½ in. x ½ in. hose barb | SSCSHB2N01 |
| Lynx Non-Metal Clamp | | ½ in. – ¾ in. TC<br>1 in. – 1 ½ in. TC | P83062<br>P83063 |
| Other Connector Types Available | • Colder Products® Quick Connects<br>• BioQuate Connectors | | Only sold in integrated systems |
| Tubing and Manifolds | • C-Flex®<br>• Platinum-cured Silicone | | Only sold in integrated systems |

## Custom Design Services

Millipore is your one point of contact for the design, development and validation support of your Mobius assembly systems. Our partnerships with various container and component vendors means you get the best combination of expertise and technology in a single, integrated solution to fit your application and specifications.




## Validation and Support Services

Validation and regulatory compliance are essential components of any process. Unlike any other partner, Millipore Access Services team (See pg. 12) can provide assistance on how to successfully integrate and validate innovative Mobius processes into your operations.

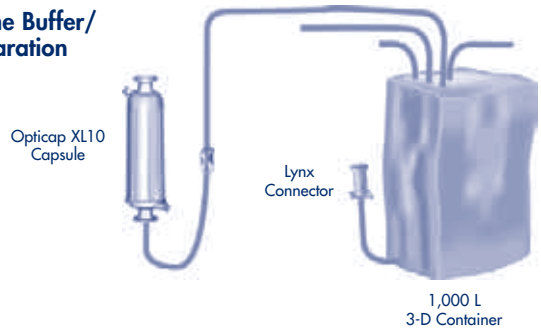
## Innovative Mobius Assembly Systems

By combining Mobius flexible manufacturing technologies – filters, connectors and valves, container systems, etc. – together with custom design services, validation services and support, Millipore offers turnkey solutions that can optimize your process. Many traditional stainless processes can be transformed with single-use, integrated and validated assemblies.

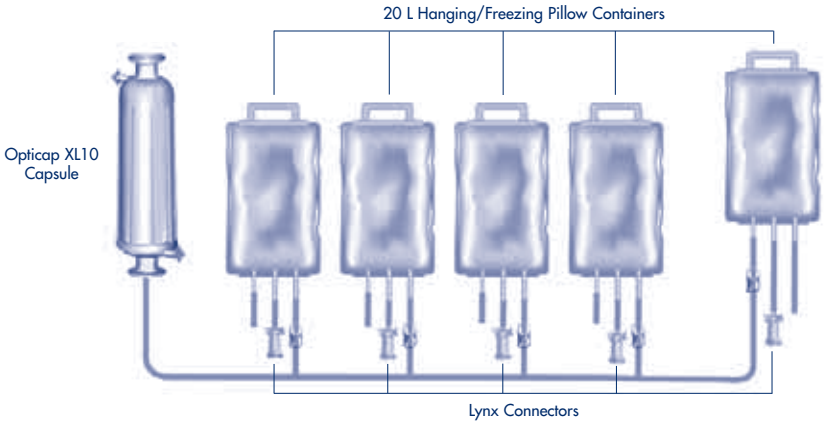
## Examples of Integrated Mobius Processes

### Small Volume Buffer/ Media Preparation

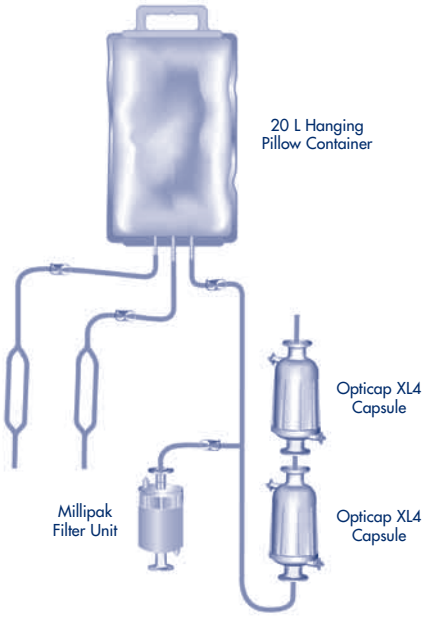
### Large Volume Buffer/ Media Preparation



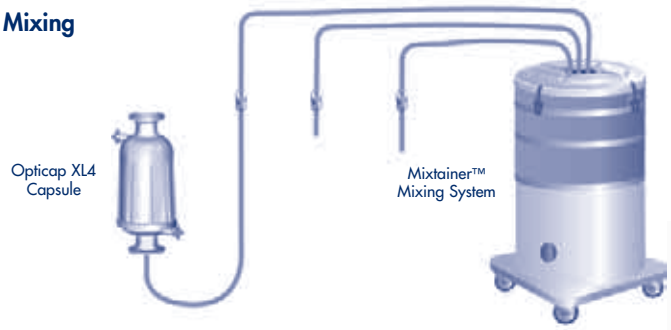

### Bulk Filling




### Final Filling and Dispensing




### Mixing




mobius

Transform your process with Mobius flexible solutions from Millipore.

Mobius Flexible Solutions

# Proven Application, Validation and Engineering Support

ACCESS
SERVICES

For over 50 years Millipore has been providing unmatched application, validation and engineering expertise to biotech and pharmaceutical companies around the globe. We understand the need for quality, cost containment and regulatory compliance at every stage from molecule to market.

Our philosophy is simple; be scientific, be practical, perform. We ask the right questions, practice excellent science, understand your application and the required validation, and provide defensible documentation. We let you concentrate on the success of your busines while the Access Team concentrates on the details.

## Streamlining Compliance

Millipore has developed a range of regulatory and compliance services designed to meet the stringent data and documentation requirements of regulatory agencies.

- Microbial Retention Testing
- Drug Product Integrity Testing
- Extractable Analysis
- Drug Product Compatibility Analysis

Our process and validation expertise, coupled with our knowledge of world regulatory guidance, has enabled many drug manufacturers to successfully prove compliance while saving time and valuable resources.

ACCESS **LAB** solutions provide access to a team of professionals and state-of-the-art facilities. Our global team is ready to provide standard service packages or individually customized solutions to all your scaling, development, validation and testing needs.

ACCESS **ON-SITE** brings our expertise directly to you. Our field-based team provides a variety of services based on your needs. From on-site trials and testing to equipment validation, operator training, and system commissioning — if you need Millipore on-site we'll be there.

## Process Development and Optimization

Whether at your site or in our lab, our comprehensive range of products, integrated technologies and support services will help solve your process development, optimization, validation and monitoring challenges.

- Design, Technology Selection, Sizing and Protocol Development
- Process Scaling, Optimization and Yield Improvements
- Validation and Engineering
- Process Monitoring, Quality Control and Technical Support

## Comprehensive Training and Certification Programs

Millipore's Access Training program is recognized around the globe for its range of courses and quality content. From scale-up without compromise to advanced aseptic processing validation school, Millipore's training courses and seminars keep pace with the industry's changing needs. Millipore is certified by IACET and is authorized to grant continuing education credits. Documentation to satisfy GMP requirements is provided for certified training courses.

## Advanced Process Design and Engineering

From process design reviews and software consulting to system commissioning and validation, our team supports the entire process.

- User Requirements Specification
- Functional Specification
- System Design and Construction
- FAT, SAT, IQ/OQ and PQ Assistance
- SOP Development
- Operator Training and Certification

**Visit www.millipore.com/accessservices today!**

ACCESS **CONSULTING** offers guidance in a variety of areas. From development, scaling and optimization strategies to system and plant design and regulatory compliance Millipore experts partner with you to ensure success.

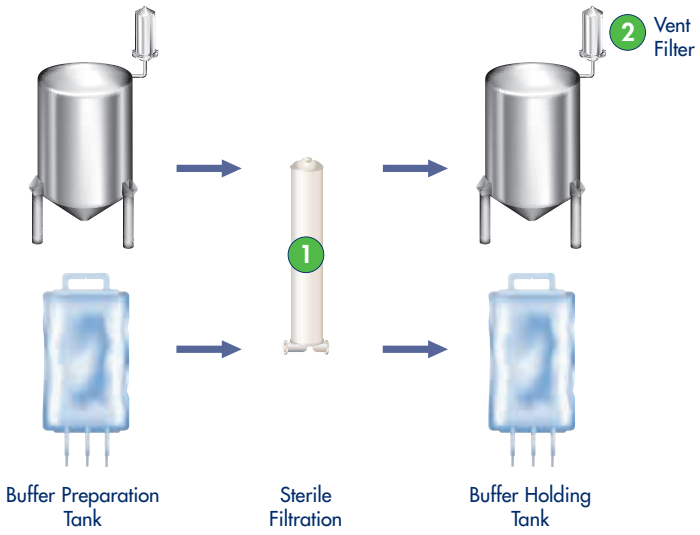
ACCESS **TRAINING** provides a broad range of training and certification courses to support the development and compliance needs of your personnel. Training includes lectures, workshops, hands-on exercises and case studies. Training is conducted in one of our worldwide training centers or at your facility.

# Buffer Preparation

Buffer solutions are required for a number of purification steps and are critical to process efficiency and final product quality. Buffer filtration is critical to protect the life of chromatography columns, downstream UF steps and to ensure an endotoxin-free final product. Buffer solutions are typically filtered using sterilizing-grade membrane filters. Depending on the salt concentration and buffer properties, prefiltration may be needed.

For details on Tank Venting 2, see page 70.

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Sterile Filtration**<br>• Utilize a sterilizing-grade membrane to remove contaminants and ensure sterility<br>• Must work with a variety of process fluids across a range of pH levels<br>• Preserve product purity<br>• Able to withstand demanding steam-in-place requirements<br>• Depending on salt concentration and fluid properties, prefiltration may be needed | 1 Single-layer Millipore Express SHF 0.2 µm Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site |
| | 1 Double-layer Millipore Express SHC 0.5 µm + 0.2 µm Filters | • Sterilizing-grade PES membrane with an additional PES prefilter layer all in one pleated device<br>• Double-layer construction provides excellent capacity even in high salt conditions >1M<br>• PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric PES pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site |

*ALTERNATIVE: If a PVDF membrane is needed, Millipore's Durapore Family of Filters have been a proven performer for decades.*

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www.lenntech.com Fax. +31-152-616-289

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| OptiScale Capsules with Single-layer Millipore Express SHF 0.2 µm Membrane | 13.8 $cm^2$ | SGEPA47FF3 |
| OptiScale Capsules with Double-layer Millipore Express SHC 0.5 µm + 0.2 µm Membrane | 13.8 $cm^2$ | SHGEA47FF3 |

## Recommended Filters

| Volume | Filter Format | Area/Filter | Catalogue No. |
|---|---|---|---|
| | Single-layer Millipore Express SHF Filters | | |
| 0–400 L | Opticap XL3 Capsule | 0.16 $m^2$ | KGEPA03TT3 |
| | Opticap XL3 Gamma-compatible Capsule | 0.17 $m^2$ | KGEPG03TT3 |
| 400–800 L | Opticap XL5 Capsule | 0.29 $m^2$ | KGEPA05TT1 |
| | Opticap XL5 Gamma-compatible Capsule | 0.31 $m^2$ | KGEPG05TT1 |
| | 5-inch Cartridge | 0.29 $m^2$ | CGEP75TP3 |
| 800–1,600 L | Opticap XL10 Capsule | 0.54 $m^2$ | KGEPA10TT1 |
| | Opticap XLT10 Capsule | 0.54 $m^2$ | KGEPA1TTT1 |
| | Opticap XL10 Gamma-compatible Capsule | 0.57 $m^2$ | KGEPG10TT1 |
| | Opticap XLT10 Gamma-compatible Capsule | 0.57 $m^2$ | KGEPG1TTT1 |
| | 10-inch Cartridge | 0.54 $m^2$ | CGEP71TP3 |
| 1,600–3,200 L | Opticap XLT20 Capsule | 1.08 $m^2$ | KGEPA2TTT1 |
| | Opticap XLT20 Gamma-compatible Capsule | 1.14 $m^2$ | KGEPG2TTT1 |
| | 20-inch Cartridge | 1.08 $m^2$ | CGEP72TP3 |
| 3,200–4,800 L | Opticap XLT30 Capsule | 1.62 $m^2$ | KGEPA3TTT1 |
| | Opticap XLT30 Gamma-compatible Capsule | 1.71 $m^2$ | KGEPG3TTT1 |
| | 30-inch Cartridge | 1.62 $m^2$ | CGEP73TP3 |
| | Double-layer Millipore Express SHC Filters | | |
| 0–200 L | Opticap XL3 Capsule | 0.13 $m^2$ | KHGEA03TT3 |
| | Opticap XL3 Gamma-compatible Capsule | 0.13 $m^2$ | KHGEG03TT3 |
| 200–450 L | Opticap XL5 Capsule | 0.23 $m^2$ | KHGEA05TT1 |
| | Opticap XL5 Gamma-compatible Capsule | 0.24 $m^2$ | KHGEG05TT1 |
| | 5-inch Cartridge | 0.23 $m^2$ | CHGE75TS3 |
| 450–1,000 L | Opticap XL10 Capsule | 0.49 $m^2$ | KHGEA10TT1 |
| | Opticap XLT10 Capsule | 0.49 $m^2$ | KHGEA1TTT1 |
| | Opticap XL10 Gamma-compatible Capsule | 0.54 $m^2$ | KHGEG10TT1 |
| | Opticap XLT10 Gamma-compatible Capsule | 0.54 $m^2$ | KHGEG1TTT1 |
| | 10-inch Cartridge | 0.49 $m^2$ | CHGE71TS3 |
| 1,000–2,000 L | Opticap XLT20 Capsule | 0.98 $m^2$ | KHGEA2TTT1 |
| | Opticap XLT20 Gamma-compatible Capsule | 1.09 $m^2$ | KHGEG2TTT1 |
| | 20-inch Cartridge | 0.98 $m^2$ | CHGE72TS3 |
| 2,000–3,000 L | Opticap XLT30 Capsule | 1.47 $m^2$ | KHGEA3TTT1 |
| | Opticap XLT30 Gamma-compatible Capsule | 1.63 $m^2$ | KHGEG3TTT1 |
| | 30-inch Cartridge | 1.47 $m^2$ | CHGE73TS3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

# Cell Culture Media Preparation

The cells used to produce therapeutic proteins require a precise balance of nutrients to support their reproduction and growth. These nutrients are provided in the form of growth media, which must be sterile. For media containing animal derived components, final sterilizing-grade filtration should assure the removal of bacteria and mycoplasma.

Media is typically mixed in bulk and then aseptically transferred to the bioreactor. Prefiltration is used to remove the bulk of particulate and colloidal contaminants from the media in order to extend the service life of the filter train. Prefilters must be sized appropriately to handle batch to batch media variability, as well as ensuring that the sterile media fill in the bioreactor is completed successfully and on time.

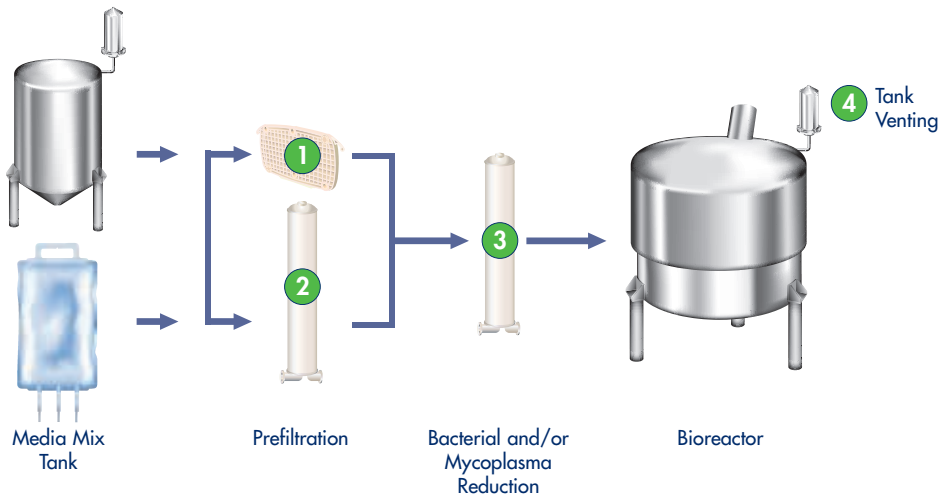
**Filter Recommendations**

Millipore's Express SHC and SHR filters are recommended for the scale-up and manufacture of tissue culture media for the production of MAbs, vaccines, and other biological therapeutics that require high throughput, flow rates and superior filtration economics.

For details on Tank Venting 4, see page 70.



## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Bacterial and Mycoplasma Retention** | | |
| **Sterile Filtration**<br>• Remove bacteria and mycoplasma to preserve the aseptic barrier around the bioreactor<br>• Filter material must have low cytotoxicity, low extractables and low binding of key nutrients<br>• Preserve cell growth components | 3 Millipore Express SHR Filters<br><br>(0.1 µm or 0.1 µm + Prefilter Layer) | • Sterilizing-grade membrane designed to remove high levels of mycoplasma and bacteria over a range of moderately plugging to highly fouling streams<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• 100% integrity tested to ensure quality<br>• Robust construction validated for multiple SIP cycles<br>• Can be integrity tested on-site<br>• Available in single-layer 0.1 µm or double-layer 0.1 µm with prefilter layer. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |

*ALTERNATIVE: If PVDF or low protein binding membrane is needed please include Durapore 0.1 µm filters in your small-scale trials.*

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Prefiltration**<br>(If sterile filter capacity is <1,000 L/m$^2$ then a prefilter should be considered.)<br>• Protect sterilizing-grade filters by effectively removing lipids, colloids and particles without binding vital media constituents<br>• Cost effectiveness and timely separation<br>• Needs to work irrespective of variation from batch to batch<br>• Preserve cell growth properties | 1 Triple-layer Millistak+ HC Filters<br><br>(Grade A1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs<br><br>*ALTERNATIVE: If media stream is less plugging, Millipore suggests testing single-layer Grade 75DE Millistak+ Filters in your small-scale trials.* |
| | 2 Triple-layer Polysep II Filters<br><br>(Grade W1, 1.0 µm + 0.2 µm + 0.1 µm) | • Designed for the protection of downstream 0.1 µm sterilizing-grade filters<br>• Triple layer construction ensures high particle loading and capacity<br>• Validated for multiple sanitization and SIP cycles<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Non-fiber releasing structure preserves product purity<br>• Cell growth studies confirm growth properties are preserved |
| **Bacterial Retention Only**<br>**Sterile Filtration**<br>• Must remove bacteria<br>• Filter material must have low cytotoxicity, low extractables and low binding of key nutrients | 3 Millipore Express SHC 0.5 µm + 0.2 µm Filters | • Sterilizing-grade PES membrane with an additional PES prefilter layer all in one pleated device<br>• Designed for media additives and prefiltered tissue culture media in batch sizes ranging from 100 to 20,000 L<br>• Asymmetric pore structure delivers superior flow rates and capacity over a range of CHO and NS0 media<br>• PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• 100% integrity tested to ensure quality<br>• Can be integrity tested on-site<br>• Robust construction validated for multiple SIP cycles<br><br>*ALTERNATIVE: If a PVDF or low protein binding membrane is needed please include Durapore 0.22 µm Filters in your small-scale trials.* |
| **Prefiltration**<br>(Not normally required for serum-free media)<br>• Protect sterilizing-grade filters by effectively removing lipids, colloids and particles without obstructing the flow of vital media constituents<br>• To ensure cost effectiveness and timely separation filters should have high flow rates and consistently high throughput<br>• Needs to work irrespective of variation from batch to batch<br>• Filter should have low extractables and low binding of key nutrients | 1 Triple-layer Millistak+ HC Filters<br><br>(Grade A1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs<br><br>*ALTERNATIVE: If media stream is less plugging, Millipore suggests testing Grade 75DE Millistak+ Filters in your small-scale trials.* |
| | 2 Double-layer Polysep II Filters<br><br>(Grade W3, 1.0 µm + 0.2 µm) | • Designed for the protection of downstream 0.22 µm sterilizing-grade filters<br>• Reliable prefilter for concentrated solutions across a full range of flow rates<br>• Robust construction ensures high particle loading and capacity<br>• Validated for multiple sanitization and SIP cycles<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Non-fiber releasing structure preserves product purity<br>• Cell growth studies confirm growth properties are preserved |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. | Filter Format | Area/Filter | Catalogue No. |
|---|---|---|---|---|---|
| **Bacterial and Mycoplasma** | | | **Bacterial** | | |
| OptiScale Capsules | | | OptiScale Capsules | | |
| Single-layer Millipore Express SHR 0.1 µm membrane | | SVEPA47FF3 | Double-layer Millipore Express SHC 0.5 µm + 0.2 µm membrane | | SHGEA47FF3 |
| Double-layer Millipore Express SHR 0.1 µm + prefilter layer | 13.8 $cm^2$ | SHVEA47FF3 | Durapore 0.22 µm membrane | 23 $cm^2$ | SVGLA47FF3 |
| Durapore 0.1 µm membrane | | SVVLA47FF3 | Double-layer Polysep II Grade W3 media | | SGW3A47FF3 |
| Triple-layer Polysep II Grade W1 media | | SGW1A47FF3 | | | |
| Millistak+ Mini Capsules | | | Millistak+ Mini Capsules | | |
| Triple-layer Grade A1HC | 23 $cm^2$ | MA1HC23HH3 | Triple-layer Grade A1HC | 23 $cm^2$ | MA1HC23HH3 |
| Single-layer Grade 75DE | | M75DE23HH3 | Single-layer Grade 75DE | | M75DE23HH3 |

## Recommended Filters

| Media/Membrane | Area/Filter | Range No Prefiltration Volume | Range With Prefiltration Volume | Cartridge | Standard Capsule | Gamma-compatible Capsule |
|---|---|---|---|---|---|---|
| **Bacterial and Mycoplasma Retention** | | | | | | |
| **Millipore Express SHR Filters*** | | | | | | |
| Single-Layer (0.1 µm) | | | | | | |
| Opticap XL3 Capsule | 0.12 $m^2$ | 70 L | 250 L | | KVEPA03TT3 | KVEPG03TT3 |
| Opticap XL5 Capsule or 5-inch Cartridge | 0.22 $m^2$ | 150 L | 480 L | CVEP75TS3 | KVEPA05TT1 | KVEPG05TT1 |
| Opticap XL10 Capsule or 10-inch Cartridge | 0.50 $m^2$ | 250 L | 950 L | CVEP71TS3 | KVEPA10TT1 | KVEPG10TT1 |
| Opticap XLT20 Capsule or 20-inch Cartridge | 1.00 $m^2$ | 550 L | 1,900 L | CVEP72TS3 | KVEPA2TTT1 | KVEPG2TTT1 |
| Opticap XLT30 Capsule or 30-inch Cartridge | 1.50 $m^2$ | 850 L | 2,800 L | CVEP73TS3 | KVEPA3TTT1 | KVEPG3TTT1 |
| Double-Layer (0.1 µm + prefilter) | | | | | | |
| Opticap XL3 Capsule | 0.14 $m^2$ | 100 L | 300 L | | KHVEA03TT3 | KHVEG03TT3 |
| Opticap XL5 Capsule or 5-inch Cartridge | 0.27 $m^2$ | 200 L | 600 L | CHVE75TS3 | KHVEA05TT1 | KHVEG05TT1 |
| Opticap XL10 Capsule or 10-inch Cartridge | 0.53 $m^2$ | 450 L | 1,400 L | CHVE71TS3 | KHVEA10TT1 | KHVEG10TT1 |
| Opticap XLT20 Capsule or 20-inch Cartridge | 1.07 $m^2$ | 950 L | 2,800 L | CHVE72TS3 | KHVEA2TTT1 | KHVEG2TTT1 |
| Opticap XLT30 Capsule or 30-inch Cartridge | 1.60 $m^2$ | 1,400 L | 4,200 L | CHVE73TS3 | KHVEA3TTT1 | KHVEG3TTT1 |

| Media/Membrane | Area/Filter | Low Range | High Range | Cartridge | Standard Capsule | |
|---|---|---|---|---|---|---|
| **Triple-layer Polysep II** | | | | | | |
| Grade W1 (1.0 µm + 0.2 µm + 0.1 µm) Filters | | | | | | |
| Opticap XL5 Capsule or 4-inch Cartridge | 0.19 $m^2$ | 95 L | 380 L | CGW1M4S03 | KGW1A05TT1 | – |
| Opticap XL10 Capsule or 10-inch Cartridge | 0.46 $m^2$ | 230 L | 920 L | CGW171S03 | KGW1A10TT1 | – |

| Media/Membrane | Area/Filter | Low Range | High Range | Stack | Capsule | Pod |
|---|---|---|---|---|---|---|
| **Triple-layer Millistak+ HC Filters** | | | | | | |
| Grade A1HC | | | | | | |
| 1-cell Pod | 0.1 $m^2$ | 100 L | 300 L | | | MA1HC01FS1 |
| 5-cell Pod | 0.5 $m^2$ | 500 L | 1,500 L | | | MA1HC05FS1 |
| Opticap Capsule, 10-inch | 650 $cm^2$ | 65 L | 195 L | | KA1HC10FF1 | |
| 2-cell Stack, 16-inch | 0.45 $m^2$ | 450 L | 1,350 L | LA1HCH6S6 | | |
| 8-cell Stack, 16-inch | 1.8 $m^2$ | 1,800 L | 5,400 L | LA1HCG6S2 | | |
| 10-cell Pod | 1.0 $m^2$ | 1,000 L | 3,000 L | | | MA1HC10FS1 |

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| Media/Membrane | Area/Filter | Range No Prefiltration Volume | Range With Prefiltration Volume | Cartridge | Standard Capsule | Gamma-compatible Capsule |
|---|---|---|---|---|---|---|
| **Bacterial Retention Only** | | | | | | |
| **Double-layer Millipore Express SHC (0.5 µm + 0.2 µm) Filters** | | | | | | |
| Opticap XL3 Capsule | 0.13 $m^2$ | 230 L | 650 L | | KHGEA03TT3 | KHGEG03TT3 |
| Opticap XL5 Capsule or 5-inch Cartridge | 0.23 $m^2$ | 440 L | 1,230 L | CHGE75TS3 | KHGEA05TT1 | KHGEG05TT1 |
| Opticap XL10 Capsule or 10-inch Cartridge | 0.49 $m^2$ | 1,000 L | 2,800 L | CHGE71TS3 | KHGEA10TT1 | KHGEG10TT1 |
| Opticap XLT20 Capsule or 20-inch Cartridge | 0.98 $m^2$ | 2,000 L | 5,600 L | CHGE72TS3 | KHGEA2TTT1 | KHGEG2TTT1 |
| Opticap XLT30 Capsule or 30-inch Cartridge | 1.47 $m^2$ | 3,000 L | 8,300 L | CHGE73TS3 | KHGEA3TTT1 | KHGEG3TTT1 |

| Media/Membrane | Area/Filter | Low Range | High Range | Cartridge | Standard Capsule | |
|---|---|---|---|---|---|---|
| **Double-layer Polysep II** Grade W3 (1.0 µm + 0.2 µm) Filters | | | | | | |
| Opticap XL5 Capsule or 4-inch Cartridge | 0.19 $m^2$ | 95 L | 380 L | CGW3M4S03 | KGW3A05TT1 | – |
| Opticap XL10 Capsule or 10-inch Cartridge | 0.46 $m^2$ | 230 L | 920 L | CGW371S03 | KGW3A10TT1 | – |

| Media/Membrane | Area/Filter | Low Range | High Range | Stack | Standard Capsule | Pod |
|---|---|---|---|---|---|---|
| **Triple-layer Millistak+ HC Filters** Grade A1HC | | | | | | |
| 1-cell Pod | 0.1 $m^2$ | 100 L | 300 L | – | – | MA1CH01FS1 |
| 5-cell Pod | 0.5 $m^2$ | 500 L | 1,500 L | – | – | MA1HC05FS1 |
| Opticap Capsule | 650 $cm^2$ | 65 L | 195 L | – | KA1HC10FF1 | – |
| 2-cell Stack, 16-inch | 0.45 $m^2$ | 450 L | 1,350 L | LA1HCH6S6 | – | – |
| 8-cell Stack, 16-inch | 1.8 $m^2$ | 1,800 L | 5,400 L | LA1HCG6S2 | – | – |
| 10-cell Pod | 1.0 $m^2$ | 1,000 L | 3,000 L | – | – | MA1HC10FS1 |

**Millipore Express SHR Filters are in final development. Specifications may change. Consult technical services for details.*

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

# Microbial Cell Culture Clarification

Microbial fermentation is used to produce products such as therapeutic proteins, antibiotics, hormones, enzymes, amino acids, blood substitutes and alcohol. The product of interest may be expressed by microbial cells or be intracellular (cytoplasmic or periplasmic in the case of bacterial cells).

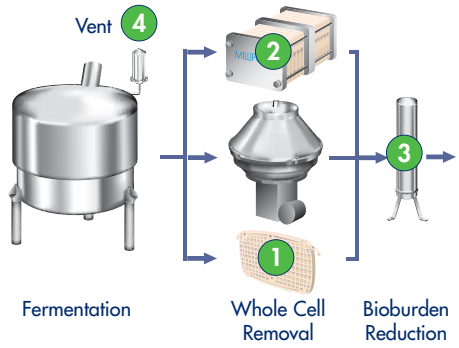
To obtain the desired product, it must first be separated from the cells and other debris in the fermentation broth. In the case of intracellular products, the cells must be lysed and the lysate must be clarified to remove the cell debris and other contaminants. Depending on the process, additional clarification steps may be needed. Filtration is also used to process fermentation additives such as nutrients and pH adjusters prior to addition into the fermenter.

Due to the variability in the expression system characteristics such as percent solids, starting turbidity, particle size distribution and more between various microbial strains, no specific sizing recommendations are provided in this guide. Please contact your local applications specialist for details regarding your application.

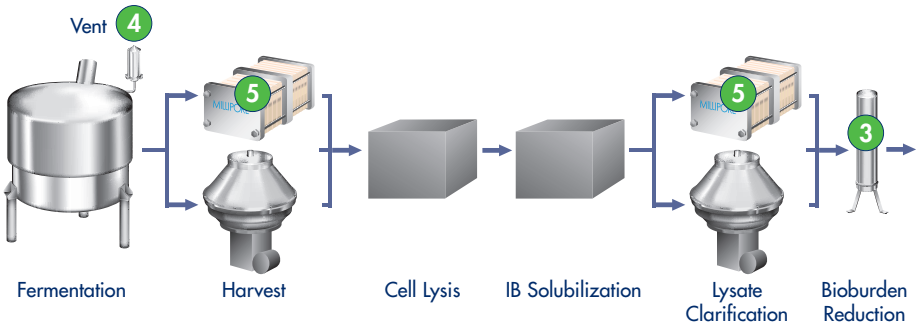
For details on Tank Venting 4, see page 70.

## 1 Typical **Process Flow**

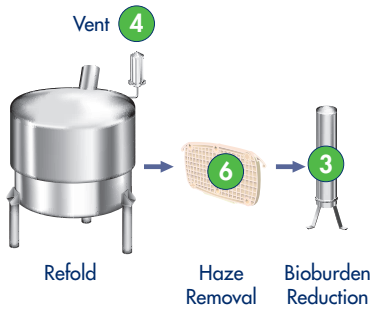
### Expressed Protein



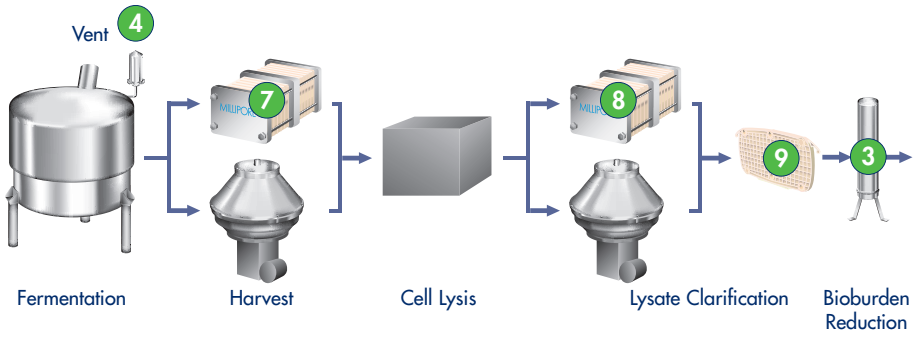

### Inclusion Body (IB) Purification



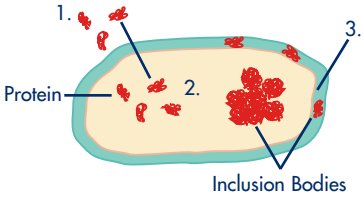

### Protein Refold Pool Clarification




### Intracellular Protein (cytoplasmic or periplasmic)




## Where Can Recombinant Proteins Be Located?




1. Secreted into the media
2. Cytoplasm: soluble or aggregated inclusion bodies
3. Periplasm: soluble or aggregated inclusion bodies

# 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Expressed Protein Clarification** | | |
| **Cell Removal**<br>• Separation of cells from fermenter broth and product recovery in filtrate fluid<br>• High solids content in feed stream, which makes centrifugation a viable option<br>• Feed stream quality can vary depending upon cell type and culture conditions | ***Depth Filtration*** | |
| | 1 Double-layer Millistak+ HC Filters<br><br>(Grade C0HC or D0HC) | • Better suited for small to medium size fermenters up to 1,000 L or larger volumes with low usage rates of less than 10 batches/year<br>• Double-layer design enhances loading capacity and filtrate quality<br>• Unique configuration allows compression of multiple process steps into one, lowering overall filtration costs<br>• Selection of C0HC or D0HC media grade depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | ***TFF with Microfiltration Membrane*** | |
| | 2 Prostak Open-Channel Modules with 0.22 µm or 0.1 µm Durapore Membrane | • Open-channel design ideal for fluids containing high cell densities and solids<br>• High flux at low transmembrane pressure allows volume reduction as fluid gets concentrated<br>• Robust construction for multiple use<br>• Validated for multiple SIP cycles<br>• Selection of 0.22 µm or 0.1 µm membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | *ALTERNATIVE: For small volumes with low cell densities, Pellicon V Screen Cassettes with 0.22 µm or 0.1 µm Durapore Membrane should be tested in your small-scale trials.* | |
| **Inclusion Body Clarification** | | |
| **Harvest/Clarification**<br>• Recovery of Inclusion Bodies post cell lysis and before solubilization step<br>• Elimination of waste fluid in the filtrate<br>• High solids content in feed stream, which makes centrifugation a viable technology option<br>• Feed stream quality can vary depending on cell type and culture conditions | ***TFF with Microfiltration Membrane*** | |
| | 5 Prostak Open-Channel Modules with 0.22 µm or 0.1 µm Durapore Membrane | • Open-channel design accommodates high loading capacity and retention for haze removal post refolding<br>• High flux at low transmembrane pressure<br>• Robust construction allows multiple use<br>• Validated for multiple SIP cycles<br>• Selection of 0.22 µm or 0.1 µm membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | *ALTERNATIVE: For small volumes with low cell densities, Pellicon V Screen Cassettes with 0.22 µm or 0.1 µm Durapore Membrane should be tested in your small-scale trials.* | |



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| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Protein Refold Pool Clarification** | | |
| **Clarification**<br>• Removal of haze formed during refold process after product protein solubilization<br>• Mostly small sub-micron particles<br>• Some fluid variability depending on refold process conditions | 6 Triple-layer Millistak+ HC Filters<br><br>(Grade A1HC or B1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs<br>• The selection of Grade A1HC or B1HC depends on the fluid particle size distribution and should be based on small-scale testing |
| **Intracellular Protein Clarification** | | |
| **Cell Harvest**<br>• Cell recovery from the fermenter broth, elimination of waste fluid in the filtrate<br>• High solids content in feed stream, which makes centrifugation a viable technology option<br>• Feed stream quality can vary depending on cell type and culture conditions | ***TFF with Microfiltration Membrane***<br>7 Prostak Open-Channel Modules with 0.22 µm or 0.1 µm Durapore Membrane | • Open-channel design ideal for fluids containing high cell densities and solids<br>• High flux at low transmembrane pressure<br>• Robust construction allows multiple use<br>• Validated for multiple SIP cycles<br>• Selection of 0.22 µm or 0.1 µm membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| **Lysate Clarification**<br>• Removal of debris, particles and colloids generated during the lysis step, and product recovery in filtrate fluid<br>• Feed stream quality can vary depending on cell culture type and lysis conditions<br>• Challenging separation due to large amount of particles and wide range in size<br>• Typically requires several process steps in series (primary clarification then polishing filtration)<br>• Centrifugation is a viable option as first separation step, but still requires downstream polishing filtration | ***Primary Clarification – TFF with Microfiltration Membrane***<br>8 Prostak Open-Channel Modules with 0.22 µm or 0.1 µm Durapore Membrane | • Open-channel design ideal for fluids with high solids levels<br>• High flux at low transmembrane pressure<br>• Robust construction allows multiple use<br>• Validated for multiple SIP cycles<br>• Selection of 0.22 µm or 0.1 µm membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | 8 Pellicon V Screen Cassettes with 0.22 µm or 0.1 µm Durapore Membrane, or 1,000 kD Biomax Membrane | • More suited for lower cell density and solid content fluids<br>• Suspended screen in feed channel allows higher turbulence enhancing separation process<br>• Complete range of devices for easy scale-up<br>• Selection of 0.22 µm, 0.1 µm or 1,000 kD membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | ***Polishing Filtration – Depth Filtration***<br>9 Triple-layer Millistak+ HC Filters<br><br>(Grade A1HC or B1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs<br>• The selection of Grade A1HC or B1HC depends on the fluid particle size distribution and should be based on small-scale testing. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Sterile Filtration** | | |
| **Bioburden Reduction**<br>• Reduces bioburden<br>• Protects downstream chromatography and UF/DF steps<br>• Maintains yield of dilute protein and preserves purity<br>• Sterilizing-grade filtration required | 3 Single-layer Durapore 0.22 µm PVDF Filters | • Sterilizing-grade PVDF membrane won't bind valuable protein<br>• 100% Integrity tested to ensure proven performance<br>• Can be integrity testable on-site<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and, in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 3 Millipore Express SHC 0.5 µm + 0.2 µm PES Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site<br>• Although double-layer 0.5 µm + 0.2 µm (SHC) is typical for this application, single-layer 0.2 µm (SHF) is also available. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| Pellicon V Screen Mini Cassettes | | |
| Durapore 0.22 µm membrane | 0.1 $m^2$ | P2GVPPV01 |
| Durapore 0.1 µm membrane | | P2VVPPV01 |
| Biomax 1,000 kD membrane | | P2B01MV01 |
| Prostak 2-stack Modules | | |
| Durapore 0.22 µm membrane | 0.17 $m^2$ | PSGVAG021 |
| Durapore 0.1 µm membrane | | PSVVAG021 |
| Millistak+ Mini Capsules | | |
| Double-layer Grade D0HC | 23 $cm^2$ | MD0HC23HH3 |
| Double-layer Grade C0HC | | MC0HC23HH3 |
| Triple-layer Grade B1HC | | MB1HC23HH3 |
| Triple-layer Grade A1HC | | MA1HC23HH3 |
| OptiScale Capsules | | |
| Durapore 0.22 µm membrane | 13.8 $cm^2$ | SVGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | | SGEPA47FF3 |
| Millipore Express SHC 0.5 µm + 0.2 µm membrane | | SHGEA47FF3 |

## Recommended Filters

| Media/Membrane | Small-Scale Processing <100 L<br>Device (area/filter) | Catalogue No. | Large-Scale Processing >100 L<br>Device (area/filter) | Catalogue No. |
|---|---|---|---|---|
| **TFF MF** | | | | |
| **Pellicon V Screen Cassettes** | | | | |
| Durapore 0.1 µm membrane | Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | P2VVPPV01<br>P2VVPPV05 | Maxi Cassette (2 $m^2$) | P2VVPPV20 |
| Durapore 0.22 µm membrane | Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | P2GVPPV01<br>P2GVPPV05 | Maxi Cassette (2 $m^2$) | P2GVPPV20 |
| Biomax 1,000 kD membrane | Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | P2B01MV01<br>P2B01MV05 | Maxi Cassette (2 $m^2$) | P2B01MV20 |
| **Prostak Open-Channel Modules** | | | | |
| Durapore 0.22 µm membrane | 2-stack (0.17 $m^2$)<br>4-stack (0.33 $m^2$) | PSGVAG021<br>PSGVAG041 | 10-stack (0.84 $m^2$)<br>20-stack (1.7 $m^2$) | PSGVAG101<br>SK2P484E0 |
| Durapore 0.1 µm membrane | 2-stack (0.17 $m^2$)<br>4-stack (0.33 $m^2$) | PSVVAG021<br>PSVVAG041 | 10-stack (0.84 $m^2$)<br>20-stack (1.7 $m^2$) | PSVVAG101<br>SK2P127E1 |
| **Depth Filtration** | | | | |
| **Triple-layer Millistak+ HC Filters Grade A1HC** | 1-cell Pod (0.1 $m^2$)<br>5-cell Pod (0.5 $m^2$)<br>10-inch Opticap (650 $cm^2$)<br>2-cell 16-inch stack (0.45 $m^2$) | MA1HC01FS1<br>MA1HC05FS1<br>KA1HC10FF1<br>LA1HCH6S6 | 10-cell Pod (1 $m^2$)<br>8-cell 16-inch stack (1.8 $m^2$) | MA1HC10FS1<br>LA1HCG6S2 |
| **Grade B1HC** | 1-cell Pod (0.1 $m^2$)<br>5-cell Pod (0.5 $m^2$)<br>10-inch Opticap (650 $cm^2$)<br>2-cell 16-inch stack (0.45 $m^2$) | MB1HC01FS1<br>MB1HC05FS1<br>KB1HC10FF1<br>LB1HCH6S6 | 10-cell Pod (1 $m^2$)<br>8-cell 16-inch stack (1.8 $m^2$) | MB1HC10FS1<br>LB1HCG6S2 |
| **Double-layer Millistak+ HC Filters Grade C0HC** | 1-cell Pod (0.1 $m^2$)<br>5-cell Pod (0.5 $m^2$)<br>10-inch Opticap (650 $cm^2$)<br>2-cell 16-inch stack (0.45 $m^2$) | MC0HC01FS1<br>MC0HC05FS1<br>KC0HC10FF1<br>LC0HCH6S6 | 10-cell Pod (1 $m^2$)<br>8-cell 16-inch stack (1.8 $m^2$) | MC0HC10FS1<br>LC0HCG6S2 |
| **Grade D0HC** | 1-cell Pod ( 0.1 $m^2$)<br>5-cell Pod (0.5 $m^2$)<br>10-inch Opticap (650 $cm^2$)<br>2-cell 16-inch stack (0.45 $m^2$) | MD0HC01FS1<br>MD0HC05FS1<br>KD0HC10FF1<br>LD0HCH6S6 | 10-cell Pod (1 $m^2$)<br>7-cell 16-inch stack (1.6 $m^2$) | MD0HC10FS1<br>LD0HCG6S2 |
| **Sterilizing-grade Filtration** | | | | |
| **Durapore 0.22 µm PVDF Filters** | Opticap XL2 Capsule (0.09 $m^2$)<br>Opticap XL4 Capsule (0.19 $m^2$)<br>Opticap XL5 Capsule (0.35 $m^2$)<br>5-inch Cartridge (0.35 $m^2$) | KVGLA02TT3<br>KVGLA04TT3<br>KVGLA05TT1<br>CVGL75S01 | Opticap XL10 Capsule (0.69 $m^2$)<br>Opticap XLT10 Capsule (0.69 $m^2$)<br>Opticap XLT20 Capsule (1.4 $m^2$)<br>Opticap XLT30 Capsule (2.1 $m^2$)<br>10-inch Cartridge (0.69 $m^2$)<br>20-inch Cartridge (1.4 $m^2$)<br>30-inch Cartridge (2.1 $m^2$) | KVGLA10TT1<br>KVGLA1TTT1<br>KVGLA2TTT1<br>KVGLA3TTT1<br>CVGL71TP3<br>CVGL72TP3<br>CVGL73TP3 |
| **Millipore Express SHC 0.5 µm + 0.2 µm PES Filters** | Opticap XL3 Capsule (0.13 $m^2$)<br>Opticap XL5 Capsule (0.24 $m^2$)<br>5-inch Cartridge (0.24 $m^2$) | KHGEA03TT3<br>KHGEA05TT1<br>CHGE75TS3 | Opticap XL10 Capsule (0.49 $m^2$)<br>Opticap XLT10 Capsule (0.49 $m^2$)<br>Opticap XLT20 Capsule (0.98 $m^2$)<br>Opticap XLT30 Capsule(1.47 $m^2$)<br>10-inch Cartridge (0.49 $m^2$)<br>20-inch Cartridge (0.98 $m^2$)<br>30-inch Cartridge (1.47 $m^2$) | KHGEA10TT1<br>KHGEA1TTT1<br>KHGEA2TTT1<br>KHGEA3TTT1<br>CHGE71TS3<br>CHGE72TS3<br>CHGE73TS3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

# Mammalian Cell Culture Clarification

Mammalian cells are cultured by a variety of methods at a range of volumes for the production of therapeutic and diagnostic proteins. The cells are grown in a bioreactor or fermentation vessel. The first step in the purification process is the removal of whole cells, cell debris, and particulates prior to further downstream unit operations.

## Understanding Cell Lines

Cell lines typically employed for mammalian cell culture include CHO, NS0 hybridoma cells, baby hamster kidney (BHK) cells, and PER.C6™ human cells. The most commonly employed mammalian cell line used for mammalian cell culture at production scale volumes are the CHO and NS0 cell lines. These cell types are relatively easy to genetically engineer, have been extensively characterized, are relatively easy to grow at large scale, and can excrete high titers of recombinant proteins in solution. Both CHO and NS0 cell lines can produce high protein expression levels, however, cell viability tends to decline with high protein expression levels. Low cell viabilities burden downstream purification with cell debris, DNA, host cell protein and other impurities. NS0 cell lines require additional media components to support cell growth (i.e. cholesterols, lipids, etc.) that can affect downstream processing. Hybridoma cells have relatively low protein expression levels (<100 mg/L) and are typically grown to low cell viabilities (<30%) which complicates the harvest operation.

## Cell Culture Media Types

Cell culture medium typically contains amino acids, vitamins, electrolytes and may contain hormones, growth factors, plant hydrolysates, animal serum, antibiotics, antioxidants, antifoams, cell stabilizers and other components.

Types of media include serum based, serum free, animal free, and protein free or chemically defined. Serum based and serum free media are widely used since they can be used to grow a broad range of cell types and cell lines such as CHO or NS0 cells.

For details on Tank Venting 5, see page 70.

## Comparison of Cell Culture Operating Modes

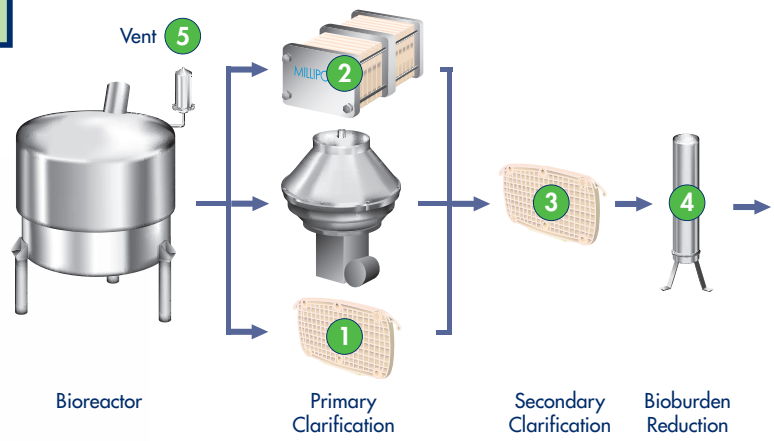
| Operating Mode | Batch | Fed-Batch | Perfusion |
|---|---|---|---|
| Media Addition | Initial | Periodic | Continuous |
| Fluid Harvest | Final | Final | Continuous |
| Benefits | Less cell debris, lower risk of contamination | High titer | High productivity<br>Low capital cost |
| Disadvantages | Fair productivity<br>Frequent equipment turnover | Maintaining sterility in bioreactor<br>Medium cell debris | Maintaining sterility in bioreactor and in the primary clarifier<br>High cell debris |

## Cell Culture Characterization

Evaluating the cell culture characteristics is a critical step in developing an effective process. Below are some generally accepted culture properties that can be used to help guide the technology selection.

| Culture Type | Batch<br>3–7 Days | Fed-Batch<br>7–15 Days | Perfusion<br>>20 Days |
|---|---|---|---|
| PSV (Solids) | Low<br><1% | Medium<br>2–3% | High<br>>3% |
| Cell Density | Low<br>$<3 \times 10^6$ cells/mL | Medium to High<br>$5–15 \times 10^6$ cells/mL | High<br>$>10–15 \times 10^6$ cells/mL |
| Cell Viability | High<br>>90% | Medium to High<br>20–90% | Medium to Low<br><50% |
| Colloids | Low | Medium to High | High |
| Turbidity | Low<br><200 NTU | High<br>500 to >1,000 NTU | Very High<br>>>1,000 NTU |
| Ease of Clarification | Easy | Medium | Difficult |

## 1 Typical **Process Flow**



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# 2 Understanding the **Options**



| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Primary Clarification**<br>• Removes whole cells and solids from bioreactor fluid and recover product in filtrate<br>• Requires high capacity<br>• Wide feed stream variability depending on cell culture type and conditions<br>• If solid content is too high, centrifugation becomes preferred technology | 1 Double-layer Millistak+ HC Filters<br><br>(Grade D0HC or C0HC) | • For bioreactors volumes up to 1,000 L or larger volumes with low usage rates of less than 10 batches/year<br>• Double layer design enhances loading capacity and filtrate quality<br>• Unique configuration allows compression of multiple process steps into one, lowering overall filtration costs.<br>• Selection of C0HC or D0HC media grade depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | 2 Prostak Open-Channel Modules with 0.22 µm or 0.65 µm Durapore Membrane | • Best suited for large bioreactors >1,000 L or bioreactors with high usage rates of more than 10 batches/year<br>• Open-channel design accommodates fluids containing low to medium cell density and solids<br>• High flux at low transmembrane pressure<br>• Robust construction allows multiple use<br>• Validated for multiple SIP cycles<br>• Selection of 0.22 µm or 0.65 µm membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| | *ALTERNATIVE: If the cell culture has high cell viability and relatively low cell counts, all polypropylene Polygard-DF depth filter cartridges is a viable option for bioreactors up to 1,000 L.* | |
| **Secondary Clarification or Polishing**<br>• Feed stream quality can vary depending on cell type, culture conditions, and primary clarification technology | 3 Triple-layer Millistak+ HC Filters<br><br>(Grades A1HC or B1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• High filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs<br>• The selection of grade A1HC or B1HC depends on the fluid particle size distribution and should be based on small-scale testing. |
| | *ALTERNATIVE: If process hardware dictates the use of pleated cartridge filters, Millipore suggests testing Polysep II multi-layer prefilters in your small-scale trials.* | |
| **Bioburden Reduction**<br>• Reduces bioburden<br>• Protects downstream chromatography and UF/DF steps<br>• Maintains yield of dilute protein and preserves purity<br>• Sterilizing-grade filtration recommended | 4 Single-layer Durapore 0.22 µm Filters | • Sterilizing-grade low-protein binding PVDF membrane<br>• 100% Integrity testing to ensure performance<br>• Can be integrity testable on-site<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and, in single-layer or multi-layer configurations to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 4 Double-layer Millipore Express SHC 0.5 µm + 0.2 µm Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site<br>• Although double-layer 0.5 µm + 0.2 µm (SHC) is typical for this application, single-layer 0.2 µm (SHF) filters are available. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| Prostak 2-stack Modules | | |
| Durapore 0.65 µm membrane | 0.17 $m^2$ | PSDVAG021 |
| Durapore 0.22 µm membrane | | PSGVAG021 |
| Millistak+ Mini Capsules | | |
| Double-layer Grade D0HC | 23 $cm^2$ | MD0HC23HH3 |
| Double-layer Grade C0HC | | MC0HC23HH3 |
| Triple-layer Grade B1HC | | MB1HC23HH3 |
| Triple-layer Grade A1HC | | MA1HC23HH3 |
| OptiScale Capsules | | |
| Durapore 0.22 µm membrane | 13.8 $cm^2$ | SVGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | | SGEPA47FF3 |
| Millipore Express SHC 0.5 µm + 0.2 µm membrane | | SHGEA47FF3 |
| Polysep II W1 1.0 µm + 0.2 µm + 0.1 µm media | | SGW1A47FF3 |
| Polysep II W3 1.0 µm + 0.2 µm media | | SGW3A47FF3 |
| Polygard DF 5.0 µm 2-inch cartridges | – | DF05M2S03 |

## Recommended Filters

| Media/Membrane | Small-Scale Processing <100 L: Device (area/filter) | Catalogue No. | Large-Scale Processing >100 L: Device (area/filter) | Catalogue No. |
|---|---|---|---|---|
| **TFF MF** | | | | |
| Prostak Open-Channel Modules 0.65 µm Membrane | 2-stack (0.17 $m^2$) | PSDVAG021 | 10-stack (0.84 $m^2$) | PSDVAG101 |
| | 4-stack (0.33 $m^2$) | PSDVAG041 | 20-stack (1.7 $m^2$) | SK2P446E0 |
| 0.22 µm Membrane | 2-stack (0.17 $m^2$) | PSGVAG021 | 10-stack (0.84 $m^2$) | PSGVAG101 |
| | 4-stack (0.33 $m^2$) | PSGVAG041 | 20-stack (1.7 $m^2$) | SK2P484E0 |
| **Depth Filtration** | | | | |
| Triple-layer Millistak+ HC Grade A1HC | 1-cell Pod (0.1 $m^2$) | MA1HC01FS1 | 10-cell Pod (1 $m^2$) | MA1HC10FS1 |
| | 5-cell Pod (0.5 $m^2$) | MA1HC05FS1 | | |
| | 10-inch Opticap (650 $cm^2$) | KA1HC10FF1 | | |
| | 2-cell stack (0.45 $m^2$) | LA1HCH6S6 | 8-cell stack (1.8 $m^2$) | LA1HCG6S2 |
| Grade B1HC | 1-cell Pod (0.1 $m^2$) | MB1HC01FS1 | 10-cell Pod (1 $m^2$) | MB1HC10FS1 |
| | 5-cell Pod (0.5 $m^2$) | MB1HC05FS1 | | |
| | 10-inch Opticap (650 $cm^2$) | KB1HC10FF1 | | |
| | 2-cell stack (0.45 $m^2$) | LB1HCH6S6 | 8-cell stack (1.8 $m^2$) | LB1HCG6S2 |
| Double-layer Millistak+ HC Filters Grade C0HC | 1-cell Pod (0.1 $m^2$) | MC0HC01FS1 | 10-cell Pod (1 $m^2$) | MC0HC10FS1 |
| | 5-cell Pod (0.5 $m^2$) | MC0HC05FS1 | | |
| | 10-inch Opticap (650 $cm^2$) | KC0HC10FF1 | | |
| | 2-cell stack (0.45 $m^2$) | LC0HCH6S6 | 8-cell stack (1.8 $m^2$) | LC0HCG6S2 |
| Grade D0HC | 1-cell Pod ( 0.1 $m^2$) | MD0HC01FS1 | 10-cell Pod (1 $m^2$) | MD0HC10FS1 |
| | 5-cell Pod (0.5 $m^2$) | MD0HC05FS1 | | |
| | 10-inch Opticap (650 $cm^2$) | KD0HC10FF1 | | |
| | 2-cell stack (0.45 $m^2$) | LD0HCH6S6 | 7-cell stack (1.6 $m^2$) | LD0HCG6S2 |
| **Sterilizing-grade Filtration** | | | | |
| Durapore 0.22 µm PVDF Filters | Opticap XL2 Capsule (0.09 $m^2$) | KVGLA02TT3 | Opticap XL10 Capsule (0.69 $m^2$) | KVGLA10TT1 |
| | Opticap XL4 Capsule (0.19 $m^2$) | KVGLA04TT3 | Opticap XLT10 Capsule (0.69 $m^2$) | KVGLA1TTT1 |
| | Opticap XL5 Capsule (0.35 $m^2$) | KVGLA05TT1 | Opticap XLT20 Capsule (1.4 $m^2$) | KVGLA2TTT1 |
| | 5-inch Cartridge (0.35 $m^2$) | CVGL75S01 | Opticap XLT30 Capsule (2.9 $m^2$) | KVGLA3TTT1 |
| | | | 10-inch Cartridge (0.69 $m^2$) | CVGL71TP3 |
| | | | 20-inch Cartridge (1.4 $m^2$) | CVGL72TP3 |
| | | | 30-inch Cartridge (2.1 $m^2$) | CVGL73TP3 |
| Millipore Express SHC 0.5 µm + 0.2 µm PES Filters | Opticap XL3 Capsule (0.13 $m^2$) | KHGEA03TT3 | Opticap XL10 Capsule (0.49 $m^2$) | KHGEA10TT1 |
| | Opticap XL5 Capsule (0.23 $m^2$) | KHGEA05TT1 | Opticap XLT10 Capsule (0.49 $m^2$) | KHGEA1TTT1 |
| | 5-inch Cartridge (0.23 $m^2$) | CHGE75TS3 | Opticap XLT20 Capsule (0.98 $m^2$) | KHGEA2TTT1 |
| | | | Opticap XLT30 Capsule(1.47 $m^2$) | KHGEA3TTT1 |
| | | | 10-inch Cartridge (0.49 $m^2$) | CHGE71TS3 |
| | | | 20-inch Cartridge (0.98 $m^2$) | CHGE72TS3 |
| | | | 30-inch Cartridge (1.47 $m^2$) | CHGE73TS3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

# Protein and Antibody Downstream Processing

This section covers the series of operations immediately following the cell culture, lysate or refold clarification process. The first of these unit operations is a capture where the product protein is typically bound to an affinity chromatography resin and then recovered by elution with a buffer solution. Once recovered, the protein solution is further purified and concentrated through filtration or additional chromatography steps until the final solution is ready for final fill operations.

See buffer preparation, mammalian cell culture clarification, microbial cell culture clarification and aseptic processing sections for details on those operations.

*The primary goals for successful protein processing are:*

- High product purity
- High product quality (or activity)
- Robustness (consistency from batch to batch)
- High product yield
- Controlled bioburden and endotoxin
- Economical

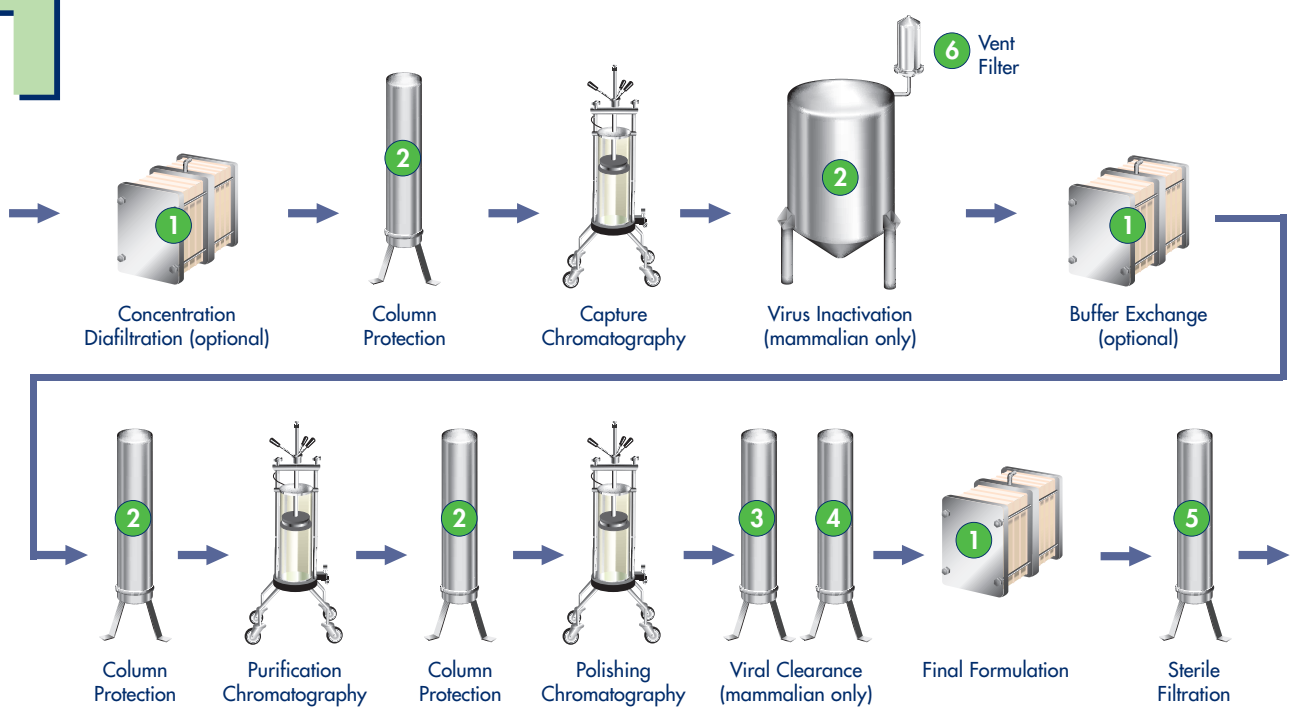
Cartridge filtration is used for chromatography column and TFF protection and sterile filtration. Ultrafiltration (Tangential Flow Filtration) steps are used to reduce batch volumes and exchange buffers for efficient column operation or final formulation. Sequential capture, purification and polishing columns remove impurities to achieve specified product purity with high product recovery. Efficient process design maximizes the difference between product and impurity binding. More than one type of virus clearance step (inactivation, filtration) is required to ensure product safety in mammalian cell and transgenic expression systems.

For details on Tank Venting 6, see page 70.

**Other Relevant Applications**


Buffer Preparation . . . . . 14
Cell Culture Media Preparation . . . . . 16
Microbial Cell Culture Clarification . . . . 20
Mammalian Cell Culture Clarification . . 25
Final Aseptic Filling . . . . . 60
Tank Venting . . . . . 70


## 1 Typical **Process Flow**





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# 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Column Protection**<br>• Reduces bioburden levels<br>• Protects and extends the life of downstream chromatographic media<br>• Preserves product purity | 2 Durapore PVDF Filters<br><br>(0.22 µm or Multilayer 0.45 µm + 0.22 µm) | • Sterilizing-grade filters assure reduction of contaminating microorganisms that shorten the life of costly chromatography media<br>• Low-binding PVDF membrane assures protein yeld<br>• 100% Integrity testing ensures quality<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br>• Can be integrity testable on-site |
| | 2 Millipore Express SHF 0.2 µm PES Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity testing ensures quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site<br>• Available in single-layer 0.2 µm (SHF) or double-layer 0.5 µm + 0.2 µm (SHC) configurations. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |
| **Viral Clearance**<br>(Optional for mammalian cell expression systems)<br>• Ensure product safety against viruses<br>• Highly validated and reliable technology<br>• Maximize product recovery<br>• Preserves product purity | 4 Viresolve NFP PVDF Filters<br>3 | • >4 log removal of parvovirus and other small viruses<br>• Robust PVDF membrane<br>• >98% recovery of protein up to 160 kD<br>• 100% Integrity testing assures performance<br>• Can be integrity tested on-site<br>• To enhance filter performance and capacity, Millipore suggests using the Viresolve Prefilter 3 in series |
| | 4 Viresolve NFR PES Filters | • >6 log removal of retroviruses (80–120 nm)<br>• >98% recovery of protein (IgG)<br>• 100% Integrity testing assures performance<br>• Can be integrity tested on-site |
| **Ultrafiltration**<br>• Concentration, buffer exchange and final formulation<br>• Maximize product recovery<br>• Fast, robust process able to accommodate feed fluid variations<br>• Wide chemical compatibility with cleaning agents<br>• Easily scalable from lab to manufacturing scale | 1 Pellicon C Screen Cassettes with Ultracel PLC Membranes | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free membranes provide excellent repeat performance<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the protein to be retained. Choice should be based on small-scale testing.<br><br>*ALTERNATIVE: Consider using chemically resistant Biomax membranes when harsh cleaning and/or decontamination chemicals are required.* |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Sterile Filtration**<br>• Sterilizing-grade step to reduce bioburden<br>• Highly validated and reliable technology<br>• Preserves product purity<br>• Ensures product safety | 5 Durapore 0.22 µm PVDF Filters | • Sterilizing-grade PVDF membrane won't bind valuable protein<br>• 100% Integrity testing and thousands of existing applications assure proven performance<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br>• Integrity testable on-site |
| | 5 Millipore Express PES Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site<br>• Although double-layer 0.5 µm + 0.2 µm (SHC) is typical for this application, single-layer 0.2 µm (SHF) is also available. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| **Pellicon XL 50 Cassettes** | | |
| Biomax 30 kD membrane | | SK1M007W01 |
| Ultracel PLC 30 kD membrane | 50 $cm^2$ | PXC030C50 |
| Ultracel PLC10 kD membrane | | PXC010C50 |
| **OptiScale Capsules** | | |
| Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Multilayer Durapore 0.45 µm + 0.22 µm membrane | 13.8 $cm^2$ | SHGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | | SGEPA47FF3 |
| Millipore Express SHC 0.5 µm + 0.2 µm membrane | | SHGEA47FF3 |
| **Evaluation Kit with OptiScale-25 Capsules*** | | |
| Viresolve NFP membrane | 3.5 $cm^2$ | SVPVA25NB9 |
| Viresolve NFR membrane | | SZRVA25NB9 |
| **OptiScale-40 Capsules** | | |
| Viresolve NFP Prefilter | 5 $cm^2$ | SSPVA40NB9 |

**Viresolve membranes are available in an Evaluation Kit containing 9 OptiScale-25 Capsules, 3 each of 3 membrane lots, and are ideal for scale-up and scale down studies.*

## Recommended Filters

| Media/Membrane | Small-Scale Processing <100 L: Device (area/filter) | Catalogue No. | Large-Scale Processing >100 L: Device (area/filter) | Catalogue No. |
|---|---|---|---|---|
| **Ultrafiltration/Diafiltration** | | | | |
| Pellicon C Screen Cassettes | | | | |
| Ultracel PLC 30 kD membrane | Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | P2C030C01<br>P2C030C05 | Maxi Cassette (2.5 $m^2$) | P2C030C25 |
| Ultracel PLC 10 kD membrane | Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | P2C010C01<br>P2C010C05 | Maxi Cassette (2.5 $m^2$) | P2C010C25 |
| **Bioburden Reduction and Sterile Filtration** | | | | |
| Single-layer Durapore 0.22 µm Filters | Opticap XL2 Capsule (0.09 $m^2$)<br>Opticap XL4 Capsule (0.19 $m^2$)<br>Opticap XL5 Capsule (0.35 $m^2$)<br>5-inch Cartridge (0.35 $m^2$) | KVGLA02TT3<br>KVGLA04TT3<br>KVGLA05TT1<br>CVGL75S01 | Opticap XL10 Capsule (0.69 $m^2$)<br>Opticap XLT20 Capsule (1.4 $m^2$)<br>Opticap XLT30 Capsule (2.9 $m^2$)<br>10-inch Cartridge (0.69 $m^2$)<br>20-inch Cartridge (1.4 $m^2$)<br>30-inch Cartridge (2.1 $m^2$) | KVGLA10TT1<br>KVGLA2TTT1<br>KVGLA3TTT1<br>CVGL71TP3<br>CVGL72TP3<br>CVGL73TP3 |
| Double-layer Multilayer Durapore 0.45 µm + 0.22 µm Filters | | | Opticap XL10 Capsule (0.55 $m^2$)<br>Opticap XLT20 Capsule (1.10 $m^2$)<br>Opticap XLT30 Capsule (1.65 $m^2$)<br>10-inch Cartridge (0.55 $m^2$)<br>20-inch Cartridge (1.10 $m^2$)<br>30-inch Cartridge (1.65 $m^2$) | KHGLA10TT1<br>KHGLA2TTT1<br>KHGLA3TTT1<br>CHGL71TP3<br>CHGL72TP3<br>CHGL73TP3 |
| Double-layer Millipore Express SHC 0.5 µm + 0.2 µm Filters | Opticap XL3 Capsule:<br>Autoclavable (0.13 $m^2$)<br>Gamma-compatible (0.13 $m^2$)<br>Opticap XL5 Capsule:<br>Autoclavable (0.23 $m^2$)<br>Gamma-compatible (0.24 $m^2$)<br>5-inch Cartridge (0.23 $m^2$) | <br>KHGEA03TT3<br>KHGEG03TT1<br><br>KHGEA05TT1<br>KHGEG05TT1<br>CHGE75TS3 | Opticap XL10 Capsule:<br>Autoclavable (0.49 $m^2$)<br>Gamma-compatible (0.54 $m^2$)<br>10-inch Cartridge (0.49 $m^2$)<br>Opticap XLT30 Capsule:<br>Autoclavable (1.47 $m^2$)<br>Gamma-compatible (1.63 $m^2$)<br>30-inch Cartridge (1.47 $m^2$) | <br>KHGEA10TT1<br>KHGEG10TT1<br>CHGE71TS3<br><br>KHGEA3TTT1<br>KHGEG3TTT1<br>CHGE73TS3 |
| Single-layer Millipore Express SHF 0.2 µm Filters | Opticap XL3 Capsule:<br>Autoclavable (0.16 $m^2$)<br>Gamma-compatible (0.17 $m^2$)<br>Opticap XL5 Capsule:<br>Autoclavable (0.29 $m^2$)<br>Gamma-compatible (0.31 $m^2$)<br>5-inch Cartridge (0.29 $m^2$) | <br>KGEPA03TT3<br>KGEPG03TT1<br><br>KGEPA05TT1<br>KGEPG05TT1<br>CGEP75TP3 | Opticap XL10 Capsule:<br>Autoclavable (0.54 $m^2$)<br>Gamma-compatible (0.57 $m^2$)<br>10-inch Cartridge (0.54 $m^2$)<br>Opticap XLT30 Capsule:<br>Autoclavable (1.62 $m^2$)<br>Gamma-compatible (1.71 $m^2$)<br>30-inch Cartridge (1.62 $m^2$) | <br>KGEPA10TT1<br>KGEPG10TT1<br>CGEP71TP3<br><br>KGEPA3TTT1<br>KGEPG3TTT1<br>CGEP73TP3 |
| **Viral Clearance (mammalian cell expression systems only)** | | | | |
| Viresolve NFP Filters | 4-inch Opticap (0.077 $m^2$)<br>Opticap XL10 Capsule (0.48 $m^2$)<br>Opticap XLT10 Capsule (0.48 $m^2$)<br>10-inch Cartridge (0.48 $m^2$)<br>Opticap XLT20 Capsule (0.97 $m^2$)<br>*Millipore suggests using multiple cartridges or capsules for volumes >750 L.* | KVPV04TT1<br>KVPVA10TT1<br>KVPVA1TTT1<br>CVPV71TP1<br>KVPVA2TTT1 | Opticap XLT30 Capsule (1.45 $m^2$)<br>20-inch Cartridge (0.97 $m^2$)<br>30-inch Cartridge (1.45 $m^2$) | KVPVA3TTT1<br>CVPV72TP1<br>CVPV73TP1 |
| Viresolve NFP Prefilter* | Opticap (850 $cm^2$) | KSPV01FF1 | Opticap (850 $cm^2$) | KSPV01FF1 |
| Viresolve NFR Filters | 4-inch Opticap Capsule (0.093 $m^2$) | KZRV04TC3 | Opticap XL10 Capsule (0.54 $m^2$)<br>Opticap XLT10 Capsule (0.54 $m^2$)<br>10-inch Cartridge (0.54 $m^2$)<br>Opticap XLT20 Capsule (0.86 $m^2$)<br>20-inch Cartridge (0.86 $m^2$)<br>Opticap XLT30 Capsule (1.29 $m^2$)<br>30-inch Cartridge (1.29 $m^2$)<br>*Millipore suggests using multiple cartridges or capsules for volumes >3,600 L.* | KZRVA10TT1<br>KZRVA1TTT1<br>CZRV71TP1<br>KZRVA2TTT1<br>CZRV72TP1<br>KZRVA3TTT1<br>CZRV73TP1 |

**Viresolve Prefilter will be available in Millipore's Pod technology late 2005.*

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

*Millipore offers a comprehensive line of chromatography columns, systems and media. Contact Millipore for details.*

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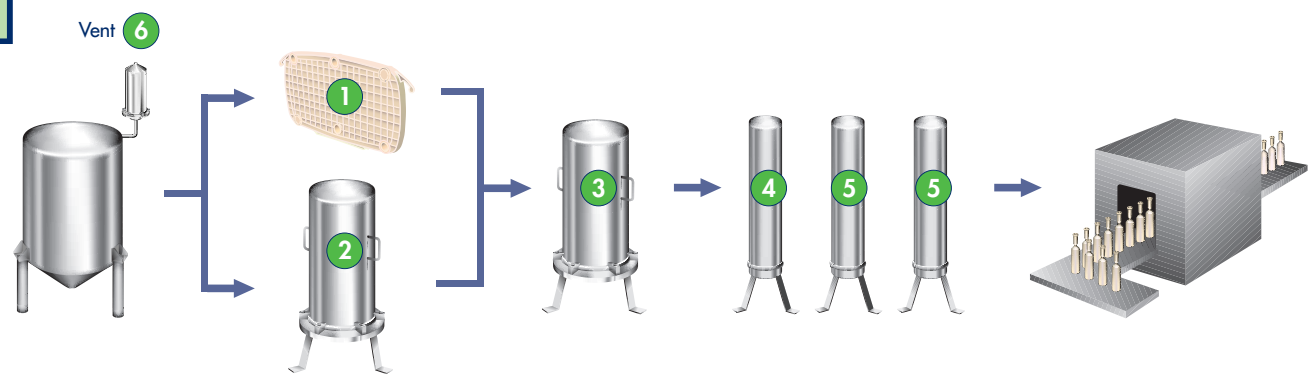
# Serum

Animal sera contain important growth factors necessary for the effective culture of mammalian cells. Serum can vary significantly, depending on the species and age of the donor animal, seasonal changes and animal diet. Fetal bovine sera tends to be relatively easy to filter while calf and adult bovine sera requires prefiltration or greater filtration area. Non-bovine sera (equine, porcine, etc) tend to have high concentrations of colloids and thus require filtration. For difficult serum, a robust clarification step using Millistak+ depth filter can be added. Depending on the nature and volume of the serum stream filters may need to be run in series to assure proper contaminant removal.

For details on Tank Venting 6, see page 70.

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Clarification and Prefiltration**<br>• Remove lipids, colloidal and particulate contaminants<br>• Operate consistently at high differential pressures and flow rates<br>• Extend the lifetime of final filters<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 1 Triple-layer Millistak+ HC Filters<br><br>(Grade A1HC or B1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs<br>• The selection of Grade A1HC or B1HC depends on the fluid particle size distribution and should be based on small-scale testing. |
| | 2 Clarigard Filters<br><br>(0.5 µm, 1.0 µm or 3.0 µm) | • Polypropylene prefilter for robust particle and colloid removal<br>• Validated for multiple sanitization and SIP cycles<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Non-fiber releasing structure preserves product purity<br>• Available in a wide-range of pore sizes to accommodate the needs of each user. Choice should be made based on small-scale testing. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Clarification and Prefiltration** continued | 3 Double-layer Milligard Filters (Grade SS, 0.5 µm + 0.2 µm, or Grade SC, 1.2 µm + 0.5 µm) | • Double-layer pleated configuration of mixed esters of cellulose membranes remove particles and colloids<br>• High porosity membranes operate at high flow rates and low pressure drops<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Available in a variety of pore sizes to accommodate the needs of each user. Grade SS is commonly used to protect downstream 0.22 µm sterilizing-grade filters. Grade SC is better suited to protect 0.45 µm membrane filters. Choice should be made based on small-scale testing. |
| | 3 Polysep II Filters (Grade W3, 1 µm + 0.2 µm) | • Depth filter consisting of a borosilicate glass layer and a layer of mixed esters of cellulose membranes<br>• Robust prefilter for concentrated solutions across a full range of flow rates<br>• High particle-loading capacity and retention<br>• Able to withstand multiple SIP or hot water sanitization cycles<br>• Non-fiber releasing |
| **Final Filtration**<br>• Reduce bacteria and mycoplasma to ensure long term storage and stability<br>• Eliminate the risk of adventitious infectious agents<br>• Operate consistently at high differential pressures and flow rates<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 4 Durapore CBR 0.1 µm Filters | • Low protein-binding PVDF membrane<br>• Retentive membrane reduces bioburden<br>• Low extractables and non-fiber releasing PVDF chemistry preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing ensures quality<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Although 0.1 µm is typical for this application, Durapore CBR 0.2 µm filters are also available. Choice should be based on small-scale screening. |
| | 5 Durapore 0.1 µm Filters | • Sterilizing-grade PVDF membrane will assure bioburden and mycoplasma clearance<br>• 100% Integrity testing and thousands of existing applications assure proven performance<br>• Integrity testable on-site<br>• Although 0.1 µm is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 5 Millipore Express SHR 0.1 µm Filters (with or without prefilter layer) | • Designed to remove high levels of mycoplasma and bacteria over a range of moderately plugging to highly fouling streams<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Sterilizing-grade PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• 100% integrity tested to ensure quality<br>• Robust construction validated for multiple SIP cycles<br>• Can be integrity tested on-site<br>• Available in single-layer 0.1 µm or double-layer 0.1 µm with prefilter layer 0.1 µm configurations. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| OptiScale Capsules | | |
| Double-layer Milligard SC 1.2 µm + 0.5 µm membrane | | SVVSCA47FF3 |
| Double-layer Milligard SS 0.5 µm + 0.2 µm membrane | | SVVSSA47FF3 |
| Double-layer Polysep II W3 1.0 µm + 0.2 µm membrane | | SGW3A47FF3 |
| Durapore 0.1 µm membrane | 13.8 $cm^2$ | SVVLA47FF3 |
| Single-layer Millipore Express SHR membrane | | SVEPA47FF3 |
| Double-layer Millipore Express SHR membrane | | SHVEA47FF3 |
| Millistak+ Mini Capsules | | |
| Triple-layer Grade A1HC | 23 $cm^2$ | MA1HC23HH3 |
| Triple-layer Grade B1HC | | MB1HC23HH3 |
| Opticap XL1 Capsules | | |
| Clarigard 0.5 µm | 1-inch* | K005A51TT1 |
| Clarigard 1.0 µm | 1-inch* | K010A51TT1 |
| Clarigard 3.0 µm | 1-inch* | K030A51TT1 |

**Filter element size*

## Recommended Filters

| Triple-layer Millistak+ HC Filters | Grade A1HC Area/Filter | Grade A1HC Catalogue No. | Grade B1HC Area/Filter | Grade B1HC Catalogue No. |
|---|---|---|---|---|
| 1-cell Pod | 0.1 $m^2$ | MA1CH01FS1 | 0.1 $m^2$ | MB1HC01FS1 |
| 5-cell Pod | 0.5 $m^2$ | MA1HC05FS1 | 0.5 $m^2$ | MB1HC05FS1 |
| 10-cell Pod | 1.0 $m^2$ | MA1HC10FS1 | 1.0 $m^2$ | MB1HC10FS1 |
| Opticap Capsule | 650 $cm^2$ | KA1HC10FF1 | 650 $cm^2$ | KB1HC10FF1 |
| 2-cell Stack | 0.45 $m^2$ | LA1HCH6S6 | 0.45 $m^2$ | LB1HCH6S6 |
| 8-cell Stack | 1.8 $m^2$ | LA1HCG6S2 | 1.8 $m^2$ | LB1HCG6S2 |

| Clarigard Filters | Filter Element Size | 0.5 µm | 1.0 µm | 3.0 µm |
|---|---|---|---|---|
| Opticap XL1 Capsule | 1-inch | K005A51TT1 | K010A51TT1 | K030A51TT1 |
| 2-inch Cartridge | 2-inch | D005N0S03 | D010N0S03 | D030N0S03 |
| Opticap XL5 Capsule | 5-inch | K005A05TT1 | K010A05TT1 | K030A05TT1 |
| Opticap XL10 Capsule | 10-inch | K005A10TT1 | K010A10TT1 | K030A10TT1 |
| 10-inch Cartridge | 10-inch | D00571S01 | D01071S01 | D03071S01 |
| 20-inch Cartridge | 20-inch | D00572S01 | D01072S01 | D03072S01 |
| 30-inch Cartridge | 30-inch | D00573S01 | D01073S01 | D03073S01 |
| 40-inch Cartridge | 40-inch | D00574S01 | D01074S01 | D03074S01 |

| Milligard Filters | Area/Filter | Grade SS Catalogue No. | Grade SC Catalogue No. |
|---|---|---|---|
| Opticap XL2 Capsule | 0.07 $m^2$ | KWSSA02TT3 | KWSCA02TT3 |
| Opticap XL4 Capsule | 0.16 $m^2$ | KWSSA04TT3 | KWSCA04TT3 |
| 4-inch Cartridge | 0.28 $m^2$ | CWSSM4S03 | CWSCM4S03 |
| Opticap XL5 Capsule | 0.28 $m^2$ | KWSSA05TT1 | KWSCA05TT1 |
| Opticap XL10 Capsule | 0.7 $m^2$ | KWSSA10TT1 | KWSCA10TT1 |
| Opticap XLT10 Capsule | 0.7 $m^2$ | KWSSA1TTT1 | KWSCA1TTT1 |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KWSSA2TTT1 | KWSCA2TTT1 |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KWSSA3TTT1 | KWSCA3TTT1 |
| 10-inch Cartridge | 0.7 $m^2$ | CWSS71S03 | CWSC71S03 |
| 20-inch Cartridge | 1.4 $m^2$ | CWSS72S03 | CWSC72S03 |
| 30-inch Cartridge | 2.1 $m^2$ | CWSS73S03 | CWSC73S03 |
| 40-inch Cartridge | 2.8 $m^2$ | CWSS74S03 | CGSC74S03 |

| Polysep II Filters | Area/Filter | Grade W3 Catalogue No. |
|---|---|---|
| Opticap XL2 Capsule | 0.06 $m^2$ | KGW3A02TT3 |
| Opticap XL4 Capsule | 0.11 $m^2$ | KGW3A04TT3 |
| 4-inch Cartridge | 0.19 $m^2$ | CGW3M4S03 |
| Opticap XL5 Capsule | 0.19 $m^2$ | KGW3A05TT1 |
| Opticap XL10 Capsule | 0.46 $m^2$ | KGW3A10TT1 |
| Opticap XLT10 Capsule | 0.46 $m^2$ | KGW3A1TTT1 |
| Opticap XLT20 Capsule | 0.92 $m^2$ | KGW3A2TTT1 |
| Opticap XLT30 Capsule | 1.38 $m^2$ | KGW3A3TTT1 |
| 10-inch Cartridge | 0.46 $m^2$ | CGW371S03 |
| 20-inch Cartridge | 0.92 $m^2$ | CGW372S03 |
| 30-inch Cartridge | 1.38 $m^2$ | CGW373S03 |
| 40-inch Cartridge | 1.84 $m^2$ | CGW374S03 |

| Durapore CBR Filters | Area/Filter | 0.1 µm |
|---|---|---|
| 10-inch Cartridge | 0.69 $m^2$ | CVVI71TPS |
| 20-inch Cartridge | 1.4 $m^2$ | CVVI72TPS |
| 30-inch Cartridge | 2.1 $m^2$ | CVVI73TPS |
| 40-inch Cartridge | 2.8 $m^2$ | CVVI74TPS |

| Durapore Sterilizing-grade Filters | Area/Filter | 0.1 µm |
|---|---|---|
| Opticap XL2 Capsule | 0.09 $m^2$ | KVVLA02TT3 |
| Opticap XL4 Capsule | 0.19 $m^2$ | KVVLA04TT3 |
| 5-inch Cartridge | 0.35 $m^2$ | CVVL75S01 |
| Opticap XL5 Capsule | 0.35 $m^2$ | KVVLA05TT1 |
| Opticap XL10 Capsule | 0.69 $m^2$ | KVVLA10TT1 |
| 10-inch Cartridge | 0.69 $m^2$ | CVVL71TP3 |
| Opticap XLT10 Capsule | 0.69 $m^2$ | KVVLA1TTT1 |
| 20-inch Cartridge | 1.4 $m^2$ | CVVL72TP3 |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KVVLA2TTT1 |
| 30-inch Cartridge | 2.1 $m^2$ | CVVL73TP3 |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KVVLA3TTT1 |
| 40-inch Cartridge | 2.8 $m^2$ | CVVL74TP3 |

| Millipore Express SHR Sterilizing-grade Filters* | Area/Filter | 0.1 µm | Area/Filter | 0.1 µm + Prefilter |
|---|---|---|---|---|
| Opticap XL3 Capsule | 0.14 $m^2$ | KVEPA03TT3 | 0.12 $m^2$ | KHVEA03TT3 |
| Opticap XL3 Gamma-compatible Capsule | 0.14 $m^2$ | KVEPG03TT3 | 0.12 $m^2$ | KHVEG03TT3 |
| Opticap XL5 Capsule | 0.27 $m^2$ | KVEPA05TT1 | 0.22 $m^2$ | KHVEA05TT1 |
| Opticap XL5 Gamma-compatible Capsule | 0.27 $m^2$ | KVEPG05TT1 | 0.22 $m^2$ | KHVEG05TT1 |
| 5-inch Cartridge | 0.27 $m^2$ | CVEP75TS3 | 0.22 $m^2$ | CHVE75TS3 |
| Opticap XL10 Capsule | 0.54 $m^2$ | KVEPA10TT1 | 0.5 $m^2$ | KHVEA10TT1 |
| Opticap XLT10 Capsule | 0.54 $m^2$ | KVEPA1TTT1 | 0.5 $m^2$ | KHVEG10TT1 |
| Opticap XL10 Gamma-compatible Capsule | 0.54 $m^2$ | KVEPG10TT1 | 0.5 $m^2$ | KHVEA1TTT1 |
| Opticap XLT10 Gamma-compatible Capsule | 0.54 $m^2$ | KVEPG1TTT1 | 0.5 $m^2$ | KHVEG1TTT1 |
| 10-inch Cartridge | 0.54 $m^2$ | CVEP71TS3 | 0.5 $m^2$ | CHVE71TS3 |
| Opticap XLT20 Capsule | 1.07 $m^2$ | KVEPA2TTT1 | 1 $m^2$ | KHVEA2TTT1 |
| Opticap XLT20 Gamma-compatible Capsule | 1.07 $m^2$ | KVEPG2TTT1 | 1 $m^2$ | KHVEG2TTT1 |
| 20-inch Cartridge | 1.07 $m^2$ | CVEP72TS3 | 1 $m^2$ | CHVE72TS3 |
| Opticap XLT30 Capsule | 1.6 $m^2$ | KVEPA3TTT1 | 1.5 $m^2$ | KHVEA3TTT1 |
| Opticap XLT30 Gamma-compatible Capsule | 1.6 $m^2$ | KVEPG3TTT1 | 1.5 $m^2$ | KVEPG3TTT1 |
| 30-inch Cartridge | 1.6 $m^2$ | CVEP73TS3 | 1.5 $m^2$ | CHVE73TS3 |

**Millipore Express SHR Filters are in final development. Specifications may change. Consult technical services for details.*

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

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# Plasma Fractionation

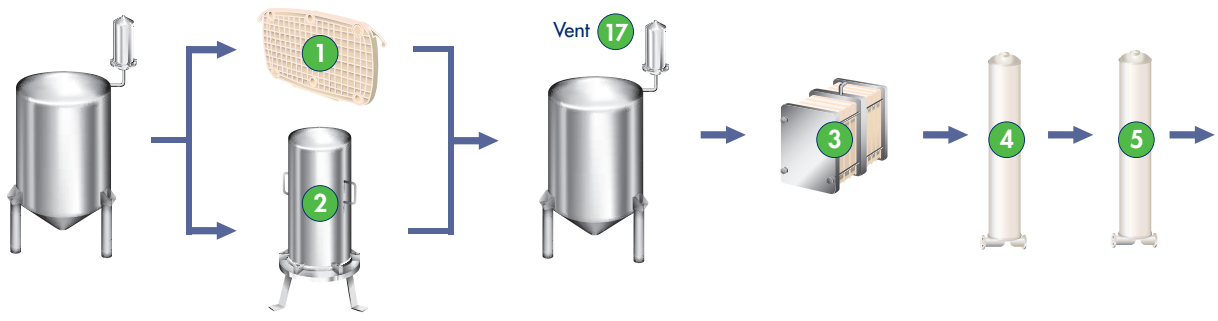
Human plasma is the source of over 700 proteins of considerable therapeutic value such as albumin, clotting factors, immunoglobulins, fibrinogen and others. The process used to extract and purify these proteins is known as plasma fractionation. Classical fractionation employs selective precipitation of proteins by manipulation of solution pH, ionic strength, temperature and ethanol content. Modern fractionation increasingly employs chromatography to make higher purity and better activity products. Contamination of plasma compounds can cause product instability as well as plugging downstream filters and should be removed via prefiltration. Clarification is used to remove contaminants prior to chromatography or UF steps, while sterilizing-grade filtration is a final step used to reduce bioburden and to sterilize heat labile proteins. A critical step, viral clearance, ensures the removal of viruses known to have contaminated source plasma such as parvovirus, hepatitis and HIV. Specialty antibodies such as hyper-immune globulin typically include a viral clearance filtration step in their manufacturing process.

For details on Tank Venting 17, see page 70.



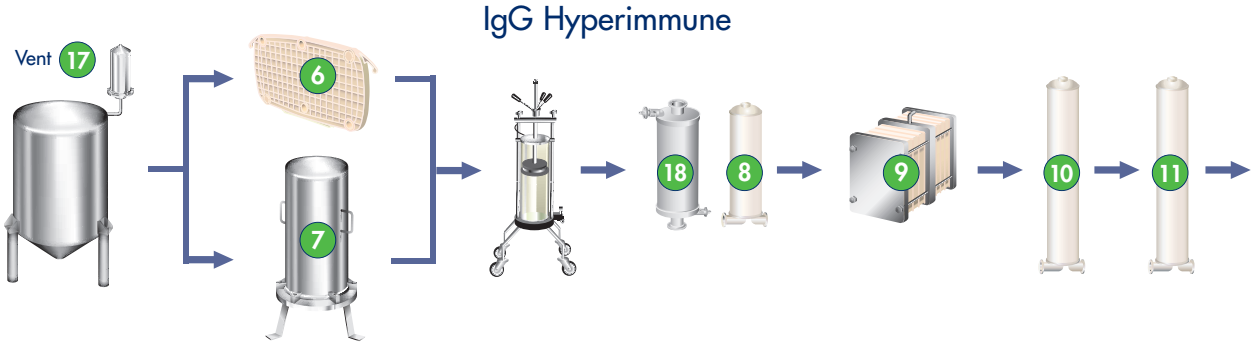
## 1 Typical **Process Flow**

### Albumin



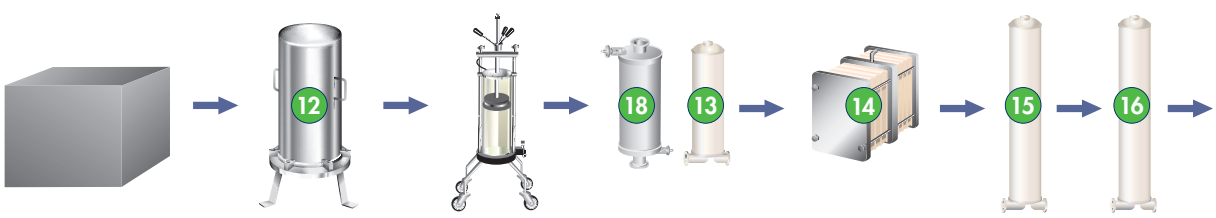

Cohn Fractionation | Clarification | Virus Inactivation | Concentration | Prefiltration | Final Sterile Filtration

### IgG Hyperimmune




Cohn Fractionation | Clarification | Chromatography | Viral Clearance | Ultrafiltration | Prefiltration | Final Sterile Filtration

### Clotting Factors




Cryoprecipitation | Clarification | Chromatography | Viral Clearance | Ultrafiltration | Prefiltration | Final Sterile Filtration

# 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Albumin**<br>**Clarification and Prefiltration**<br>• Remove colloids, aggregated and non-product proteins, lipids and particles prior to downstream purification<br>• Protect downstream sterilizing-grade filters, chromatography media and TFF membranes<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 2 Single-layer Millistak+ DE Filters<br><br>(Grade 55DE) | • Better suited for large volumes >500 L<br>• High internal surface area for maximum particle capture loading<br>• Graded density matrix allows retention of particle range<br>• High porosity provides low pressure drop<br>• Although Grade 55DE is typical for this application, Millistak+ filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 1 Double-layer Millistak+ HC Filters<br><br>(Grade C0HC) | • Better suited for volumes <500 L or with low usage rates of less than 10 batches/year<br>• Double-layer design enhances loading capacity and filtrate quality<br>• Unique configuration allows compression of multiple process steps so prefiltration may not be required. This can lower overall filtration costs.<br>• Although Grade C0HC is ideal for this application, Millistak+ filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 4 Double-layer Milligard Filters<br><br>(Grade SS, 0.5 µm + 0.2 µm) | • Double-layer pleated configuration of mixed esters of cellulose membranes provide high dirt-holding capacity and retention efficiency<br>• High porosity membranes operate at high flow rates and low pressure drops<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Grade SS is commonly used for this application; Milligard filters are available in numerous pore sizes and, in double-layer or triple-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 4 Double-layer Polysep II Filters<br><br>(Grade W3, 1.0 µm + 0.2 µm) | • Borosilicate glass top layer enhances particle and loading capacity<br>• Mixed esters of cellulose membrane bottom layer ensures high retention and filtrate quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Available in a variety of pore sizes to accommodate the needs of each user. Grade W3 is commonly used to protect downstream 0.22 µm membrane filters. Choice should be made based on small-scale testing. |



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| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Ultrafiltration**<br>• Reduce batch volumes and exchange buffer systems for efficient column operation and final formulation<br>• Run efficiently to ensure process economics | 3 Pellicon Cassettes with Biomax 10 kD Membrane | • Biomax void-free membrane has exceptional caustic stability and excellent repeat performance<br>• Low feed flow requirement minimizes pumping, working and hold up volumes.<br>• Higher product recovery and flux<br>• Suspended screen in feed channel allows higher turbulence enhancing the separation process<br>• Complete range of Pellicon devices allow for easy scale-up |
| **Sterile Filtration (liquid)**<br>(Also see Aseptic Filling page 60)<br>• Sterilizing-grade filters reduce bioburden and sterilize heat labile proteins<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 5 Durapore 0.22 µm Filters | • Low protein binding sterilizing-grade PVDF membrane<br>• 100% Integrity testing and thousands of existing applications assure proven performance<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and, in single-layer or multi-layer configurations to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br>• Integrity testable on-site<br><br>*ALTERNATIVE: If a PES membrane or broad chemical compatibility is a requirement Millipore suggests testing Millipore Express SHF 0.2 µm Filters in your small-scale trials.* |
| **IgG Hyper Immune**<br>**Clarification and Prefiltration**<br>• Remove colloids, aggregated and non-product proteins, lipids and large particles<br>• Protect downstream sterilizing-grade filters, chromatography media and TFF membranes<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 6 Double-layer Millistak+ HC Filters<br><br>(Grade C0HC) | • Better suited for volumes <500 L or with low usage rates of less than 10 batches/year<br>• Double-layer design enhances loading capacity and filtrate quality<br>• Unique configuration allows compression of multiple process steps so prefiltration may not be required. This can lower overall filtration costs.<br>• Although grade C0HC is ideal for this application, Millistak+ filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 7 Single-layer Millistak+ DE Filters<br><br>(Grade 75DE) | • Better suited for large volumes >500 L<br>• High internal surface area for maximum particle capture loading<br>• Graded density matrix allows retention of particle range<br>• High porosity provides low pressure drop<br>• Although grade 75DE is typical for this application, Millistak+ filters are available in several pore sizes and, in single-layer or multi-layer configurations to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 10 Double-layer Milligard Filters<br><br>(Grade SS, 0.5 µm + 0.2 µm) | • Double-layer pleated configuration of mixed esters of cellulose membranes provide high dirt-holding capacity and retention efficiency<br>• High porosity membranes operate at high flow rates and low pressure drops<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Although grade SS is commonly used for this application, Milligard filters are available in numerous pore sizes and in double-layer or triple-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br><br>*ALTERNATIVE: If adsorption is a concern, or a robust bioburden reduction is needed before the final filter Millipore suggests running Durapore 0.45 µm filters in your small-scale trials.* |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Viral Clearance**<br>• Critical step to ensure removal of viruses known to have contaminated source plasma such as parvovirus, hepatitis viruses and HIV<br>• Following current regulatory guidelines, 2 orthogonal methods are normally utilized to remove or inactivate viruses<br>• Validated log removal of viruses is a dedicated process step<br>• Filtration products should easily scale-up and down for simple validation | 8 Viresolve NFR Filters | • >6 log removal of retroviruses (80–120 nm)<br>• >98% recovery of protein (IgG)<br>• 100% Integrity testing assures performance<br>• Robust PES membrane<br>• Can be integrity tested on-site |
| | 8 18 Viresolve NFP Filters | • >4 log removal of parvovirus and other small viruses<br>• >98% recovery of protein up to 160kD<br>• Robust PVDF membrane<br>• 100% Integrity testing assures performance<br>• Can be integrity tested on-site<br>• To enhance filter performance and capacity, Millipore suggests using the Viresolve Prefilter 18 in series. |
| **Ultrafiltration**<br>• Reduce batch volumes and exchange buffer systems for efficient column operation and final formulation<br>• Run efficiently to ensure process economics | 9 Pellicon Cassettes with Biomax 30 kD Membrane or Ultracel PLC 30 kD Membrane | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Higher product recovery and flux<br>• Highly retentive void-free membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes provide excellent repeat performance<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Sterile Filtration**<br>(Also see Aseptic Filling page 60)<br>• Sterilizing-grade filters reduce bioburden and sterilize heat labile proteins<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 11 Durapore 0.22 µm Filters | • Sterilizing-grade PVDF low-binding membrane is ideal when adsorption is a concern<br>• 100% Integrity testing and thousands of existing applications assure proven performance<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br>• Integrity testable on-site |
| | 11 Millipore Express PES Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates even with clogging streams<br>• Can be integrity tested on-site<br>• Available in single-layer 0.2 µm (SHF) or double-layer 0.5 µm + 0.2 µm (SHC) configurations. The degree of protection required for the downstream process and the plugging characteristics of the fluid will guide this selection. Choice should be based on small-scale testing. |

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| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Clotting Factors** | | |
| **Clarification and Prefiltration**<br>• Remove colloids, aggregated and non-product proteins, lipids and particles prior to downstream purification<br>• Protect downstream sterilizing-grade filters, chromatography media and TFF membranes<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 12 Single-layer Millistak+ DE Filters<br><br>(Grade 65DE) | • Better suited for large volumes >500 L<br>• High internal surface area for maximum particle capture loading<br>• Graded density matrix enables retention of a wide range of particle sizes<br>• High porosity provides low pressure drop<br>• Although Grade 65DE is typical for this application, Millistak+ filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 15 Double-layer Milligard Filters<br><br>(Grade SC, 1.2 µm + 0.5 µm) | • Double-layer pleated configuration of mixed esters of cellulose membranes provide high dirt-holding capacity and retention efficiency<br>• High porosity membranes operate at high flow rates and low pressure drops<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Grade SC is commonly used for this application; Milligard filters are available in numerous pore sizes and in single-layer or double-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | *ALTERNATIVE: If adsorption is a concern, or a robust bioburden reduction is needed before the final filter Millipore suggests running Durapore 0.45 µm filters in your small-scale trials.* | |
| **Viral Clearance**<br>• Critical step to ensure removal of viruses known to have contaminated source plasma such as parvovirus, hepatitis viruses and HIV<br>• Following current regulatory guidelines, 2 orthogonal methods are normally utilized to remove or inactivate viruses<br>• Validated log removal of viruses is a dedicated process step<br>• Filtration products should easily scale-up and down for simple validation | 13 Viresolve NFR Filters | • >6 log removal of retroviruses (80–120 nm)<br>• >98% recovery<br>• Utilizes size exclusion technology<br>• Robust PES membrane<br>• 100% integrity tested to ensure performance<br>• Can be integrity tested on-site |
| | 13 18 Viresolve NFP Filters | • >4 log removal of parvoviruses and other small viruses<br>• >98% recovery of protein up to 160 kD<br>• Utilizes size exclusion technology<br>• Robust PVDF membrane<br>• 100% integrity tested to ensure performance<br>• Can be integrity tested on-site<br>• To enhance filter performance and capacity, Millipore suggests using the Viresolve Prefilter 18 series. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Ultrafiltration**<br>• Reduce batch volumes and exchange buffer systems for efficient column operation and final formulation<br>• Run efficiently to ensure process economics | 14 Pellicon Cassettes with Biomax or Ultracel PLC Membranes | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Higher product recovery and flux<br>• Highly retentive void-free membranes offer good permeate flux and withstand process upsets<br>• Robust low binding Ultracel PLC void-free membranes provide excellent repeat performance<br>• For sera with caustic stability constraints Millipore suggests Biomax membranes. For low adsorption utilize Ultracel PLC membranes.<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing |
| **Sterile Filtration**<br>(Also see Aseptic Filling page 60)<br>• Sterilizing-grade filters reduce bioburden and sterilize heat labile proteins<br>• Must be able to withstand multiple steam-in-place or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 16 Durapore 0.22 µm Filters<br><br>*ALTERNATIVE: For broad chemical compatibility and high flow rates or if PES membranes are required, Millipore suggests testing Millipore Express SHF filters in your small-scale trials.* | • Sterilizing-grade filters assure reduction of contaminating microorganisms that shorten the life of costly chromatography media<br>• Low-binding PVDF membrane assures protein yield<br>• 100% Integrity testing ensures quality<br>• Although 0.22 µm is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br>• Integrity testable on-site |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| **Albumin** | | |
| Pellicon XL50 Cassettes | | |
| Biomax 10 kD membrane | 50 $cm^2$ | PXB010A50 |
| OptiScale Capsules | | |
| Double-layer Milligard SS 0.5 µm + 0.2 µm membrane | 13.8 $cm^2$ | SVWSSA47FF3 |
| Double-layer Polysep II W3 1.0 µm + 0.2 µm membrane | | SGW3A47FF3 |
| Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | | SGEPA47FF3 |
| Millistak+ Mini Capsules | | |
| Single-layer Grade 55DE | 23 $cm^2$ | M55DE23HH3 |
| Double-layer Grade C0HC | | MC0HC23HH3 |
| **IgG Hyper Immune** | | |
| Pellicon XL50 Cassettes | | |
| Biomax 10 kD membrane | 50 $cm^2$ | PXB010A50 |
| Biomax 30 kD membrane | | PXB030A50 |
| Biomax 50 kD membrane | | PXB050A50 |
| Ultracel PLC 30 kD membrane | | PXC030C50 |
| OptiScale Capsules | | |
| Double-layer Milligard SS 0.5 µm + 0.2 µm membrane | 13.8 $cm^2$ | SVWSSA47FF3 |
| Durapore 0.45 µm membrane | | SVHLA47FF3 |
| Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | | SGEPA47FF3 |
| Double-layer Millipore Express SHC membrane | | SHGEA47FF3 |
| Millistak+ Mini Capsules | | |
| Single-layer Grade 75DE | 23 $cm^2$ | M75DE23HH3 |
| Double-layer Grade C0HC | | MC0HC23HH3 |
| Evaluation Kit with OptiScale-25 Capsules* | | |
| Viresolve NFP membrane | 3.5 $cm^2$ | SVPVA25NB9 |
| Viresolve NFR membrane | | SZRVA25NB9 |
| OptiScale-40 Devices | | |
| Viresolve Prefilter | 5 $cm^2$ | SSPVA40NB9 |
| **Clotting Factors** | | |
| Pellicon XL50 Cassettes | | |
| Biomax membrane is available in 5, 8,10,30,50,100,300,500 or 1,000 kD | | |
| Biomax 10 kD membrane | 50 $cm^2$ | PXB010A50 |
| Biomax 30 kD membrane | | PXB030A50 |
| Biomax 50 kD membrane | | PXB050A50 |
| Ultracel membrane is available in 5, 10, 30, 100, 300 or 1,000 kD | | |
| Ultracel PLC10 kD membrane | | PXC010C50 |
| Ultracel PLC 30 kD membrane | | PXC030C50 |
| OptiScale Capsules | | |
| Double-layer Milligard SC 1.2 µm + 0.5 µm membrane | 13.8 $cm^2$ | SVWSCA47FF3 |
| Durapore 0.45 µm membrane | | SVHLA47FF3 |
| Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | | SGEPA47FF3 |
| Millistak+ Mini Capsules | | |
| Single-layer Grade 65DE | 23 $cm^2$ | M65DE23HH3 |
| Evaluation Kit with OptiScale-25 Capsules* | | |
| Viresolve NFP membrane | 3.5 $cm^2$ | SVPVA25NB9 |
| Viresolve NFR membrane | | SZRVA25NB9 |
| OptiScale-40 Devices | | |
| Viresolve Prefilter | 5 $cm^2$ | SSPVA40NB9 |

**Viresolve membranes are available in an Evaluation Kit containing 9 OptiScale-25 Capsules, 3 each of 3 membrane lots, and are ideal for scale-up and scale down studies.*



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## Recommended Filters

| Media/Membrane | Small-Scale Processing: Device (area/filter) | Small-Scale Processing: Catalogue No. | Large-Scale Processing: Device (area/filter) | Large-Scale Processing: Catalogue No. |
|---|---|---|---|---|
| **Clarification and Prefiltration** | | | | |
| Single-layer Millistak+ DE | | | | |
| Grade 55DE | 10-inch Opticap Capsule (930 $cm^2$) | K55DE10FF1 | 12-inch, 6-cell stack (0.63 $m^2$)<br>16-inch*, 16-cell stack (3.47 $m^2$) | L55DEF2S3<br>L55DET6S1 |
| Grade 65DE | 10-inch Opticap Capsule (930 $cm^2$) | K65DE10FF1 | 12-inch, 6-cell stack (0.63 $m^2$)<br>16-inch*, 16-cell stack (3.47 $m^2$) | L65DEF2S3<br>L65DET6S1 |
| Grade 75DE | 10-inch Opticap Capsule (930 $cm^2$) | K75DE10FF1 | 12-inch, 6-cell stack (0.63 $m^2$)<br>16-inch*, 16-cell stack (3.47 $m^2$) | L75DEF2S3<br>L75DET6S1 |
| Double-layer Millistak+ HC Filters | | | | |
| Grade C0HC | 1-cell Pod (0.1 $m^2$)<br>5-cell Pod (0.5 $m^2$) | MC0HC01FS1<br>MC0HC05FS1 | 16-inch, 2-cell stack (0.45 $m^2$)<br>16-inch, 8-cell stack (1.8 $m^2$)<br>10-cell Pod (1 $m^2$) | LC0HCH6S6<br>LC0HCG6S2<br>MC0HC10FS1 |
| Double-layer Milligard Filters | | | | |
| Grade SS (0.5 µm + 0.2 µm) | Opticap XL2 Capsule (0.07 $m^2$)<br>Opticap XL4 Capsule (0.16 $m^2$)<br>Opticap XL5 Capsule ( 0.28 $m^2$)<br>4-inch Cartridge (0.28 $m^2$) | KWSSA02TT3<br>KWSSA04TT3<br>KWSSA05TT1<br>CWSSM4S03 | Opticap XL10 Capsule (0.7 $m^2$)<br>Opticap XLT10 Capsule (0.7 $m^2$)<br>10-inch Cartridge (0.7 $m^2$)<br>Opticap XLT20 Capsule (1.4 $m^2$)<br>20-inch Cartridge (1.4 $m^2$)<br>Opticap XLT30 Capsule (2.1 $m^2$)<br>30-inch Cartridge (2.1 $m^2$) | KWSSA10TT1<br>KWSSA1TTT1<br>CWSS71S03<br>KWSSA2TTT1<br>CWSS72S03<br>KWSSA3TTT1<br>CWSS73S03 |
| Grade SC (1.2 µm + 0.5 µm) | Opticap XL2 Capsule (0.07 $m^2$)<br>Opticap XL4 Capsule (0.16 $m^2$)<br>Opticap XL5 Capsule (0.28 $m^2$)<br>4-inch Cartridge (0.28 $m^2$) | KWSCA02TT3<br>KWSCA04TT3<br>KWSCA05TT1<br>CWSCM4S03 | Opticap XL10 Capsule (0.7 $m^2$)<br>Opticap XLT10 Capsule (0.7 $m^2$)<br>10-inch Cartridge (0.7 $m^2$)<br>Opticap XLT20 Capsule (1.4 $m^2$)<br>20-inch Cartridge (1.4 $m^2$)<br>Opticap XLT30 Capsule (2.1 $m^2$)<br>30-inch Cartridge (2.1 $m^2$) | KWSCA10TT1<br>KWSCA1TTT1<br>CWSC71S03<br>KWSCA2TTT1<br>CWSC72S03<br>KWSCA3TTT1<br>CWSC73S03 |
| Double-layer Polysep II Filters | | | | |
| Grade W3 (1.0 µm + 0.2 µm) | Opticap XL2 Capsule (0.06 $m^2$)<br>Opticap XL4 Capsule (0.11 $m^2$)<br>Opticap XL5 Capsule (0.19 $m^2$)<br>4-inch Cartridge (0.19 $m^2$) | KGW3A02TT3<br>KGW3A04TT3<br>KGW3A05TT1<br>CGW3M4S03 | Opticap XL10 Capsule (0.46 $m^2$)<br>Opticap XLT10 Capsule (0.46 $m^2$)<br>10-inch Cartridge (0.46 $m^2$)<br>Opticap XLT20 Capsule (0.92 $m^2$)<br>20-inch Cartridge (0.92 $m^2$)<br>Opticap XLT30 Capsule (1.38 $m^2$)<br>30-inch Cartridge (1.38 $m^2$) | KGW3A10TT1<br>KGW3A1TTT1<br>CGW371S03<br>KGW3A2TTT1<br>CGW372S03<br>KGW3A3TTT1<br>CGW373S03 |
| **Ultrafiltration/Diafiltration** | | | | |
| Pellicon Cassettes | | | | |
| Biomax 10 kD membrane | A Screen<br>Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | <br>P2B010A01<br>P2B010A05 | A Screen<br>Maxi Cassette (2.5 $m^2$) | <br>P2B010A25 |
| Biomax 30 kD membrane | A Screen<br>Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | <br>P2B030A01<br>P2B030A05 | A Screen<br>Maxi Cassette (2.5 $m^2$) | <br>P2B030A25 |
| Biomax 50 kD membrane | A Screen<br>Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | <br>P2B050A01<br>P2B050A05 | A Screen<br>Maxi Cassette (2.5 $m^2$) | <br>P2B050A25 |
| Ultracel PLC 10 kD membrane | C Screen<br>Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | <br>P2C010C01<br>P2C010C05 | C Screen<br>Maxi Cassette (2.5 $m^2$) | <br>P2C010C25 |
| Ultracel PLC 30 kD membrane | C Screen<br>Mini Cassette (0.1 $m^2$)<br>Cassette (0.5 $m^2$) | <br>P2C030C01<br>P2C030C05 | C Screen<br>Maxi Cassette (2.5 $m^2$) | <br>P2C030C25 |

**Millistak+ DE Filters are available in a range of sizes and diameters. Contact Millipore for more details.*

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

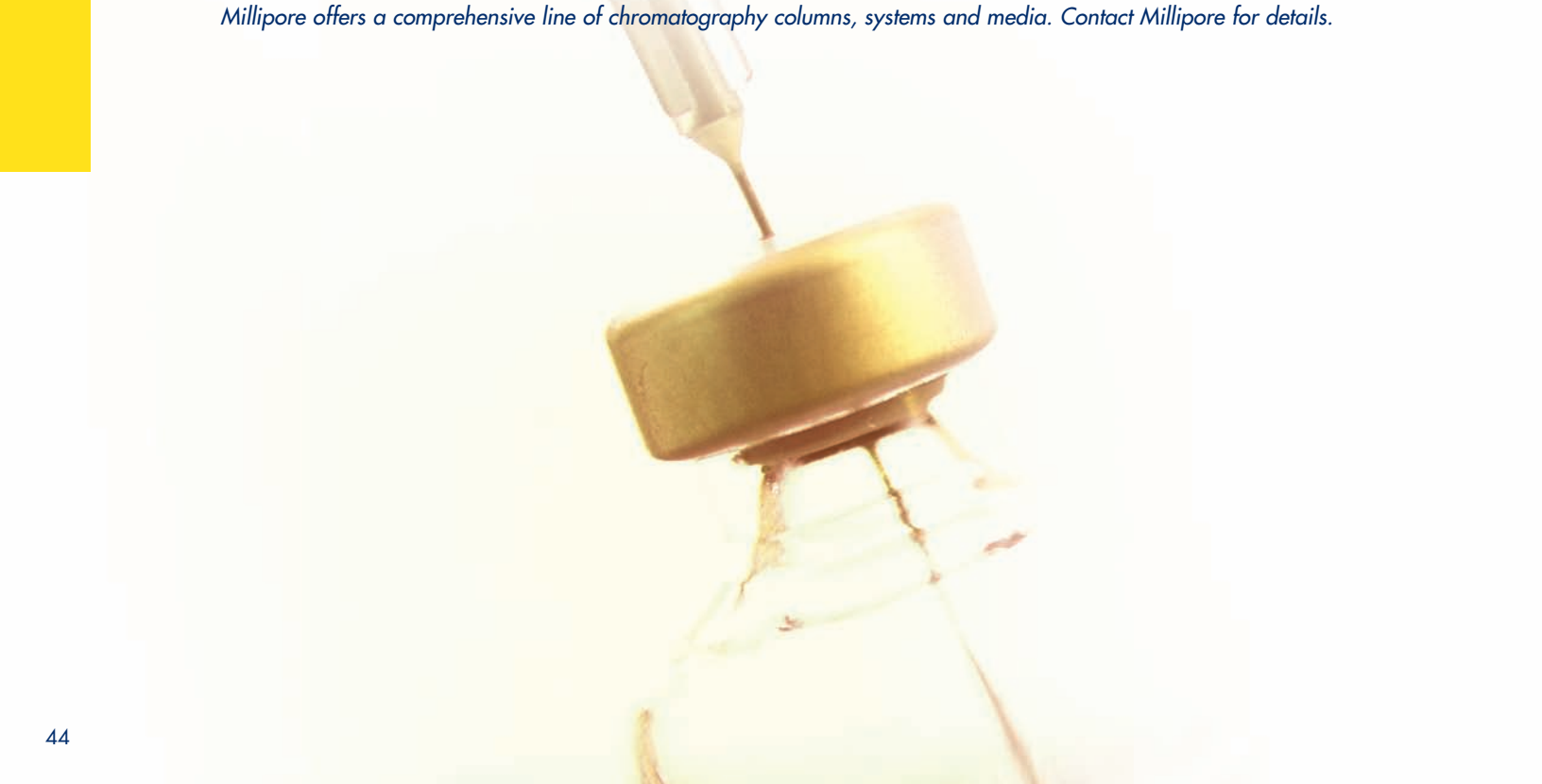
# Filter Quick **Reference Guide** continued

| Media/Membrane | Small-Scale Processing: Device (area/filter) | Small-Scale Processing: Catalogue No. | Large-Scale Processing: Device (area/filter) | Large-Scale Processing: Catalogue No. |
|---|---|---|---|---|
| **Viral Clearance** | | | | |
| Viresolve NFP Filters | 4-inch Opticap (0.077 $m^2$) | KVPV04TT3 | Opticap XLT30 Capsule (1.45 $m^2$) | KVPVA3TTT1 |
| | Opticap XL10 Capsule (0.48 $m^2$) | KVPVA10TT1 | 20-inch Cartridge (0.97 $m^2$) | CVPV72TP1 |
| | Opticap XLT10 Capsule (0.48 $m^2$) | KVPVA1TTT1 | 30-inch Cartridge (1.45 $m^2$) | CVPV73TP1 |
| | 10-inch Cartridge (0.48 $m^2$) | CVPV71TP1 | | |
| | Opticap XLT20 Capsule (0.97 $m^2$) | KVPVA2TTT1 | | |
| | *Millipore suggests using multiple cartridges or capsules for volumes > 750 L.* | | | |
| Viresolve Prefilter* | Opticap (850 $cm^2$) | KSPV01FF1 | Opticap (850 $cm^2$) | KSPV01FF1 |
| Viresolve NFR Filters | 4-inch Opticap Capsule (0.093 $m^2$) | KZRV04TC3 | Opticap XL10 Capsule (0.54 $m^2$) | KZRVA10TT1 |
| | | | Opticap XLT10 Capsule (0.54 $m^2$) | KZRVA1TTT1 |
| | | | 10-inch Cartridge (0.54 $m^2$) | CZRV71TP1 |
| | | | Opticap XLT20 Capsule (0.86 $m^2$) | KZRVA2TTT1 |
| | | | 20-inch Cartridge (0.86 $m^2$) | CZRV72TP1 |
| | | | Opticap XLT30 Capsule (1.29 $m^2$) | KZRVA3TTT1 |
| | | | 30-inch Cartridge (1.29 $m^2$) | CZRV73TP1 |
| | *Millipore suggests using multiple cartridges or capsules for values >3,600 L.* | | | |
| **Sterilizing-grade Filtration** | | | | |
| Durapore 0.22 µm Filters | Opticap XL2 Capsule (0.09 $m^2$) | KVGLA02TT3 | Opticap XL10 Capsule (0.69 $m^2$) | KVGLA10TT1 |
| | Opticap XL4 Capsule (0.19 $m^2$) | KVGLA04TT3 | Opticap XLT10 Capsule (0.69 $m^2$) | KVGLA1TTT1 |
| | Opticap XL5 Capsule (0.35 $m^2$) | KVGLA05TT1 | Opticap XLT20 Capsule (1.4 $m^2$) | KVGLA2TTT1 |
| | 5-inch Cartridge (0.35 $m^2$) | CVGL75S01 | Opticap XLT30 Capsule (2.1 $m^2$) | KVGLA3TTT1 |
| | | | 10-inch Cartridge (0.69 $m^2$) | CVGL71TP3 |
| | | | 20-inch Cartridge (1.4 $m^2$) | CVGL72TP3 |
| | | | 30-inch Cartridge (2.1 $m^2$) | CVGL73TP3 |
| Millipore Express SHF 0.2 µm Filters | Opticap XL3 Capsule (0.16 $m^2$) | KGEPA03TT3 | Opticap XL10 Capsule (0.54 $m^2$) | KGEPA10TT1 |
| | Opticap XL5 Capsule (0.29 $m^2$) | KGEPA05TT1 | Opticap XLT10 Capsule (0.54 $m^2$) | KGEPA1TTT1 |
| | 5-inch Cartridge (0.29 $m^2$) | CGEP75TP3 | Opticap XLT20 Capsule (1.08 $m^2$) | KGEPA2TTT1 |
| | | | Opticap XLT30 Capsule (1.62 $m^2$) | KGEPA3TTT1 |
| | | | 10-inch Cartridge (0.54 $m^2$) | CGEP71TP3 |
| | | | 20-inch Cartridge (1.08 $m^2$) | CGEP72TP3 |
| | | | 30-inch Cartridge (1.62 $m^2$) | CGEP73TP3 |
| Millipore Express SHC 0.5 µm + 0.2 µm PES Filters | Opticap XL3 Capsule (0.13 $m^2$) | KHGEA03TT3 | Opticap XL10 Capsule (0.49 $m^2$) | KHGEA10TT1 |
| | Opticap XL5 Capsule (0.24 $m^2$) | KHGEA05TT1 | Opticap XLT10 Capsule (0.49 $m^2$) | KHGEA1TTT1 |
| | 5-inch Cartridge (0.24 $m^2$) | CHGE75TS3 | Opticap XLT20 Capsule (0.98 $m^2$) | KHGEA2TTT1 |
| | | | Opticap XLT30 Capsule (1.47 $m^2$) | KHGEA3TTT1 |
| | | | 10-inch Cartridge (0.49 $m^2$) | CGEP71TS3 |
| | | | 20-inch Cartridge (0.98 $m^2$) | CGEP72TS3 |
| | | | 30-inch Cartridge (1.47 $m^2$) | CGEP73TS3 |

**Viresolve Prefilter will be available in Millipore's Pod technology late 2005.*

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

*Millipore offers a comprehensive line of chromatography columns, systems and media. Contact Millipore for details.*



# Vaccines

Vaccines are biologically active products designed to stimulate the immune system against future invasion of a pathogen by inducing memory to specific antigens. Vaccines may be produced from viral pathogens such as those causing polio, influenza and Lyme Disease, or from bacterial pathogens such as pertussis, tetanus, diphtheria and anthrax. Recombinant fermentation techniques such as those used for hepatitis vaccine, produce highly purified antigen-specific subunits that stimulate immunity without concern of pathogen infection. Vaccine production typically uses several filtration and purification steps. To obtain a purified vaccine the selected microorganism must first be grown then the selected antigen must be separated, purified, formulated and sterilized prior to delivery.

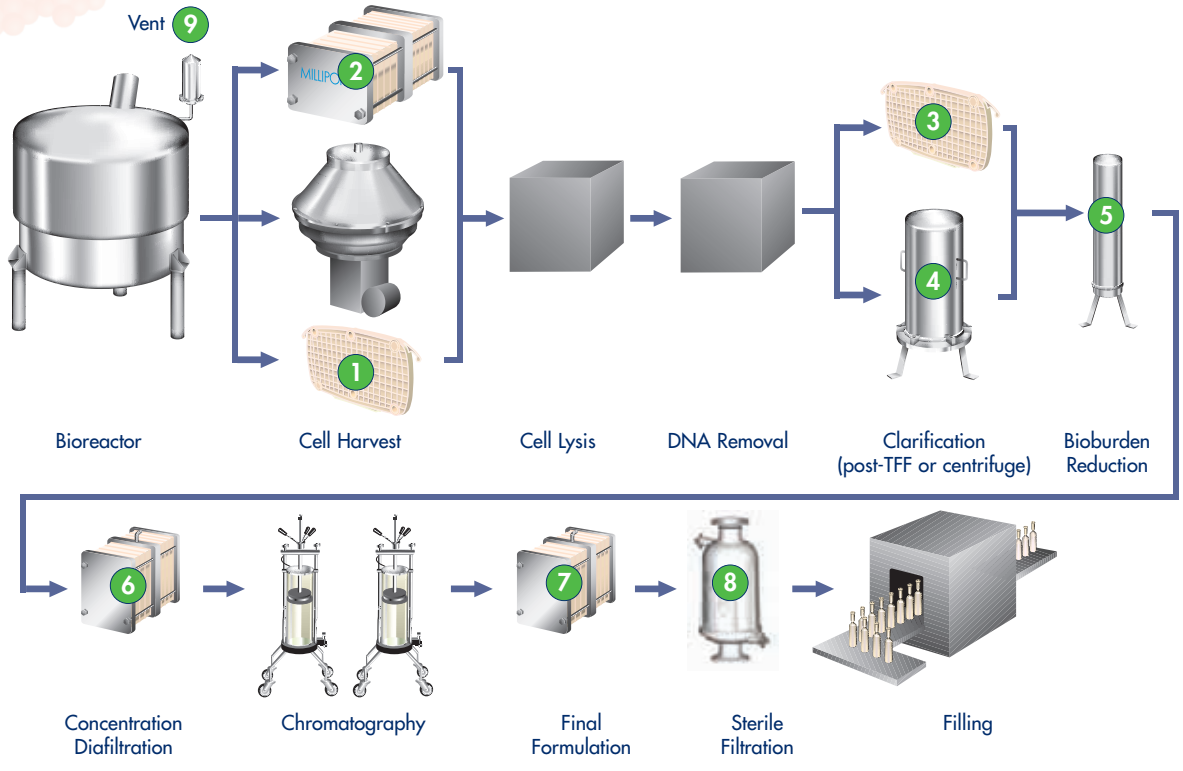
**Application Requirements**

- Vaccine broths have moderate to high solids concentrations that require effective removal before downstream purification. Millipore products are designed for high yield, throughput and efficiency
- Highly purified vaccines are often required to minimize adverse reaction.
- Injectable vaccines require sterilization.


| Vaccines | Batch Volumes | |
|---|---|---|
| Mammalian Cell | <2,000 L | 45 |
| Viral Vectors | <500 L | 48 |
| Plasmid DNA | <5,000 L | 50 |
| Conjugates | <1,000 L | 52 |
| Polysaccharides | <2,000 L | 54 |
| Filter Quick Reference Guide | | 56 |


# Vaccines: Mammalian Cell

## 1 Typical **Process Flow**



# 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Cell Harvesting**<br>(In place of TFF/Centrifuge, post fermentation)<br>• Remove heavy solid loads from bioreactor fluid and recover product in filtrate<br>• Requires high capacity<br>• Wide feed stream variability depending on cell culture type and conditions<br>• If solid content is too high, centrifugation becomes preferred technology | 2 Prostak Open-Channel Modules with Durapore 0.22 µm Membrane | • Best suited for large bioreactors >1,000 L or bioreactors with high usage rates of more than 10 batches/year<br>• Open-channel design accommodates fluids containing low to medium density and solids<br>• High flux at low transmembrane pressure<br>• Robust construction allows multiple use<br>• Validated for multiple SIP cycles<br>• Although Durapore 0.22 µm membrane is typical for this application, Prostak Modules are available in with a wide range of membranes to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |
| | 1 Double-layer Millistak+ HC Filters<br><br>(Grade D0HC or C0HC) | • For bioreactor volumes up to 1,000 L or larger volumes with low usage rates of less than 10 batches/year<br>• Double layer design enhances loading capacity and filtrate quality<br>• Unique configuration allows compression of multiple process steps into one, lowering overall filtration costs<br>• Selection of C0HC or D0HC media grade depends on particle size distribution and feed solution. Choice should be based upon small-scale testing. |
| | *ALTERNATIVE: For smaller batch sizes where no centrifuge or TFF step is required Millipore suggests using Clarigard 0.3 µm or Double-layer Milligard 0.5 µm + 0.2 µm (Grade SS) Filters in your process. Choice should be based on small-scale testing.* | |
| **Clarification or Polishing**<br>(Post TFF or Centrifuge)<br>• Remove cell debris, small particles and colloids passed through the primary clarification step<br>• Potential for variations in fluid particle size distribution<br>• Must have high capacity and protect downstream sterilizing-grade filters | 3 Triple-layer Millistak+ HC Filters<br><br>(Grade B1HC) | • Ideal solution post-centrifuge for medium and small volume bioreactors with <2,000 L volume<br>• Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• High filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Unique design enables the compression of multiple process steps into one, lowering overall filtration costs. |
| | 4 Double-layer Milligard Filters<br><br>(Grade SS, 0.5 µm + 0.2 µm) | • Ideal solution post-TFF when additional clarification of whole cells and colloids is needed<br>• Double-layer pleated configuration increases particle and colloid loading capacity<br>• Mixed esters of cellulose filter material with low protein-binding characteristics<br>• Low extractables and non-fiber releasing<br>• High flow rate at low pressure drop<br>• Validated for multiple SIP cycles<br>• Decades of proven performance protecting membrane filters<br>• 100% integrity tested to ensure quality |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Bioburden Reduction**<br>• Reduces bioburden at intermediate process step<br>• Protects downstream filters, media and equipment<br>• Preserves product purity<br>• Sterilizing-grade filtration required | 5 Double-layer Millipore Express SHC 0.5 µm + 0.2 µm Filters | • Sterilizing-grade PES 0.2 µm membrane with an additional 0.5 µm prefilter layer all in one pleated device<br>• Designed for bulk intermediate processing where fluids may be fouling in batch sizes ranging from 100 to 20,000 L.<br>• PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site |
| **Concentration and Diafiltration**<br>(Prior to column chromatography steps)<br>• Concentration of process fluids and buffer exchange<br>• Will extend the life of expensive chromatography media and improve their speed and efficiency<br>• Fast, robust process able to accommodate feed fluid variations<br>• Wide chemical compatibility with cleaning agents<br>• Easily scalable from lab to manufacturing scale | 6 Pellicon C Screen Cassettes with Ultracel PLC 100, 300 or 1,000 kD Membrane | • Low feed flow requirements minimize pumping, working and hold up volumes<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Concentration and Diafiltration**<br>(For final formulation)<br>• Concentration and diafiltration adjusts the end product to the proper dosage conditions prior to final packaging<br>• Fast, robust process able to accommodate feed fluid variations<br>• Easily scalable from lab to manufacturing scale | 7 Pellicon C Screen Cassettes with Ultracel PLC 100 or 300 kD Membrane | • Low feed flow requirements minimize pumping, working and hold up volumes<br>• Higher product recovery and flux<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Sterile Filtration**<br>• Sterilizing-grade step to reduce bioburden or sterilize heat labile products<br>• Highly validated and reliable technology<br>• Preserves product purity<br>• Ensures product safety | 8 Durapore 0.22 µm Filters | • Low protein-binding sterilizing-grade PVDF membrane<br>• Low extractables preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assure proven performance<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Available in Millipak stacked disc format which allows minimal hold-up volume<br>• Although 0.22 µm membrane is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user. Choice should be based on small-scale testing. |

For details on Tank Venting 9, see page 70.

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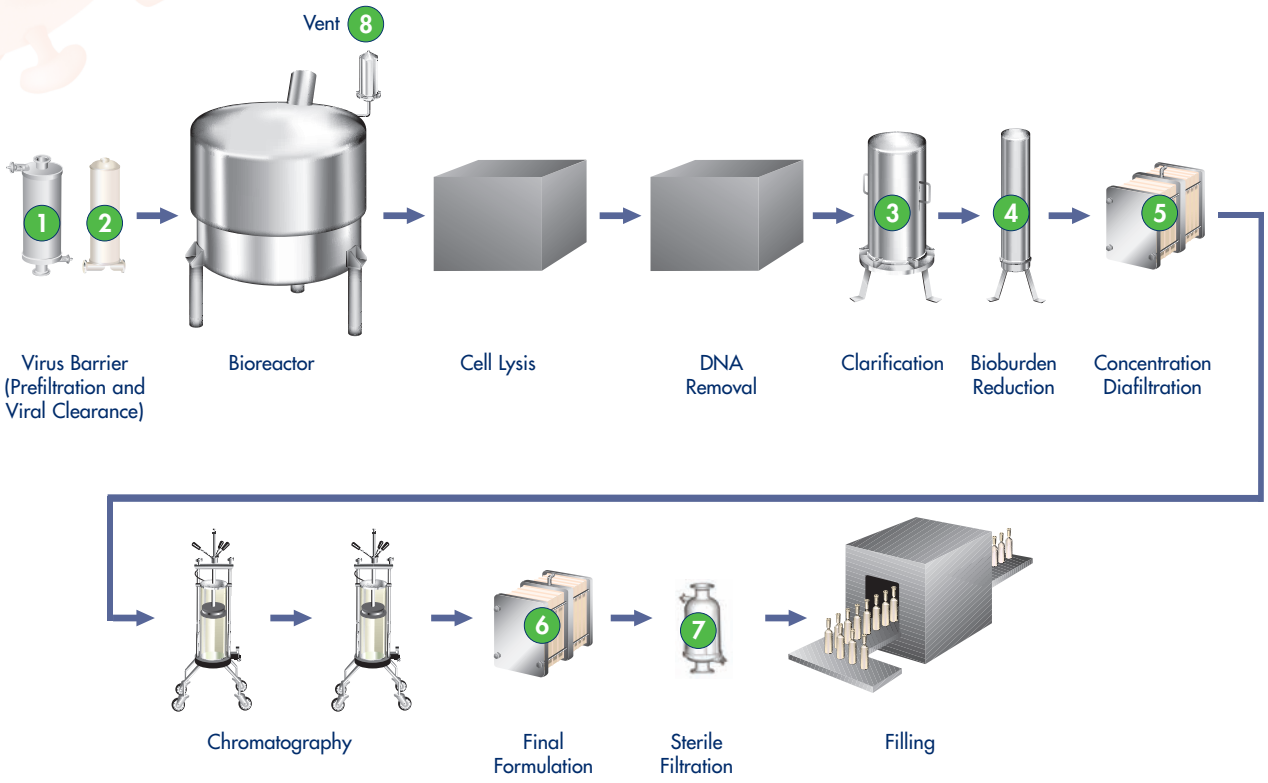
# Vaccines: Viral Vectors

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

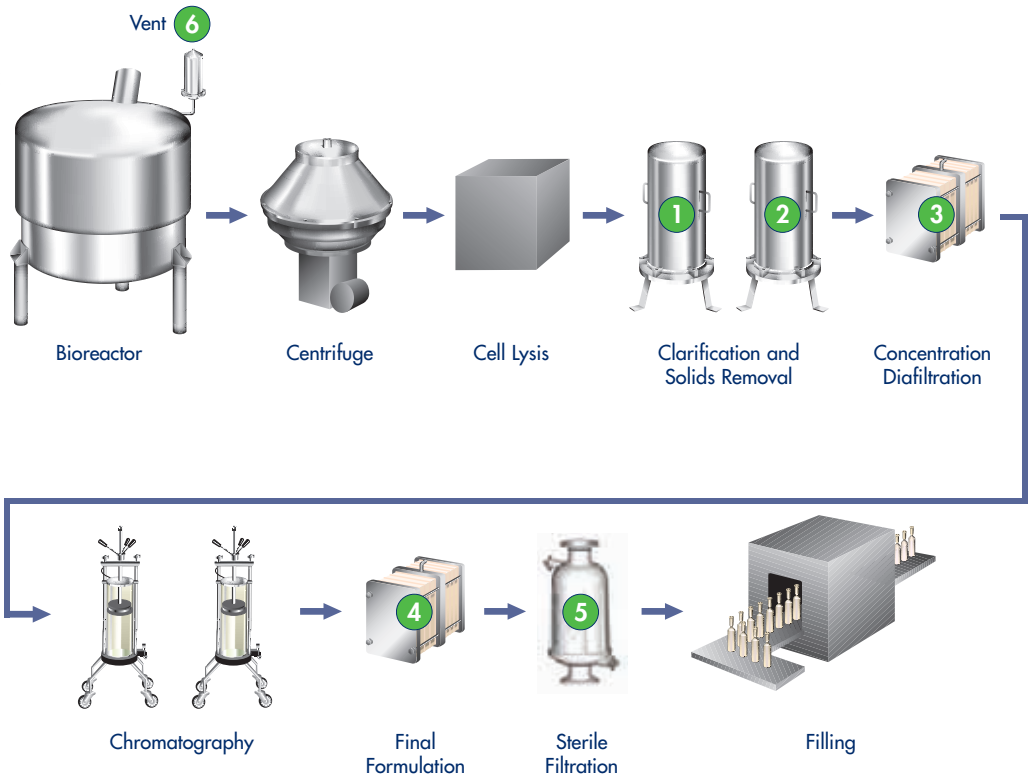
| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Virus Barrier**<br>• Removes adventitious viruses<br>• Ensures product safety<br>• Requires a highly validated and reliable technology<br>• Maximizes product recovery<br>• Preserves and ensures product purity | 2 Viresolve NFP Filters<br>1 | • >4 log removal of parvovirus and other small viruses without compromising flow rate or removing vital media nutrients<br>• Robust PVDF membrane<br>• >98% protein recovery up to 160 kD<br>• Available in multiple formats for easy scale-up and scale-down<br>• 100% Integrity testing assures performance<br>• Can be integrity tested on-site<br>• To ensure performance and capacity, Millipore suggests using in series with the Viresolve Prefilter 1. |
| **Clarification**<br>• Removes cell debris, small particles and colloids after the cell lysis step<br>• Must have high throughput capacity<br>• Protects downstream sterilizing-grade membrane filters | 3 Single-layer Millistak+ CE Filters<br><br>(Grade 40CE, 45CE, or 50CE) | • Better suited for volumes <2,000 L<br>• High internal surface area for maximum particle capture loading<br>• Filter matrix exhibits positive charge properties to enhance filtration<br>• High porosity provides low pressure drop<br>• Available in several media grades to accommodate the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Bioburden Reduction**<br>• Reduces bioburden<br>• Protects downstream chromatography and UF/DF steps<br>• Preserves product purity | 4 Double-layer Durapore 0.45 µm Filters<br><br>(with 0.5 µm prefilter layer) | • Low protein-binding PVDF membrane with prefilter layer<br>• Highly retentive membrane reduces bioburden<br>• Low extractables and non-fiber releasing PVDF chemistry preserves product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assures proven performance<br>• Validated for multiple SIP and hot water sanitization cycles |
| **Concentration and Diafiltration**<br>(Prior to column chromatography steps)<br>• Concentration of process fluids and buffer exchange<br>• Will extend the life of expensive chromatography media and improve their speed and efficiency<br>• Fast, robust process able to accommodate feed fluid variations<br>• Wide chemical compatibility with cleaning agents<br>• Easily scalable from lab to manufacturing scale | 5 Pellicon V Screen Cassettes with Ultracel PLC 300 kD Membrane | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Concentration and Diafiltration**<br>(For final formulation)<br>• Concentration and diafiltration adjusts the end product to the proper dosage conditions prior to final packaging<br>• Fast, robust process able to accommodate feed fluid variations<br>• Easily scalable from lab to manufacturing scale | 6 Pellicon C Screen Cassettes with Ultracel PLC 300 kD Membrane | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Higher product recovery and flux<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Sterile Filtration**<br>• Sterilizing-grade step reduces bioburden<br>• Highly validated and reliable technology<br>• Preserves and ensures product purity<br>• Ensures product safety | 7 Durapore 0.22 µm Filters | • Low protein-binding sterilizing-grade PVDF membrane<br>• Low extractables preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assure proven performance<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Available in Millipak stacked disc format which allows minimal hold-up volume<br>• Although 0.22 µm membrane is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user. Choice should be based on small-scale testing. |

For details on Tank Venting 8, see page 70.

# Vaccines: Plasmid DNA

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Clarification and Solids Removal**<br>(In place of bag filter)<br>• Remove solids after the cell lysis step<br>• Have high debris holding capacity<br>• Protect downstream membranes<br>• Charged medias should be avoided due to plasmid interaction<br>• Typically operated at low delta P to minimize precipitate or breakthrough<br>• Process is more efficient in cases of flocculants that float<br>• Washing of precipitate to reduce endotoxin and genomic DNA contaminants | 1 Polygard CR 10 µm Filters | • For use in place of a bag filter or for extra clarification after cell lysis<br>• Multi-stage graded density design retains solids or sediment within the depth matrix<br>• Polypropylene media provides excellent solids capacity and high throughput. |
| | 2 Clarigard 0.5 µm Filters | • For use in series after the Polygard CR filter when no bag filter is used for solids removal<br>• Polypropylene graded density prefilter for robust particle and colloid removal<br>• 1–2 log bioburden reduction<br>• Validated for multiple sanitization and SIP cycles<br>• Higher filtrate quality allows smaller size requirements for downstream sterilizing-grade filtration step<br>• Non-fiber releasing structure preserves product purity. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Concentration and Diafiltration**<br>(Prior to column chromatography steps)<br>• Concentration of process fluids and buffer exchange<br>• Will extend the life of expensive chromatography media and improve their speed and efficiency<br>• Fast, robust process able to accommodate feed fluid variations<br>• Wide chemical compatibility with cleaning agents<br>• Easily scalable from lab to manufacturing scale | 3 Pellicon V Screen Cassettes with Ultracel PLC 30 or 100 kD Membrane | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Concentration and Diafiltration**<br>(For final formulation)<br>• Concentration and diafiltration adjusts the end product to the proper dosage conditions prior to final packaging<br>• Fast, robust process able to accommodate feed fluid variations<br>• Easily scalable from lab to manufacturing scale | 4 Pellicon C Screen Cassettes with Ultracel PLC 30 or 100 kD Membranes<br><br>*ALTERNATIVE: In case of high concentrations (>5 g/L) Pellicon V Screen cassettes are recommended.* | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Higher product recovery and flux<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Sterile Filtration**<br>• Sterilizing-grade step removes bacteria prior to aseptic fill<br>• Ensures product safety<br>• Highly validated and reliable technology<br>• Preserves product purity<br><br>*NOTE: Membrane chemistries other than PES are known to cause gel formation at the membrane surface. We strongly recommend a PES filter for this step.* | 5 Double-layer Millipore Express SHC 0.5 µm + 0.2 µm Filters | • Sterilizing-grade PES 0.2 µm membrane with an additional 0.5 µm PES prefilter layer all in one pleated device<br>• Double-layer construction provides excellent capacity even in high salt conditions<br>• PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric PES pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site |

For details on Tank Venting 6, see page 70.

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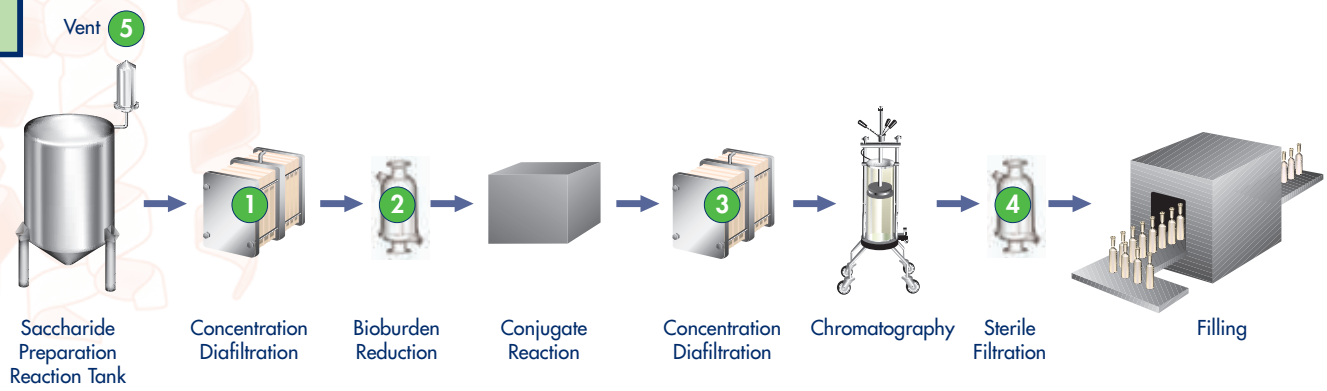
# Vaccines: Conjugates

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

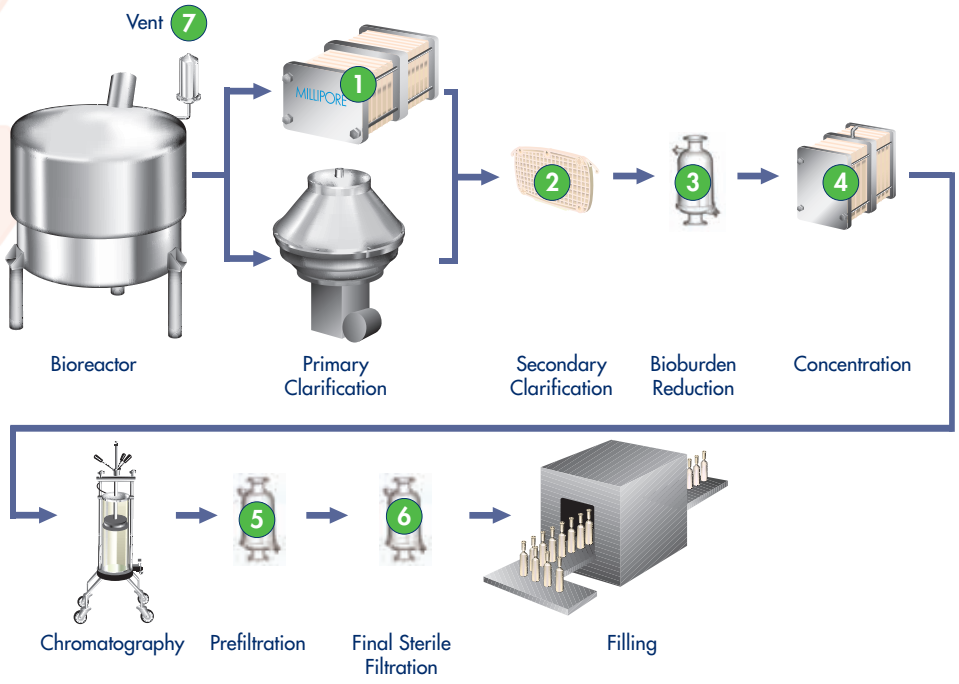
| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Concentration and Diafiltration**<br>(Prior to additional purification)<br>• Concentration and diafiltration of conjugate prior to reacting with the polysaccharide assures the proper formulation and conditions<br>• Fast, robust process able to accommodate feed fluid variations<br>• Easily scalable from lab to manufacturing scale | 1 Pellicon C Screen Cassettes with Ultracel PLC 100, 300 or 1,000 kD Membranes | • Low feed flow requirement minimizes pumping, working and hold up volumes.<br>• Higher product recovery and flux<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up |
| **Bioburden Reduction**<br>• Reduces bioburden<br>• Protects downstream chromatography and UF/DF steps<br>• Preserves product purity | 2 Double-layer Multilayer Durapore 0.45 µm + 0.22 µm Filters | • Sterilizing-grade PVDF 0.22 µm membrane with an additional 0.45 µm prefilter layer all in one pleated device<br>• Low-binding membranes assure product yield and sterility<br>• 100% Integrity testing ensures quality<br>• Double-layer construction provides excellent capacity and protection of downstream equipment<br>• Can be integrity tested on-site |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Concentration and Diafiltration**<br>(Prior to column chromatography steps)<br>• Concentration of process fluids and buffer exchange<br>• Will extend the life of expensive chromatography media and improve their speed and efficiency<br>• Fast, robust process able to accommodate feed fluid variations<br>• Wide chemical compatibility with cleaning agents<br>• Easily scalable from lab to manufacturing scale | 3 Pellicon V Screen Cassettes with Ultracel PLC 30, 100, 300 or 1,000 kD Membranes | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing.<br><br>*ALTERNATIVE: For applications where organic solvents are used, Millipore suggests utilizing a Prostak UF Module with Ultracel membrane.* |
| **Sterile Filtration**<br>• Sterilizing-grade step reduces bioburden<br>• Highly validated and reliable technology<br>• Preserves product purity<br>• Ensures product safety | 4 Durapore 0.22 µm Filters | • Low protein-binding sterilizing-grade PVDF membrane<br>• Low extractables preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assure proven performance<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Available in Millipak stacked disc format which allows minimal hold-up volume<br>• Although 0.22 µm membrane is typical for this application, Durapore filters are available in several pore sizes and, in single-layer or multi-layer configurations to accommodate the needs of each user. Choice should be based on small-scale testing. |

For details on Tank Venting 5, see page 70.

# Vaccines: Polysaccharides

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Primary Clarification**<br>• Remove whole cells and solids from bioreactor fluid and recover product in filtrate<br>• Requires high capacity<br>• Wide feed stream variability depending on cell culture type and conditions<br>• If solid content is too high, centrifugation becomes preferred technology<br>• Membrane selection will depend upon the size of the polysaccharide | 1 Prostak Open-Channel Modules with Durapore 0.22, 0.45 or 0.65 µm Membrane | • Best suited for large bioreactors >1,000 L or more than 10 batches/year<br>• Open-channel design to accommodate high cell density and high solids cell culture fluids<br>• High flux at low transmembrane pressure<br>• Allows volume reduction as fluid is concentrated<br>• Robust construction enables multiple use<br>• Validated for multiple SIP cycles<br>• Selection of Durapore membrane depends on particle size distribution in feed solution. Choice should be based upon small-scale testing. |
| **Secondary Clarification**<br>• Cell recovery from the fermenter broth, elimination of waste fluid in the filtrate<br>• High solids content in feed stream<br>• Feed stream quality can vary depending on cell type and culture conditions | 2 Triple-layer Millistak+ HC Filters<br><br>(Grade B1HC) | • Triple-layer configuration includes a membrane bottom layer to enhance filter loading capacity and retention<br>• Unique design enables the compression of multiple steps to one, lowering overall filtration costs. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Bioburden Reduction**<br>• Reduces bioburden at intermediate process step to reduce the risk of pyrogenic contamination and damage<br>• Protects downstream filters, media and equipment<br>• Preserves product purity<br>• Sterilizing-grade filtration required | 3 Millipore Express SHC 0.5 µm + 0.2 µm Filters | • Sterilizing-grade PES 0.2 µm membrane with an additional 0.5 µm prefilter layer all in one pleated device may eliminate the need for a prefilter<br>• Designed for bulk intermediate processing where fluids may be fouling in batch sizes ranging from 100 to 20,000 L.<br>• PES membrane provides broad chemical compatibility across a wide pH range (1–14)<br>• Robust construction validated for multiple SIP cycles<br>• 100% integrity tested to ensure quality<br>• Asymmetric pore structure delivers extremely high flow rates at low pressure drop<br>• Can be integrity tested on-site<br><br>*ALTERNATIVE: If a PVDF or low-protein binding membrane is required, Millipore suggests testing Multilayer Durapore 0.45 µm + 0.22 µm in your small-scale trials.* |
| **Concentration and Diafiltration**<br>(For final formulation)<br>• Concentration and diafiltration adjusts the end product to the proper dosage conditions prior to final packaging<br>• Fast, robust process able to accommodate feed fluid variations<br>• Easily scalable from lab to manufacturing scale | 4 Pellicon C Screen Cassettes with Ultracel PLC 30 or 100 kD Membranes | • Low feed flow requirement minimizes pumping, working and hold up volumes<br>• Higher product recovery and flux<br>• Highly retentive regenerated cellulose membranes offer good permeate flux and withstand process upsets<br>• Robust low binding void-free Ultracel PLC membranes assure consistent processing from batch to batch, have good chemical compatibility and are easy to clean<br>• Complete range of devices for easy scale-up<br>• Choose a membrane molecular weight cut-off 3–5X smaller than the biomolecule. Choice should be based on small-scale testing. |
| **Prefiltration**<br>(Bulk intermediate)<br>• Removes colloidal and particulate contaminants and extend the life of final filters<br>• Should preserve polysaccharide purity and operate consistently at high differential pressures and flow rates<br>• Must be able to withstand multiple SIP or hot water sanitization cycles<br>• Run efficiently to ensure process economics | 5 Double-layer Milligard Filters<br><br>(Grade LS, 0.5 µm + 0.2 µm) | • Prefiltration for Durapore 0.22 µm Filters<br>• Double-layer pleated configuration of mixed esters of cellulose membranes provide high dirt-holding capacity, and retention efficiency<br>• Low protein-binding media preserves polysaccharide purity<br>• High porosity membranes operate at high flow rates and low pressure drops<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Grade LS is commonly used for this application; Milligard filters are available in numerous pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br><br>*ALTERNATIVE: When choosing Multilayer Durapore 0.45 µm + 0.22 µm for Final Filtration, this step is not required. The prefilter layer is built into the final filter.* |

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| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Final Sterile Filtration**<br>• Sterilizing-grade step reduces bioburden<br>• Highly validated and reliable technology<br>• Preserves product purity<br>• Ensures product safety | 6 Single-layer Durapore 0.22 µm Filters | • Use in series with Milligard LS Filters<br>• Low protein-binding sterilizing-grade PVDF membrane<br>• Low extractables preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assures proven performance<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Available in Millipak stacked disc format which allows minimal hold-up volume<br>• Although 0.22 µm membrane is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user. Choice should be based on small-scale testing. |
| | 6 Double-layer Durapore Multilayer 0.45 µm + 0.22 µm Filters | • Low protein-binding sterilizing-grade PVDF 0.22 µm membrane layer combined with a 0.5 µm prefilter layer<br>• Very low extractables preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assure proven performance<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Prefiltration step 5 not required with this choice. |

For details on Tank Venting 7, see page 70.



# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| **Mammalian Cell** | | |
| Prostak MF Open-Channel 2-stack Modules | | |
| Durapore 0.22 µm membrane | 0.17 $m^2$ | PSGVAG021 |
| Millistak+ Mini Capsules | | |
| Grade B1HC | | MB1HC23HH3 |
| Grade C0HC | 23 $cm^2$ | MC0HC23HH3 |
| Grade D0HC | | MD0HC23HH3 |
| Opticap XL1 Capsules | | |
| Clarigard 0.3 µm media | 1-inch* | K003A51TT1 |
| OptiScale Capsules | | |
| Double-layer Milligard SS 0.5 µm + 0.2 µm membrane | | SVSSA47FF3 |
| Durapore 0.22 µm membrane | 13.8 $cm^2$ | SVGLA47FF3 |
| Double-layer Millipore Express SHC 0.5 µm + 0.2 µm membrane | | SHGEA47FF3 |
| Pellicon 2 C Screen Mini-Cassettes | | |
| Ultracel PLC C Screen 100 kD membrane | | P2C100C01 |
| Ultracel PLC C Screen 300 kD membrane | 0.1 $m^2$ | P2C300C01 |
| Ultracel PLC C Screen 1,000 kD membrane | | P2C01MC01 |

**Filter element size*

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| **Viral Vectors** | | |
| Millistak+ Mini Devices | | |
| Grade CE40 | 23 $cm^2$ | M40CE23HH3 |
| Grade CE45 | | M45CE23HH3 |
| Grade CE50 | | M50CE23HH3 |
| Evaluation Kit with OptiScale-25 Capsules** | | |
| Viresolve NFP membrane | 3.5 $cm^2$ | SVPVA25NB9 |
| OptiScale-40 Devices | | |
| Viresolve Prefilter | 5 $cm^2$ | SSPVA40NB9 |
| OptiScale Capsules | | |
| Durapore 0.22 µm membrane | 13.8 $cm^2$ | SVGLA47FF3 |
| Durapore 0.45 µm membrane (order with 0.5 µm prefilter SW06A47FF3) | | SVHLA47FF3 |
| Pellicon 2 V Screen Mini-Cassettes | | |
| Ultracel PLC 300 kD membrane | 0.1 $m^2$ | P2C300V01 |
| **Plasmid DNA** | | |
| Opticap XL1 Capsules | | |
| Polygard CR 10 µm media | 1-inch* | KR10A51TT1 |
| Clarigard 0.5 µm media | | K005A51TT1 |
| OptiScale Capsules | | |
| Double-layer Millipore Express SHC membrane | 13.8 $cm^2$ | SHGEA47FF3 |
| Pellicon 2 V Screen Mini-Cassettes | | |
| Ultracel PLC 30 kD membrane | 0.1 $m^2$ | P2C030V01 |
| Ultracel PLC 100 kD membrane | | P2C100V01 |
| Pellicon 2 C Screen Mini-Cassettes | | |
| Ultracel PLC 30 kD membrane | 0.1 $m^2$ | P2C030C01 |
| Ultracel PLC 100 kD membrane | | P2C100C01 |
| **Conjugates** | | |
| Pellicon V Screen Mini-Cassettes | | |
| Ultracel PLC 30 kD membrane | 0.1 $m^2$ | P2C030V01 |
| Ultracel PLC 100 kD membrane | | P2C100V01 |
| Ultracel PLC 300 kD membrane | | P2C300V01 |
| Ultracel PLC 1,000 kD membrane | | P2C01MV01 |
| Pellicon C Screen Mini-Cassettes | | |
| Ultracel PLC 30 kD membrane | 0.1 $m^2$ | P2C030C01 |
| Ultracel PLC 100 kD membrane | | P2C100C01 |
| Ultracel PLC 300 kD membrane | | P2C300C01 |
| Ultracel PLC 1,000 kD membrane | | P2C01MC01 |
| Prostak UF 4-stack Modules | | |
| Ultracel PL 5 kD membrane | 0.39 $m^2$ | PSLCSP041 |
| Ultracel PL 10 kD membrane | | PSLGSP041 |
| Ultracel PL 30 kD membrane | | PSLTSP041 |
| OptiScale Devices | | |
| Durapore 0.22 µm membrane | 13.8 $cm^2$ | SVGLA47FF3 |
| Multilayer Durapore 0.45 µm + 0.22 µm membrane | | SHGLA47FF3 |
| **Polysaccharides** | | |
| Prostak MF Open-Channel 2-stack Modules | | |
| Durapore 0.22 µm membrane | 0.17 $m^2$ | PSGVAG021 |
| Durapore 0.45 µm membrane | | PSHVAG021 |
| Durapore 0.65 µm membrane | | PSDVAG021 |
| OptiScale Devices | | |
| Double-layer Milligard LS 0.5 µm + 0.2 µm media | 13.8 $cm^2$ | SWLSA47FF3 |
| Double-layer Millipore Express SHC membrane | | SHGEA47FF3 |
| Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Multilayer Durapore 0.45 µm + 0.22 µm membrane | | SHGLA47FF3 |
| Pellicon 2 C Screen Mini-Cassettes | | |
| Ultracel PLC 30 kD membrane | 0.1 $m^2$ | P2C030C01 |
| Ultracel PLC 100 kD membrane | | P2C100C01 |
| Millistak+ Mini-Capsules | | |
| Grade B1HC | 23 $cm^2$ | MB1HC23HH3 |

**Filter element size*
***Viresolve membranes are available in an Evaluation Kit containing 9 OptiScale-25 Capsules, 3 each of 3 membrane lots, and are ideal for scale-up and scale down studies.*

Vaccines

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## Recommended Filters

Prostak MF Open-Channel Modules with Durapore Membrane

| | Area/Filter | 0.22 µm | 0.45 µm | 0.65 µm |
|---|---|---|---|---|
| 2-stack | 0.17 $m^2$ | PSGVAG021 | PSHVAG021 | PSDVAG021 |
| 4-stack | 0.33 $m^2$ | PSGVAG041 | PSHVAG041 | PSDVAG041 |
| 10-stack | 0.84 $m^2$ | PSGVAG101 | PSHVAG101 | PSDVAG101 |
| 20-stack | 1.7 $m^2$ | SK2P484E0 | SK2P242E9 | SK2P446E0 |

Pellicon 2 C Screen Cassettes with Ultracel PLC Membrane

| | Area/Filter | 30 kD | 100 kD | 300 kD | 1,000 kD |
|---|---|---|---|---|---|
| Mini-cassette | 0.1 $m^2$ | P2C030C01 | P2C100C01 | P2C300C01 | P2C01MC01 |
| Cassette | 0.5 $m^2$ | P2C030C05 | P2C100C05 | P2C300C05 | P2C01MC05 |
| Maxi-cassette | 2.5 $m^2$ | P2C030C25 | P2C100C25 | P2C300C25 | P2C01MC25 |

Pellicon 2 V Screen Cassettes with Ultracel PLC Membrane

| | Area/Filter | 30 kD | 100 kD | 300 kD | 1,000 kD |
|---|---|---|---|---|---|
| Mini-cassette | 0.1 $m^2$ | P2C030V01 | P2C100V01 | P2C300V01 | P2C01MV01 |
| Cassette | 0.5 $m^2$ | P2C030V05 | P2C100V05 | P2C300V05 | P2C01MV05 |
| Maxi-cassette | 2.0 $m^2$ | P2C030V20 | P2C100V20 | P2C300V20 | P2C01MV20 |

| Millistak+ HC Filters | Area/Filter | Grade B1HC | Grade C0HC | Area/Filter | Grade D0HC |
|---|---|---|---|---|---|
| 1-cell Pod | 0.1 $m^2$ | MB1HC01FS1 | MC0HC01FS1 | 0.1 $m^2$ | MD0HC01FS1 |
| 5-cell Pod | 0.5 $m^2$ | MB1HC05FS1 | MC0HC05FS1 | 0.5 $m^2$ | MD0HC05FS1 |
| 10-cell Pod | 1.0 $m^2$ | MB1HC10FS1 | MC0HC10FS1 | 1.0 $m^2$ | MD0HC10FS1 |
| Opticap Capsule | 650 $cm^2$ | KB1HC10FF1 | KC0HC10FF1 | 650 $cm^2$ | KD0HC10FF1 |
| 2-cell Stack, 16-inch dia. | 0.45 $m^2$ | LB1HCH6S6 | LC0HCH6S6 | 0.45 $m^2$ | LD0HCH6S6 |
| 8-cell Stack, 16-inch dia. | 1.8 $m^2$ | LB1HCG6S2 | LC0HCG6S2 | 1.6 $m^2$ | LD0HCG6S2* |

| Millistak+ CE Filters | Area/Filter | Grade 40CE | Grade 45CE | Grade 50CE |
|---|---|---|---|---|
| Opticap Capsule | 930 $cm^2$ | K40CE10FF1 | K45CE10FF1 | K50CE10FF1 |
| 6-cell Stack, 12-inch dia. | 0.63 $m^2$ | L40CEF2S3 | L45CEF2S3 | L50CEF2S3 |
| 9-cell Stack, 12-inch dia. | 0.95 $m^2$ | L40CEJ2S3 | L45CEJ2S3 | L50CEJ2S3 |
| 13-cell Stack, 12-inch dia. | 1.37 $m^2$ | L40CEN2S2 | L45CEN2S2 | L50CEN2S2 |
| 16-cell Stack, 12-inch dia. | 1.68 $m^2$ | L40CER2S2 | L45CER2S2 | L50CER2S2 |
| 16-cell Stack, 16-inch dia. | 3.47 $m^2$ | L40CET6S1 | L45CET6S1 | L50CET6S1 |

| Clarigard Filters | Filter Element Size | 0.3 µm | 0.5 µm |
|---|---|---|---|
| Opticap XL1 Capsule | 1-inch | K003A51TT1 | K005A51TT1 |
| 2-inch Cartridge | 2-inch | D003N0S03 | D005N0S03 |
| Opticap XL5 Capsule | 5-inch | K003A05TT1 | K005A05TT1 |
| Opticap XL10 Capsule | 10-inch | K003A10TT1 | K005A10TT1 |
| 10-inch Cartridge | 10-inch | D00371S01 | D00571S01 |
| 20-inch Cartridge | 20-inch | D00372S01 | D00572S01 |
| 30-inch Cartridge | 30-inch | D00373S01 | D00573S01 |
| 40-inch Cartridge | 40-inch | D00374S01 | D00574S01 |

| Polygard CR Filters | Filter Element Size | 10 µm |
|---|---|---|
| Opticap XL1 Capsule | 1-inch | KR10A51TT1 |
| 2-inch Cartridge | 2-inch | CR10M0203 |
| Opticap XL5 Capsule | 5-inch | KR10A05TT1 |
| Opticap XL10 Capsule | 10-inch | KR10A10TT1 |
| 10-inch Cartridge | 10-inch | CR1071006 |
| 20-inch Cartridge | 20-inch | CR1072006 |
| 30-inch Cartridge | 30-inch | CR1073006 |
| 40-inch Cartridge | 40-inch | CR1074006 |

| Milligard Filters | Area/Filter | Grade SS | Grade LS |
|---|---|---|---|
| Opticap XL2 Capsule | 0.07 $m^2$ | KWSSA02TT3 | KWLSA02TT3 |
| Opticap XL4 Capsule | 0.16 $m^2$ | KWSSA04TT3 | KWLSA04TT3 |
| 4-inch Cartridge | 0.28 $m^2$ | CWSSM4S03 | CWLSM4S03 |
| Opticap XL5 Capsule | 0.28 $m^2$ | KWSSA05TT1 | KWLSA05TT1 |
| Opticap XL10 Capsule | 0.7 $m^2$ | KWSSA10TT1 | KWLSA10TT1 |
| Opticap XLT10 Capsule | 0.7 $m^2$ | KWSSA1TTT1 | – |
| 10-inch Cartridge | 0.7 $m^2$ | CWSS71S03 | CWLS71S03 |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KWSSA2TTT1 | – |
| 20-inch Cartridge | 1.4 $m^2$ | CWSS72S03 | CWLS72S03 |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KWSSA3TTT1 | – |
| 30-inch Cartridge | 2.1 $m^2$ | CWSS73S03 | CWLS73S03 |
| 40-inch Cartridge | 2.8 $m^2$ | CWSS74S03 | CWLS74S03 |

**Millistak+ Grade D0HC comes in 7-cell 16-inch stacks.*

| Viresolve NFP Filters | Area/Filter | Catalogue No. | Viresolve Prefilter | Area/Filter | Catalogue No. |
|---|---|---|---|---|---|
| 4-inch Opticap Capsule | 0.077 $m^2$ | KVPV04TT3 | | | |
| | – | – | 10-inch Opticap Capsule | 850 $cm^2$ | KSPV01FF1 |
| Opticap XL10 Capsule | 0.48 $m^2$ | KVPVA10TT1 | | | |
| Opticap XLT10 Capsule | 0.48 $m^2$ | KVPVA1TTT1 | | | |
| 10-inch Cartridge | 0.48 $m^2$ | CVPV71TP1 | | | |
| Opticap XLT20 Capsule | 0.97 $m^2$ | KVPVA2TTT1 | | | |
| 20-inch Cartridge | 0.97 $m^2$ | CVPV72TP1 | | | |
| Opticap XLT30 Capsule | 1.45 $m^2$ | KVPVA3TTT1 | | | |
| 30-inch Cartridge | 1.45 $m^2$ | CVPV73TP1 | | | |

| Durapore Filters | Area/Filter | 0.22 µm Sterilizing-grade | 0.45 µm + 0.5 µm Prefilter Layer | Area/Filter | 0.45 µm + 0.22 µm Sterilizing-grade Multilayer |
|---|---|---|---|---|---|
| Opticap XL2 Capsule | 0.09 $m^2$ | KVGLA02TT3 | | | |
| Opticap XL4 Capsule | 0.19 $m^2$ | KVGLA04TT3 | | | |
| 5-inch Cartridge | 0.35 $m^2$ | CVGL75S01 | | | |
| Opticap XL5 Capsule | 0.35 $m^2$ | KVGLA05TT1 | | | |
| Opticap XL5 Gamma-compatible Capsule | 0.35 $m^2$ | KVGLG05TT1 | | | |
| Opticap XL10 Capsule | 0.69 $m^2$ | KVGLA10TT1 | KVHLA10TT1 | 0.55 $m^2$ | KHGLA10TT1 |
| Opticap XL10 Gamma-compatible Capsule | 0.69 $m^2$ | KVGLG10TT1 | | | |
| 10-inch Cartridge | 0.69 $m^2$ | CVGL71TP3 | CVHL71TP3 | 0.55 $m^2$ | CHGL71TP3 |
| Opticap XLT10 Capsule | 0.69 $m^2$ | KVGLA1TTT1 | | 0.55 $m^2$ | KHGLA1TTT1 |
| Opticap XLT10 Gamma-compatible Capsule | 0.69 $m^2$ | KVGLG1TTT1 | | | |
| 20-inch Cartridge | 1.4 $m^2$ | CVGL72TP3 | CVHL72TP3 | 1.1 $m^2$ | CHGL72TP3 |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KVGLA2TTT1 | | 1.2 $m^2$ | KHGLA2TTT1 |
| Opticap XLT20 Gamma-compatible Capsule | 1.4 $m^2$ | KVGLG2TTT1 | | | |
| 30-inch Cartridge | 2.1 $m^2$ | CVGL73TP3 | CVHL73TP3 | 1.65 $m^2$ | CHGL73TP3 |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KVGLA3TTT1 | | 1.75 $m^2$ | KHGLA3TTT1 |
| Opticap XLT30 Gamma-compatible Capsule | 2.1 $m^2$ | KVGLG3TTT1 | | | |
| 40-inch Cartridge | 2.76 $m^2$ | CVGL74TP3 | CVHL74TP3 | | |

| Millipore Express SHC Sterilizing-grade Filters | Area/Filter | 0.5 µm + 0.2 µm |
|---|---|---|
| Opticap XL3 Capsule | 0.13 $m^2$ | KHGEA03TT3 |
| Opticap XL3 Gamma-compatible Capsule | 0.13 $m^2$ | KHGEG03TT3 |
| Opticap XL5 Capsule | 0.23 $m^2$ | KHGEA05TT1 |
| Opticap XL5 Gamma-compatible Capsule | 0.24 $m^2$ | KHGEG05TT1 |
| 5-inch Cartridge | 0.23 $m^2$ | CHGE75TS3 |
| Opticap XL10 Capsule | 0.49 $m^2$ | KHGEA10TT1 |
| Opticap XLT10 Capsule | 0.49 $m^2$ | KHGEA1TTT1 |
| Opticap XL10 Gamma-compatible Capsule | 0.54 $m^2$ | KHGEG10TT1 |
| Opticap XLT10 Gamma-compatible Capsule | 0.54 $m^2$ | KHGEG1TTT1 |
| 10-inch Cartridge | 0.49 $m^2$ | CHGE71TS3 |
| Opticap XLT20 Capsule | 0.98 $m^2$ | KHGEA2TTT1 |
| Opticap XLT20 Gamma-compatible Capsule | 1.09 $m^2$ | KHGEG2TTT1 |
| 20-inch Cartridge | 0.98 $m^2$ | CHGE72TS3 |
| Opticap XLT30 Capsule | 1.47 $m^2$ | KHGEA3TTT1 |
| Opticap XLT30 Gamma-compatible Capsule | 1.63 $m^2$ | KHGEG3TTT1 |
| 30-inch Cartridge | 1.47 $m^2$ | CHGE73TS3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

*Millipore offers a comprehensive line of chromatography columns, systems and media. Contact Millipore for details.*

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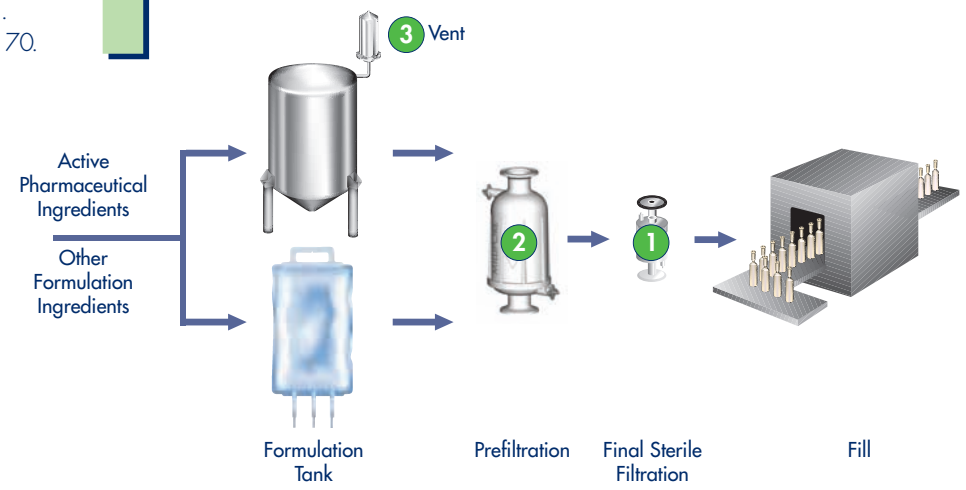
# Final Aseptic Fill

Small volume parenterals (SVP) are typically packaged in small vials <20 mL and can include pre-filled syringes, ampules, or lyophilized powder. Sterile filtration is used after compounding or at the filling head.

For details on Tank Venting 3, see page 70.

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Final Sterile Filtration**<br>• High sterility assurance<br>• Highly validated and reliable technology<br>• Ensure product purity<br>• High flow rate<br>• Easily Integrity tested pre- and post-sterilization<br>• Robust construction to withstand demanding sanitization cycles<br>• Low hold-up volume | 1 Durapore 0.22 µm Filters | • Low protein-binding sterilizing-grade PVDF membrane<br>• Bacterial retentive membrane has been the proven industry standard for decades<br>• Very low extractables preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity testing and thousands of applications assures proven performance<br>• Validated for multiple SIP and hot water sanitization cycles<br>• Integrity testable on-site<br>• Available in Millipak stacked disc format which allows minimal hold-up volume<br>• Although 0.22 µm membrane is ideal for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user. Choice should be based on small-scale testing.<br><br>*ALTERNATIVE: For high flow applications or if a PES membrane is requested, sterilizing-grade Millipore Express PES Filters are available.* |
| **Prefilter**<br>• Typically needed only for more concentrated solutions (>10 mg/mL)<br>• Must prevent plugging of down-stream sterilizing-grade<br>• Preserves product purity<br>• High flow rate<br>• Robust construction to withstand SIP | 2 Milligard Filters<br><br>(Grade SS, 0.5 µm + 0.2 µm) | • Available in double-layer pleated configurations for increased particle and colloid loading capacity<br>• Mixed esters of cellulose filter material with low protein-binding characteristics<br>• Low extractables and non-fiber releasing<br>• High flow rate at low pressure drop<br>• Validated for multiple SIP cycles<br>• Decades of proven performance protecting membrane filters<br>• 100% integrity tested<br>• Although grade SS, 0.5 µm + 0.2 µm is commonly used to protect downstream 0.22 µm sterilizing-grade membrane filters, Milligard filters are available in several pore sizes and in single-layer or multi-layer configurations. Choice should be based on small-scale testing. |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening for the best candidates. If capacity data illustrates that fluid is a non-plugging stream (≥1,000 L/m²) then sizing is based on flow rate and pressure drop requirements.

Millipore recommends normalizing for pressure and area of the OptiScale small-scale screening capsules. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| OptiScale Devices | | |
| Milligard SC 1.2 µm + 0.5 µm membrane | | SWSCA47FF3 |
| Milligard SS 0.5 µm + 0.2 µm membrane | | SWSSA47FF3 |
| Milligard 1.2 µm membrane | 13.8 cm² | SW19A47FF3 |
| Milligard 0.5 µm membrane | | SW06A47FF3 |
| Milligard 0.2 µm membrane | | SW03A47FF3 |
| OptiScale Devices | | |
| Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Millipore Express SHF 0.2 µm membrane | 13.8 cm² | SGEPA47FF3 |
| Double-layer Millipore Express SHC 0.5 µm + 0.2 µm membrane | | SHGEA47FF3 |

## Recommended Filters

Recommendation table based on filter capacity of approximately 1,000 L/m²

| | Prefiltration (optional) | | Final Sterilizing-grade Filtration | |
|---|---|---|---|---|
| **Volume** | **Device (area/filter)** | **Catalogue No.** | **Device (area/filter)** | **Catalogue No.** |
| **Solution Concentration < 10 mg/mL** | | | | |
| | | | Durapore 0.22 µm Filters | |
| 5–10 L | NOT REQUIRED | | Millipak Gold 20 Unit (0.01 m²) | MPGL02GF2 |
| 10–50 L | NOT REQUIRED | | Millipak Gold 40 Unit (0.02 m²)<br>Millipak Gold 60 Unit (0.03 m²)<br>Millipak Gold 100 Unit (0.05 m²) | MPGL04GF2<br>MPGL06GF3<br>MPGL1GCF3 |
| 50–300 L | NOT REQUIRED | | Opticap XL2 Capsule (0.09 m²)<br>Millipak Gold 200 Unit (0.1 m²)<br>Opticap XL4 Capsule (0.19 m²)<br>OptiSeal Cartridge (0.18 m²)<br>Opticap XL5 Capsule (0.35 m²)<br>5-inch Cartridge (0.35 m²) | KVGLA02TT3<br>MPGL2GCF3<br>KVGLA04TT3<br>LAGL04TP6<br>KVGLA05TT1<br>CVGL75S01 |
| 300–1,500 L | NOT REQUIRED | | Opticap XL10 Capsule (0.69 m²)<br>Opticap XLT10 Capsule (0.69 m²)<br>10-inch Cartridge (0.69 m²) | KVGLA10TT1<br>KVGLA1TTT1<br>CVGL71TP3 |
| **Solution Concentration > 10 mg/mL** | | | | |
| | Milligard SS 0.5 µm + 0.2 µm Prefilters | | Durapore 0.22 µm Filters | |
| 5–10 L | NOT REQUIRED | | Millipak Gold 20 Unit (0.01 m²) | MPGL02GF2 |
| 10–50 L | Opticap XL2 Capsule (0.07 m²) | KWSSA02TT3 | Millipak Gold 40 Unit (0.02 m²)<br>Millipak Gold 60 Unit (0.03 m²)<br>Millipak Gold 100 Unit (0.05 m²) | MPGL04GF2<br>MPGL06GF3<br>MPGL1GCF3 |
| 50–300 L | Opticap XL2 Capsule ( 0.07 m²)<br>Opticap XL4 Capsule (0.16 m²)<br>Opticap XL5 Capsule (0.28 m²)<br>4-inch Cartridge (0.28 m²) | KWSSA02TT3<br>KWSSA04TT3<br>KWSSA05TT1<br>CWSSM4S03 | Opticap XL2 Capsule (0.09 m²)<br>Millipak Gold 200 Unit (0.11 m²)<br>Opticap XL4 Capsule (0.19 m²)<br>Optiseal Cartridge (0.18 m²)<br>Opticap XL5 Capsule (0.35 m²)<br>5-inch Cartridge (0.35 m²) | KVGLA02TT3<br>MPGL2GCL3<br>KVGLA04TT3<br>LAGL04TP6<br>KVGLA05TT1<br>CVGL75S01 |
| 300–1,500 L | Opticap XL10 Capsule (0.7 m²)<br>Opticap XLT10 Capsule (0.7 m²)<br>10-inch Cartridge (0.7 m²) | KWSSA10TT1<br>KWSSA10TTT1<br>CWSS71S03 | Opticap XL10 Capsule (0.69 m²)<br>Opticap XLT10 Capsule (0.69 m²)<br>10-inch Cartridge (0.69 m²) | KVGLA10TT1<br>KVGLA1TTT1<br>CVGL71TP3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

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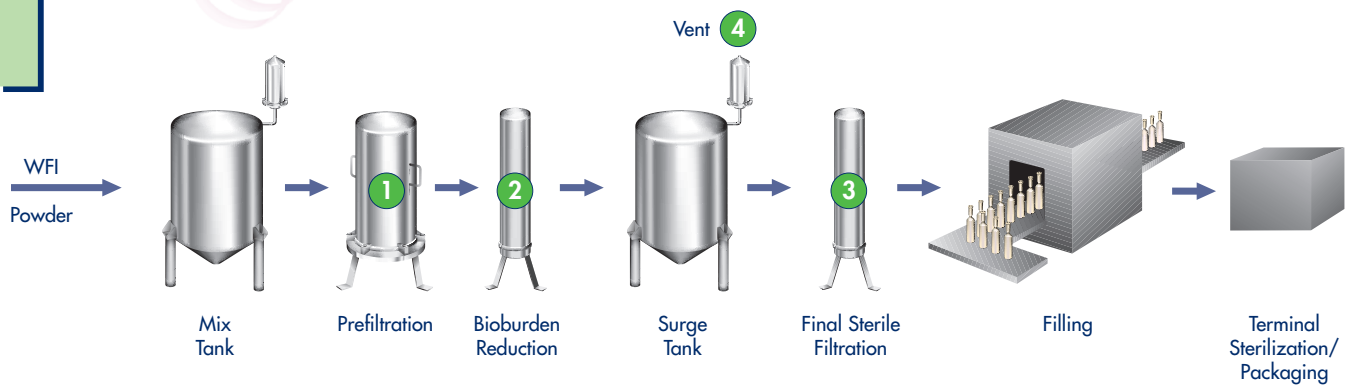
# Large Volume Parenterals (LVP)

Large volume parenterals are single unit doses >100 mL in volume. Typical solutions include water, dextrose (5–50%), amino acids, salts and viscous Total Parenteral Nutrition (TPN) components with batch sizes in the tens of thousands of liters. Filtration is used for particle and colloid removal as well as bioburden reduction.

For details on Tank Venting 4, see page 70.

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Prefiltration**<br>• Remove colloidal and particulate contaminants<br>• Preserve product purity<br>• Operate consistently at high differential pressures and flow rates<br>• Prevent plugging and extend the life of downstream filters<br>• Able to withstand demanding sanitization cycles<br>• Run efficiently to ensure process economics<br>• Solute concentration impacts filter selection | 1 Double-layer Milligard Filters<br>(Grade SS, 0.5 µm + 0.2 µm, or Grade SC, 1.2 µm + 0.5 µm) | • Double-layer pleated configuration of mixed esters of cellulose membranes remove particles and colloids<br>• High porosity membranes operate at high flow rates and low pressure drops<br>• Better suited for low-solute concentrations<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Available in a variety of pore sizes to accommodate the needs of each user. Grade SS is commonly used to protect downstream 0.22 µm sterilizing-grade filters. Grade SC is better suited to protect 0.45 µm membrane filters. Choice should be made based on small-scale testing. |
| | 1 Double-layer Polysep II Filters<br>(Grade W6, 1 µm+ 0.5 µm, or Grade W3, 1 µm + 0.2 µm) | • Borosilicate glass top layer enhances particle and loading capacity in high solute applications<br>• Mixed esters of cellulose membrane bottom layer ensures high retention and filtrate quality<br>• Ideal for high solute concentration such as 5% Dextrose<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Available in a variety of pore sizes to accommodate the needs of each user. Grade W3 is commonly used to protect downstream 0.22 µm membrane filters. Grade W6 is better suited to protect 0.45 µm membrane filters. Choice should be made based on small-scale testing. |

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Bioburden Reduction**<br>• Reduce bioburden prior to terminal sterilization<br>• Preserve product purity<br>• Operate consistently at high flow rates<br>• Able to withstand demanding sanitization requirements | 2 Double-layer Durapore 0.45 µm Filters<br><br>(with 0.5 µm prefilter layer) | • Low protein-binding PVDF membrane with prefilter<br>• Retentive membrane reduces bioburden<br>• Low extractables and non-fiber releasing PVDF chemistry preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity tested to ensure quality<br>• Validated for multiple SIP and hot water sanitization cycles |
| | 2 Durapore CBR 0.2 µm Filters | • Low protein-binding 0.2 µm PVDF membrane<br>• Bacterial retentive membrane reduces bioburden<br>• Low extractables and non-fiber releasing PVDF chemistry preserve product purity and yield<br>• High flow rate at low pressure drop for reliable economic processing<br>• 100% integrity tested to ensure quality<br>• Validated for multiple SIP and hot water sanitization cycles |
| **Final Sterile Filtration**<br>• Sterile filtration prior to terminal sterilization<br>• Operate consistently at high differential pressures and flow rates<br>• Able to withstand rigorous sanitization and process requirements<br>• Ensure product safety | 3 Durapore 0.22 µm Filters<br><br>*ALTERNATIVE: If a PES membrane is required, Millipore suggests including Millipore's Express SHF Filters in your screening trials.* | • Sterilizing-grade PVDF membrane<br>• 100% Integrity testing and thousands of existing applications assure proven performance<br>• Although 0.22 µm membrane is typical for this application, Durapore filters are available in several pore sizes and in single-layer or multi-layer configurations to accommodate the needs of each user, the degree of protection required for the downstream process and the plugging characteristics of the fluid. Choice should be based on small-scale testing.<br>• Integrity testable on-site |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| OptiScale Capsules | | |
| Double-layer Milligard SC 1.2 µm + 0.5 µm membrane | 13.8 $cm^2$ | SWSCA47FF3 |
| Double-layer Milligard SS 0.5 µm + 0.2 µm membrane | | SWSSA47FF3 |
| Double-layer Polysep II W6 1.0 µm + 0.5 µm membrane | | SGW6A47FF3 |
| Double-layer Polysep II W3 1.0 µm + 0.2 µm membrane | | SGW3A47FF3 |
| Durapore 0.45 µm membrane (order with 0.5 µm prefilter SW06A47FF3) | | SVHLA47FF3 |
| Durapore CBR 0.2 µm membrane | | SVGLA47FF3 |
| Single-layer Durapore 0.22 µm membrane | | SVGLA47FF3 |
| Single-layer Millipore Express SHF membrane | | SGEPA47FF3 |

## Recommended Filters

**Prefiltration and Bioburden Reduction used in combination.**

**Low Solute Concentration (e.g. 5% Dextrose)**

| | Area/Filter | Catalogue No. | | Area/Filter | Catalogue No. |
|---|---|---|---|---|---|
| Milligard SS (0.5 µm + 0.2 µm) Filters | | | Durapore CBR 0.2 µm Filters | | |
| Opticap XL10 Capsule | 0.7 $m^2$ | KWSSA10TT1 | 10-inch Cartridge | 0.69 $m^2$ | CVDI71TPS |
| Opticap XLT10 Capsule | 0.7 $m^2$ | KWSSA1TTT1 | 20-inch Cartridge | 1.4 $m^2$ | CVDI72TPS |
| 10-inch Cartridge | 0.7 $m^2$ | CWSS71S03 | 30-inch Cartridge | 2.1 $m^2$ | CVDI73TPS |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KWSSA2TTT1 | 40-inch Cartridge | 2.8 $m^2$ | CVDI74TPS |
| 20-inch Cartridge | 1.4 $m^2$ | CWSS72S03 | | | |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KWSSA3TTT1 | | | |
| 30-inch Cartridge | 2.1 $m^2$ | CWSS73S03 | | | |
| 40-inch Cartridge | 2.8 $m^2$ | CWSS74S03 | | | |
| Milligard SC (1.2 µm + 0.5 µm) Filters | | | Durapore 0.45 µm Filters + 0.5 µm Prefilter Layer | | |
| Opticap XL10 Capsule | 0.7 $m^2$ | KWSCA10TT1 | Opticap XL10 Capsule | 0.69 $m^2$ | KVHLA10TT1 |
| Opticap XLT10 Capsule | 0.7 $m^2$ | KWSCA1TTT1 | 10-inch Cartridge | 0.69 $m^2$ | CVHL71TP3 |
| 10-inch Cartridge | 0.7 $m^2$ | CWSC71S03 | 20-inch Cartridge | 1.4 $m^2$ | CVHL72TP3 |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KWSCA2TTT1 | 30-inch Cartridge | 2.1 $m^2$ | CVHL73TP3 |
| 20-inch Cartridge | 1.4 $m^2$ | CWSC72S03 | 40-inch Cartridge | 2.8 $m^2$ | CVHL74TP3 |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KWSCA3TTT1 | | | |
| 30-inch Cartridge | 2.1 $m^2$ | CWSC73S03 | | | |
| 40-inch Cartridge | 2.8 $m^2$ | CWSC74S03 | | | |

## Prefiltration and Bioburden Reduction used in combination.

### High Solute Concentration (e.g. up to 50% Dextrose)

| | Area/Filter | Catalogue No. | | Area/Filter | Catalogue No. |
|---|---|---|---|---|---|
| **Polysep II W3 (1.0 µm + 0.2 µm) Filters** | | | **Durapore CBR 0.2 µm Filters** | | |
| Opticap XL10 Capsule | 0.46 $m^2$ | KGW3A10TT1 | 10-inch Cartridge | 0.69 $m^2$ | CVDI71TPS |
| Opticap XLT10 Capsule | 0.46 $m^2$ | KGW3A1TTT1 | 20-inch Cartridge | 1.4 $m^2$ | CVDI72TPS |
| 10-inch Cartridge | 0.46 $m^2$ | CGW371S03 | 30-inch Cartridge | 2.1 $m^2$ | CVDI73TPS |
| Opticap XLT20 Capsule | 0.92 $m^2$ | KGW3A2TTT1 | 40-inch Cartridge | 2.8 $m^2$ | CVDI74TPS |
| 20-inch Cartridge | 0.92 $m^2$ | CGW372S03 | | | |
| Opticap XLT30 Capsule | 1.38 $m^2$ | KGW3A3TTT1 | | | |
| 30-inch Cartridge | 1.38 $m^2$ | CGW373S03 | | | |
| 40-inch Cartridge | 1.84 $m^2$ | CGW374S03 | | | |
| **Polysep II W6 (1.0 µm + 0.5 µm) Filters** | | | **Durapore 0.45 µm Filters + 0.5 µm Prefilter Layer** | | |
| Opticap XL10 Capsule | 0.46 $m^2$ | KGW6A10TT1 | Opticap XL10 Capsule | 0.69 $m^2$ | KVHLA10TT1 |
| Opticap XLT10 Capsule | 0.46 $m^2$ | KGW6A1TTT1 | 10-inch Cartridge | 0.69 $m^2$ | CVHL71TP3 |
| 10-inch Cartridge | 0.46 $m^2$ | CGW671S03 | 20-inch Cartridge | 1.4 $m^2$ | CVHL72TP3 |
| Opticap XLT20 Capsule | 0.92 $m^2$ | KGW6A2TTT1 | 30-inch Cartridge | 2.1 $m^2$ | CVHL73TP3 |
| 20-inch Cartridge | 0.92 $m^2$ | CGW672S03 | 40-inch Cartridge | 2.8 $m^2$ | CVHL74TP3 |
| Opticap XLT30 Capsule | 1.38 $m^2$ | KGW6A3TTT1 | | | |
| 30-inch Cartridge | 1.38 $m^2$ | CGW673S03 | | | |
| 40-inch Cartridge | 1.84 $m^2$ | CGW674S03 | | | |

## Final Sterile Filtration

| | Area/Filter | Catalogue No. |
|---|---|---|
| **Durapore 0.22 µm Filters** | | |
| Opticap XL10 Capsule | 0.69 $m^2$ | KVGLA10TT1 |
| Opticap XLT10 Capsule | 0.69 $m^2$ | KVGLA1TTT1 |
| Opticap XL10 Gamma-compatible Capsule | 0.69 $m^2$ | KVGLG10TT1 |
| XLT10 Gamma-compatible Capsule | 0.69 $m^2$ | KVGLG1TTT1 |
| 10-inch Cartridge | 0.69 $m^2$ | CVGL71TP3 |
| Opticap XLT20 Capsule | 1.4 $m^2$ | KVGLA2TTT1 |
| XLT20 Gamma-compatible Capsule | 1.4 $m^2$ | KVGLG2TTT1 |
| 20-inch Cartridge | 1.4 $m^2$ | CVGL72TP3 |
| Opticap XLT30 Capsule | 2.1 $m^2$ | KVGLA3TTT1 |
| XLT30 Gamma-compatible Capsule | 2.1 $m^2$ | KVGLG3TTT1 |
| 30-inch Cartridge | 2.1 $m^2$ | CVGL73TP3 |
| 40-inch Cartridge | 2.8 $m^2$ | CVGL74TP3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

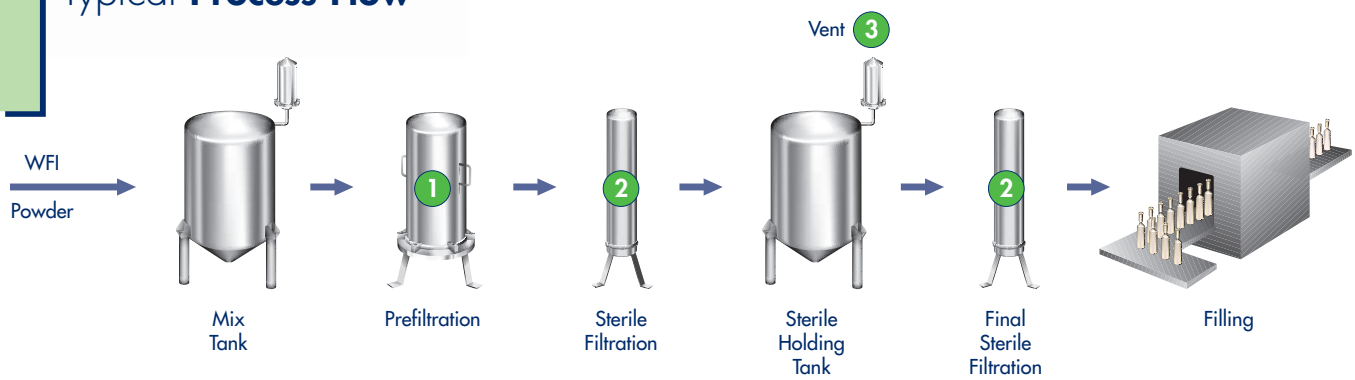
# Ophthalmic Solutions

Ophthalmic solutions range from contact lens cleaning and storage solutions to eye surgery and treatment products. These preparations must meet stringent regulatory requirements and product specifications.

Though the major component in ophthalmics is water, many contain salts such as NaCl, preservatives, petrolatum for ointments and thixotropic polymeric substances for lubricating agents. Heat-labile components are processed via sterile filtration for particle and bioburden reduction and microorganism removal.

For details on Tank Venting 3, see page 70.

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Prefiltration**<br>• Reduce particles and bioburden<br>• Extend the life of final filters<br>• Must be robust for high volume processes<br>• Run efficiently for optimal process economics | 1 Double-layer Polysep II Filters (Grade W6, 1 µm + 0.5 µm) | • Borosilicate glass top layer enhances particle and loading capacity in high solute applications<br>• Mixed esters of cellulose membrane bottom layer ensures high retention and filtrate quality<br>• Robust construction validated to withstand multiple SIP or hot water sanitization cycles<br>• Non-fiber releasing structure preserves product purity<br>• 100% integrity tested to ensure quality<br>• Available in a variety of pore sizes to accommodate the needs of each user. Grade W6 is commonly used in this application. Choice should be made based on small-scale testing. |
| **Sterile Filtration**<br>• Sterilizing-grade filter to remove microorganisms<br>• Operate consistently at high flow rates<br>• Must be robust for high volume processes<br>• Run efficiently to ensure process economics | 2 Charged Durapore 0.22 µm Filters | • Sterilizing-grade PVDF membrane<br>• Ideal solution when preservative binding is a concern<br>• High flow rates and throughput, low extractables and protein binding<br>• 100% Integrity testing to ensure performance |
| | 2 Millipore Express SHF 0.2 µm Filters | • Sterilizing-grade PES membrane providing broad chemical compatibility across a wide pH range (1–14)<br>• Asymmetric pore structure delivers extremely high flow rates at low preservative binding<br>• 100% integrity tested to ensure quality |

# 3 Filter Quick **Reference Guide**

## Process Development Screening

Millipore recommends running small-scale trials for capacity and throughput screening. This table provides details on process development devices for recommended filters and alternatives since the ideal solution will vary based on each fluid stream. The following order table is for recommended devices only.

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| OptiScale Capsules<br>Polysep II W6 1.0 µm + 0.5 µm membrane<br>Millipore Express SHF membrane | 13.8 $cm^2$ | <br>SGW6A47FF3<br>SGEPA47FF3 |
| Charged Durapore 0.22 µm, 47 mm filter discs | 13.8 $cm^2$ | CCGL04725 |

## Recommended Filters

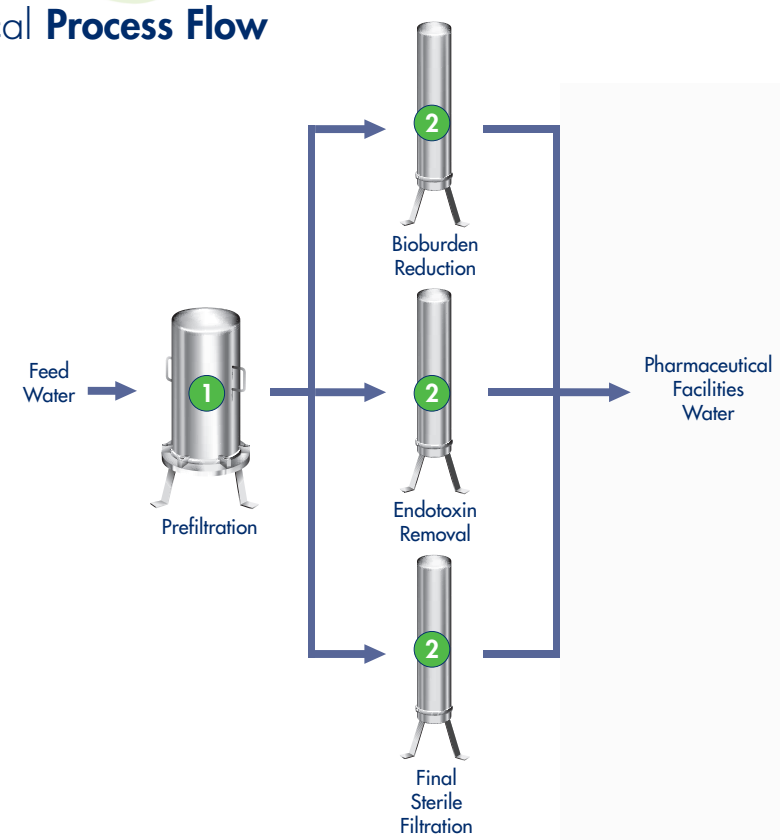
| | Small-Scale Processing <100 L | | Large-Scale Processing >100 L | |
|---|---|---|---|---|
| **Media/Membrane** | **Device (area/filter)** | **Catalogue No.** | **Device (area/filter)** | **Catalogue No.** |
| **Prefiltration** | | | | |
| Double-layer Polysep II Filters (Grade W6, 1.0 µm + 0.5 µm) | Opticap XL2 Capsule (0.06 $m^2$)<br>Opticap XL4 Capsule (0.11 $m^2$)<br>Opticap XL5 Capsule (0.19 $m^2$)<br>4-inch Cartridge (0.19 $m^2$) | KGW6M02TT3<br>KGW6A04TT3<br>KGW6A05TT1<br>CGW674S03 | Opticap XL10 Capsule (0.46 $m^2$)<br>Opticap XLT10 Capsule (0.46 $m^2$)<br>10-inch Cartridge (0.46 $m^2$)<br>Opticap XLT20 Capsule (0.92 $m^2$)<br>20-inch Cartridge (0.92 $m^2$)<br>Opticap XLT30 Capsule (1.38 $m^2$)<br>30-inch Cartridge (1.38 $m^2$) | KGW6A10TT1<br>KGW6A1TTT1<br>CGW671S03<br>KGW6A2TTT1<br>CGW672S03<br>KGW6A3TTT1<br>CGW673S03 |
| **Sterilizing-grade Filtration** | | | | |
| Charged Durapore 0.22 µm PVDF Filters | Optiseal Cartridge ( 0.18 $m^2$) | LCGL04TP6 | 10-inch Cartridge (0.69 $m^2$)<br>20-inch Cartridge (1.4 $m^2$)<br>30-inch Cartridge (2.1 $m^2$) | CCGL71TP1<br>CCGL72TP1<br>CCGL73TP1 |
| Millipore Express SHF 0.2 µm PES Filters | Opticap XL3 Capsule (0.16 $m^2$)<br>Opticap XL5 Capsule (0.29 $m^2$)<br>5-inch Cartridge (0.29 $m^2$) | KGEPA03TT3<br>KGEPA05TT1<br>CGEP75TP3 | Opticap XL10 Capsule (0.54 $m^2$)<br>Opticap XLT10 Capsule (0.54 $m^2$)<br>10-inch Cartridge (0.54 $m^2$)<br>Opticap XLT20 Capsule (1.08 $m^2$)<br>20-inch Cartridge (1.08 $m^2$)<br>Opticap XLT30 Capsule (1.62 $m^2$)<br>30-inch Cartridge (1.62 $m^2$) | KGEPA10TT1<br>KGEPA1TTT1<br>CGEP71TP3<br>KGEPA2TTT1<br>CGEP72TP3<br>KGEPA3TTT1<br>CGEP73TP3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

# Facilities Water

Pharmaceutical grade water is defined as feed water common to process systems such as washers, autoclaves or secondary water purification systems such as WFI distillation. Filters in central water systems may be exposed to a variety of contaminants. The filter train should reduce the bioburden and contaminant load while maintaining a low pressure drop for extended periods of time. Filters in DI systems must maintain low pressure drops throughout long throughput cycles and may be exposed to particle loads for resin beds.

## 1 Typical **Process Flow**




## 2 Understanding the **Options**

| Essential Process Requirements | Recommended Filter | Filter Characteristics |
|---|---|---|
| **Prefiltration** | 1 Clarigard 3.0 µm Filters | • All-polypropylene filters have a 99.99% retention rating with high particle holding capacity and low extractables |
| **Bioburden Reduction** | 2 Durapore CBR 0.2 µm PVDF Filters | • An economical solution when only bioburden reduction is required |
| **Endotoxin Removal** | 2 Charged Durapore 0.22 µm PVDF Filters | • A great choice when endotoxin and bioburden reduction is required |
| **Final Sterile Filtration** | 2 Millipore Express SHF 0.2 µm PES Sterilizing-grade Filters | • The best alternative where high flow rates are required |

# 3 Filter Quick **Reference Guide**

## Recommended Filters

| Flowrate (Lpm) | Prefiltration | Bioburden Reduction | Endotoxin Removal | Sterilizing Filtration |
|---|---|---|---|---|
| | Clarigard 3.0 µm Filters | Durapore CBR 0.2 µm Filters | Charged Durapore 0.22 µm Filters | Millipore Express SHF 0.2 µm Filters |
| 1–15 | 10-inch Cartridge: D03071S01 | 10-inch Cartridge: CVDI71TPS | 10-inch Cartridge: CCGL71TP1 | 10-inch Cartridge: CGEP71TP3 |
| 15–30 | 20-inch Cartridge: D03072S01 | 20-inch Cartridge: CVDI72TPS | 20-inch Cartridge: CCGL72TP1 | 20-inch Cartridge: CGEP72TP3 |
| 30–45 | 20-inch Cartridge: D03072S01 | 20-inch Cartridge: CVDI72TPS | 30-inch Cartridge: CCGL73TP1 | 30-inch Cartridge: CGEP73TP3 |
| Per 45 | 30-inch Cartridge: D03073S01 | 30-inch Cartridge: CVDI73TPS | 30-inch Cartridge: CCGL73TP1 | 30-inch Cartridge: CGEP73TP3 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

*For details on Millipore's lab water systems visit www.millipore.com/H2O*

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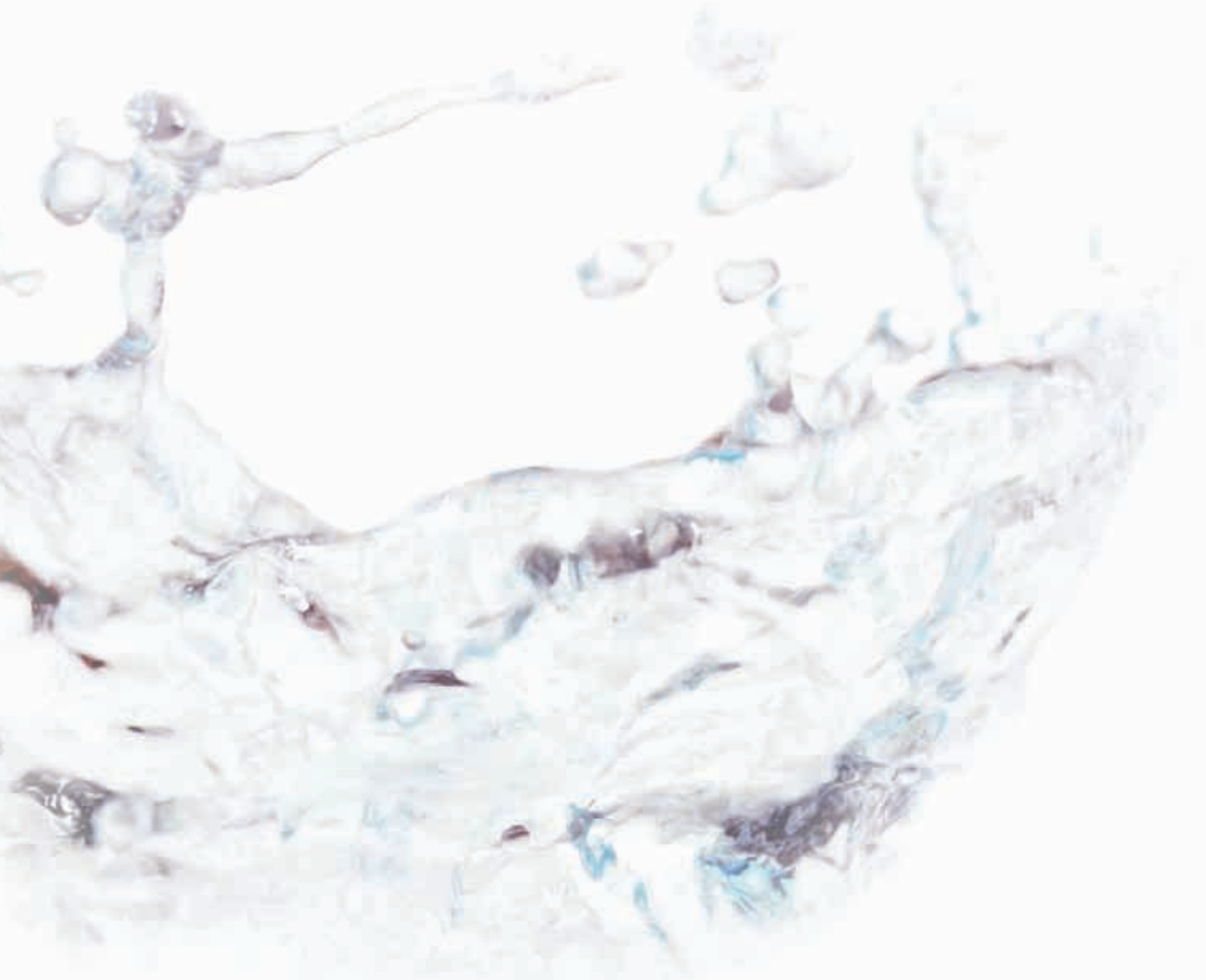

# Tank Venting and Air Filtration

Hydrophobic sterilizing-grade filters are commonly used as air vents on processing tanks. The goal of the application is to maintain near ambient pressure in the tank while ensuring sterility in the tank. The tank vent filter removes viruses and microorganisms from the gas as it flows in or out of the tank.

### Filter requirements

- Sterilizing-grade PTFE membrane
- Integrity testable, bacteria and virus retentive
- Robust construction validated for multiple SIP cycles
- Delivers high flow rates
- 100% integrity tested to ensure quality

### Sizing Your Vent Filter

Air flows in and out of a process tank for two reasons. The first is to replace a volume of liquid as it is pumped in or out of the tank. Sizing the tank vent filter for pump-out or fill rate is relatively simple. The air flow rate will be equal to the pump-out or fill rate. With flow rate and pressure determined, a flow/$\Delta$P curve can be used to determine sizing.

The second reason air will flow into a process tank is to compensate for the volume change associated with steam condensation. At the end of a tank steam-in-place procedure, steam in the tank will cool and undergo a phase change to liquid water. There is over 1,000X difference in volume between an amount of water in gas phase vs. liquid phase. During cooling, sterilized ambient air must be allowed into the tank to prevent vacuum. Sizing the vent filter for steam collapse requires knowing the vacuum rating of the tank and the convective cooling rate. These can be calculated based on the tank dimensions including height, diameter and wall thickness. Millipore has developed a computer program to facilitate these calculations.

Improper tank vent sizing can result in low pump-out rates, loss of sterility due to rupture disk or filter failure, or worst case, tank implosion. Fortunately, proper sizing is not difficult as long as the flow requirements and driving force are understood.

## 1 Typical **Process Flow**

## 3 Filter Quick **Reference Guide**

### Recommended Filters

| Filter Format | Area/Filter | Catalogue No. |
|---|---|---|
| Aervent Hydrophobic Filters | | |
| Aervent-50 capsule | 19.6 $m^2$ | MTGR15010 |
| Opticap XL2 capsule | 0.10 $m^2$ | KTGRA02TT3 |
| Optiseal cartridge | 0.18 $m^2$ | LAGR04TP6 |
| Opticap XL4 capsule | 0.21 $m^2$ | KTGRA04TT3 |
| Opticap XL5 capsule | 0.32 $m^2$ | KTGRA05TT1 |
| 5-inch cartridge | 0.32 $m^2$ | CTGR75S01 |
| Opticap XL10 capsule | 0.65 $m^2$ | KTGRA10TT1 |
| 10-inch cartridge | 0.65 $m^2$ | CTGR71TP1 |
| 20-inch cartridge | 1.3 $m^2$ | CTGR72TP1 |
| 30-inch cartridge | 1.95 $m^2$ | CTGR73TP1 |

*Filters are available in many sizes, configurations and formats. See the quick reference tables on page 2 for a detailed list.*

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