Millipore®

Preparation, Separation,
Filtration & Testing Products

MOBIUS® SINGLE-USE FINAL FILL SOLUTIONS

The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

MERCK

Mobius® Single-Use Final Fill Solutions

The Mobius® single-use final fill offering allows end users to design robust, easy-to-use assemblies that ensure product quality and patient safety.

We have a comprehensive library of single-use assembly components which includes filters, tubing connectors, needles and pumps. We provide customers with high quality assemblies, technical expertise, and the services and support needed to minimize their risk.

Efficient and Cost-Effective

Whether you are looking to introduce single-use technologies into an existing process or you are building a new single-use facility, Mobius® products and solutions can help meet your evolving manufacturing needs.

Mobius® single-use products can increase your speed and efficiency, while also being cost effective. Our single use specialists will partner with you from initial specification of single-use components to optimization of your single-use operation.

At the heart of our Mobius® solutions are industry leading Durapore® and Millipore Express® filtration technologies.

Flexible Filling Productivity

Mobius® single-use final fill assemblies provide flexibility, allowing you to meet evolving manufacturing needs. They minimize costly cleaning validations and maximize change-over efficiency. In one customer case study, filling campaign setup, installation and production time was reduced from 36 to 12 hours through the use of a Mobius® single-use final fill solution versus a traditional stainless steel system.

Features and Benefits

- Reduced upfront capital investment
- Reduced risk of cross contamination and enhanced operator safety
- Flexibility and increased filling productivity
- Advanced single-use filtration technologies to maximize yields

PROCESS DESIGN CONSIDERATIONS

Sterility Assured

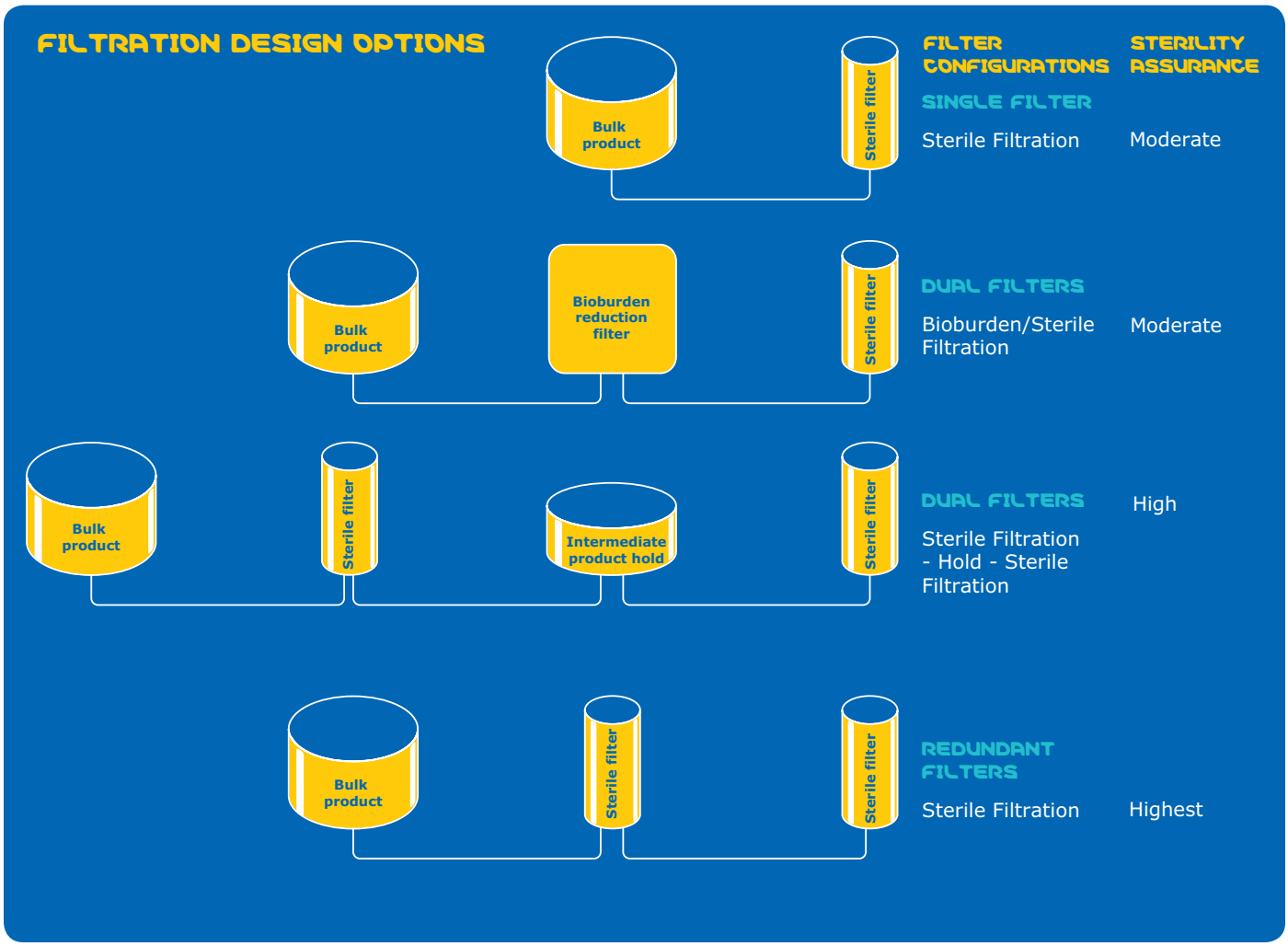
When claiming sterility, regulatory agencies worldwide recommend pre-use integrity testing and require post-use integrity testing of sterilizing-grade filters. Successful filter integrity tests are a critical link between your filter validation, successful processing, and product release.

Sterile filtration is a critical operation in final filling and there are multiple options for system design, either single, dual or redundant filtration. Regulatory requirements, costs, facility fit and risk profile are all important factors when designing your filtration system.

Questions to consider when designing your single-use final filtration assembly:

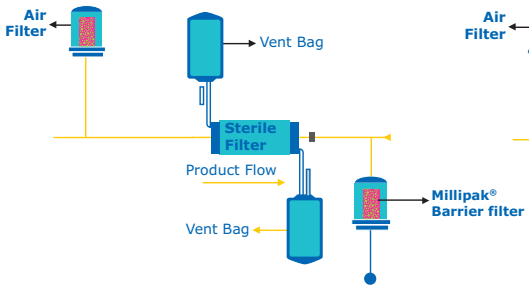
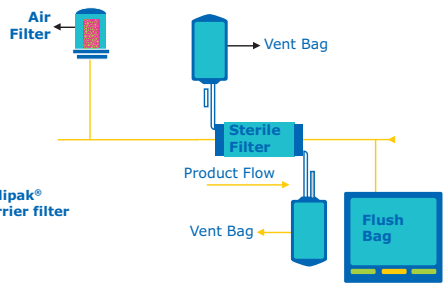
1. Do you require single, dual or redundant filtration?

2. Do you require the filter in or out of the isolator?



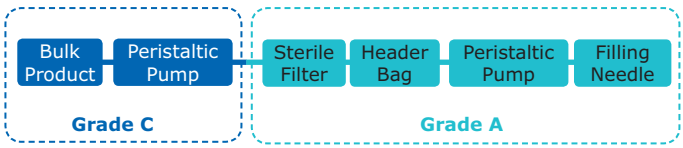
Filter Flushing Design Options: Bag vs. Millipak® Barrier Filter

Performing pre-use and post-use integrity testing (IT) requires careful flushing and manipulation of the assembly to ensure you do not compromise the downstream sterility. The diagrams below show possible filter configurations for in-line integrity testing. Millipak® Barrier filters, containing both hydrophobic and hydrophilic sterilizing-grade membrane, were developed to faciliate in-line integrity testing of sterilized liquid filtration systems.

Sterile Boundary Attribute		
Sterility of Product Filter Maintained During Pre-Use Test	✓	✓
Ability to retest	✓	✗ Limited by the size of the flush bag
Ability to Dry the Product Filter	✓	✗
Simple Design	✓	✓

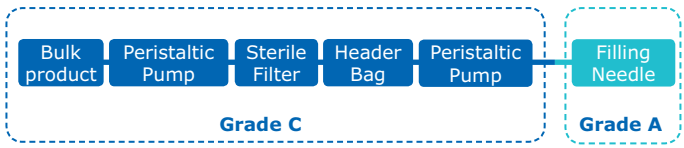
Sterile Filter Placement Considerations: Inside or Outside the Isolator/RABS

Sterile Filter in Grade A/ISO 5/Class 100 Space



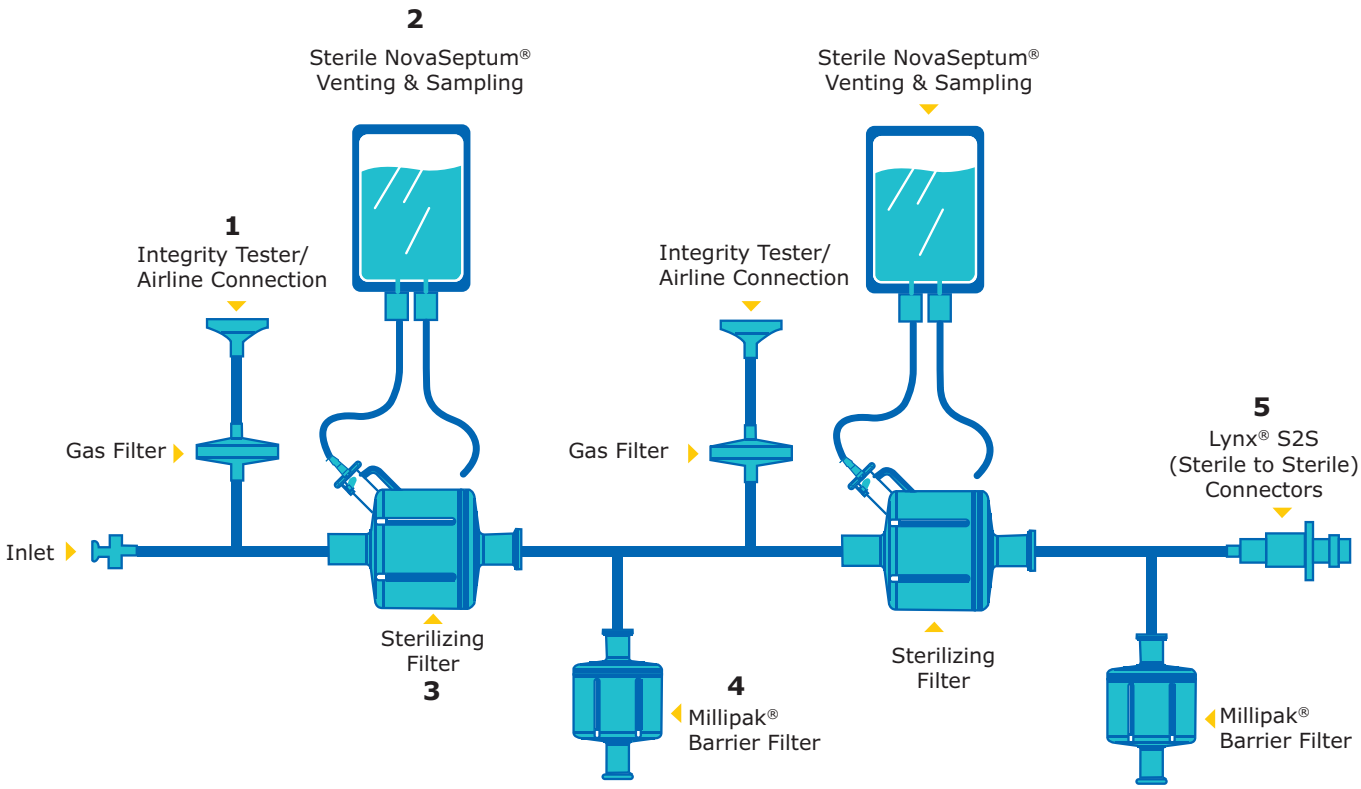
Complete SUS transferred to Grade A	
Benefits	**Considerations**
Low risk of fluid path contamination with majority of operations (venting, connections, etc.) occuring inside isolator/ RABS	Sterile environment risk if performing open venting
	Handling challenges • Large number of components to transfer from Grade C into Grade A • Pre-use integrity testing challenge

Sterile Filter in Grade C/ISO 7/Class 10,000 Space

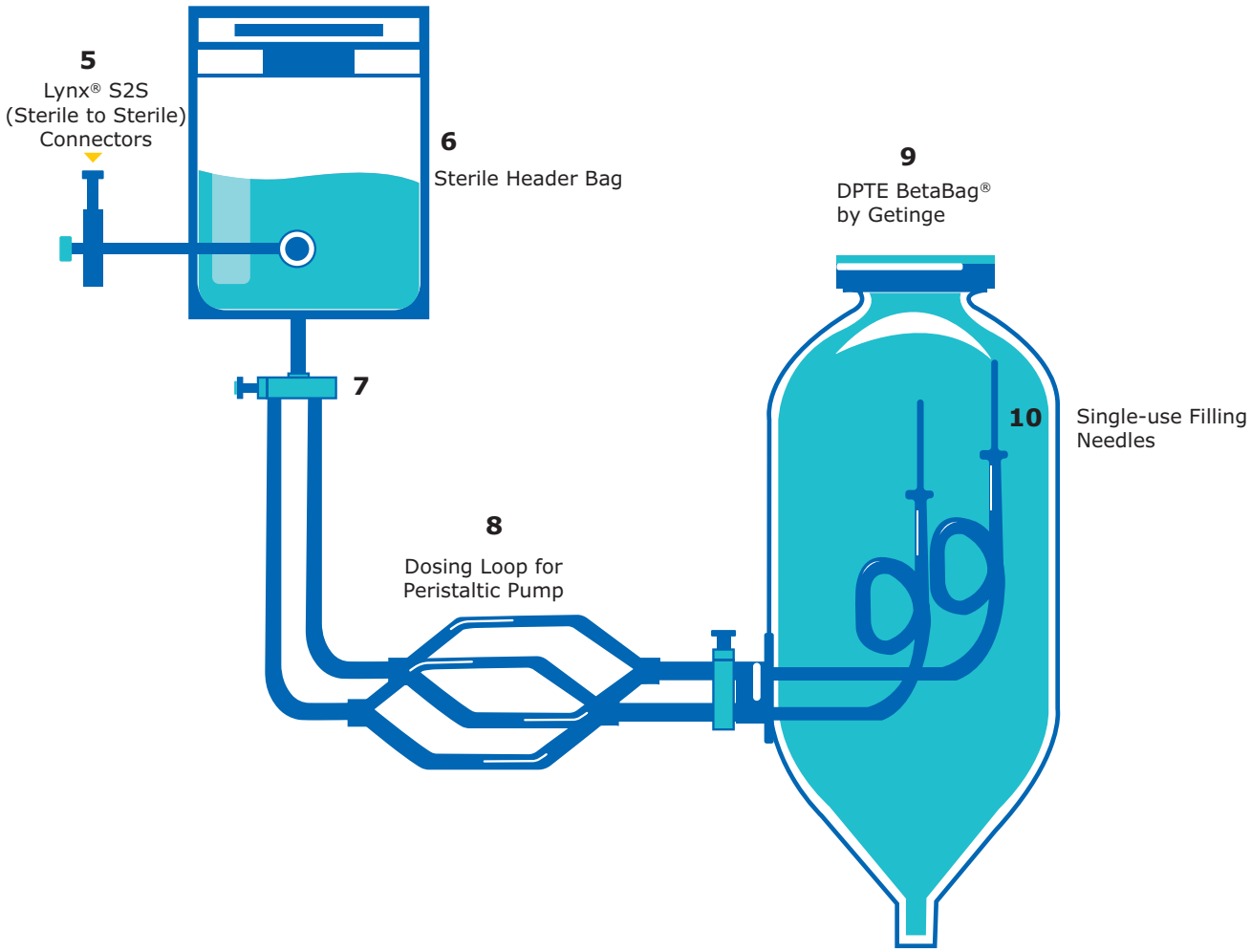


Only filling needles transferred to Grade A	
Benefits	**Considerations**
Majority of operations (installation, flushing, etc.) occur outside isolator/RABS	More potential points for microbial ingress
Potential to replace filter if integrity test fails	Demonstration of assembly integrity more critical

CLOSED SYSTEM FILLING TRANSFER SET TO ISOLATOR



No.	Description
1	Sterile air line to attach Integritest® for in-line filter integrity test pre-use or post-use.
2	Closed and sterile NovaSeptum® sampling capabilities with a variety of container types and volumes ranging from 5mL to 1L.
3	Millipak® Final Fill Filter or Opticap® Product Filter
4	Millipak® Barrier filters have both a hydrophobic and hydrophillic membrane, allowing flushing of water and blowdown with air, maintaining sterility during filter integrity testing operations.
5	The Lynx® S2S connector has been subjected to rigorous microbiological validation studies to demonstrate its robust design and functionality. The results indicate that the connector provides sterility assurance during a sterile fluid transfer process. Please refer to tech brief TB1008N00 (Validation of the Lynx® S2S Connector for Sterile Fluid Transfer) for additional information.
6	Hanging header bags are available in a range of volumes from 1L to 50L, and in a range of inlet/outlet port configurations and sizes from 1/4 inch to 1 inch hosebarbs.
7	The header bag outlet uses an overmolded 1.5” TC Multi-tube Manifold or individual bag ports to accomodate 1 to 10 line filling machines or larger.



No.	Description
8	Pump tubings from several suppliers available in various sizes to fit a variety of peristaltic dosing pumps
9	The DPTE BetaBag® is a Rapid Transfer Port (RTP) bag that attaches to an Alpha port of an isolator so the single-use components can be transferred into the Class A space in a sterile manner after the isolator is cleaned and sterilized.
10	Single-use Filling needles are available in a range of sizes and styles to fit a variety of filling machine models and needle holders

FORMULATION

Mobius® Single-Use Mixing System

Key Features
Easy-to-use
Low sheer impeller design
No particulate generation
Broad range of sizes available (10 L – 1000 L)
Jacket and load cells available as standard options in sizes 100 L – 1000 L
Standard and custom bag options available

BioReliance® Services

Formulation, Filtration & Final Filling

BioReliance® Services are customized to address your specific needs and backed by an industry leading team of scientists, engineers and validation specialists.

Standard Offerings

- Filter compatibility
- Bacterial retention
- Product specific bubble point
- Standard model solvents extractables
- Mobius® compatibility
- Mobius® extractables
- Mobius® leachables
- Patient toxicological assessment
- Particle shedding

Custom Offerings

- Shipping validation

INDUSTRY LEADING EXPERTISE AND QUALITY TO EASE YOUR IMPLEMENTATION

Our Mobius® team of experts will work with you to determine your specific final fill requirements. The result: a pre-sterilized, single-use final fill system that's ready to use out of the box, featuring modular, fully-optimized assemblies. The assemblies are connected to create a closed, disposable system that meets your filling needs/requirements. These systems are replicable, scalable, sterile and simplify technology transfer across multiple sites.

As your sterile filtration partner, you will have the peace of mind that comes from working with the industry leader who has over 50 years of expertise in sterile filtration with market leading Durapore® (PVDF) and Millipore Express® (PES) membranes.

QUALITY

Component Qualification

We have a well-defined and documented process for qualifying single-use components into our library, to ensure the most stringent quality requirements are met.

Criteria
Gamma compatibility >40kGy
Functional testing
Regulatory statements (Animal Origin, Latex, BPA, etc.)
USP <88> Class VI
USP <85> Endotoxin
USP <788> Particulates
USP <661> Physiochemical
Shelf life > 2 years
Sterility per ANSI/AAMI/ISO 11737
Bacteriastasis/Fungistasis
Bioburden

Mobius® Assembly Leak Testing

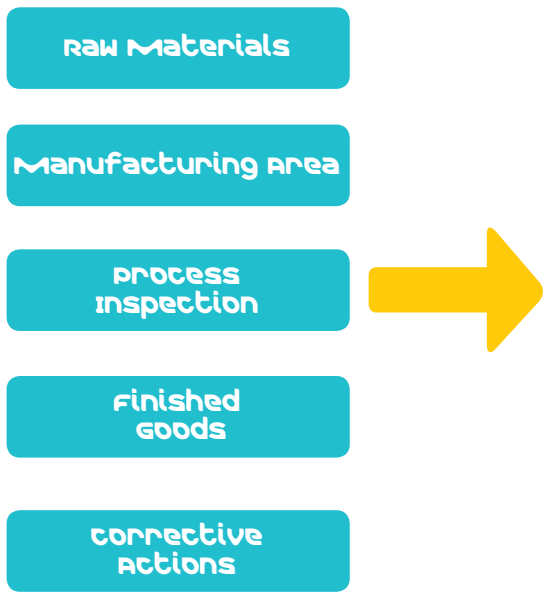
- Gold certified assemblies are 100% tested
- Testing performed using a pressure decay method

Packaging and Transport Validation

Mobius® packaging protects assemblies from the rigors of typical shipping conditions. Representative Mobius® Final Fill assemblies have been proven to be integral after being subjected to a packaging validation per the International Safe Transit Association (ISTA) 2A Procedure.

Particulate Mitigation and Control Strategy

Particle mitigation and control requires a holistic approach for single-use assemblies. We have assessed risk at all stages of the raw material sourcing and assembly manufacturing lifecycle, and continuously monitor, correct, control and improve.



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