Millipore®
Expert Pharm/BioPharm
Products & CTDMO Services

Data Sheet

# Mobius® iPUPSIT Filtration System

## For reducing risks in final sterile filtration


### Introduction

EU GMP Annex 1 requires for sterilizing grade filter that is used to sterilize a fluid should be pre-use post sterilization integrity tested (PUPSIT). While single-use assemblies facilitate implementation of PUPSIT, manual intervention creates multiple areas of concern including operator error and maintaining sterility of the drug product.

PUPSIT is complicated and relies on highly trained operators to avoid test failure and minimize the risk of contamination or batch loss. The Mobius® iPUPSIT Filtration System is designed to facilitate PUPSIT with single-use filtration assemblies, thereby minimizing the risk of operator error which is a critical element of the contamination control strategy (CCS).

### Benefits

- **Gain flexibility:** A modular system designed to accommodate **multiple filtration configurations** enabling easy transition between batch sizes and molecules
- **Optimize footprint:** **Compact system design** that includes a feed pump, flush bag, human-machine interface (HMI), and integrity tester
- **Maximize product recovery:** Optimized system and consumables engineered to **reduce loss** of valuable drug product
- **Tailor automation:** Provides multiple automation options from **local recording to fully automated** solution



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## Automated System Components


**HMI:**
Enabling recipe edition and data recording; 21 CFR part 11 compliant

**Integrity Tester:**
Embedded integrity testing system to test single-use assembly and sterilizing grade filters.

**Flowmeter:**
Non-invasive, measure of flow for enhanced process control
0 – 20L/min with accuracy of +/- 1,5%

**Peristaltic Pump:**
Embedded pump to allow for filter wetting (pre-use IT) and product filtration

**Liquid Sensor:**
Non-invasive, ultrasonic air bubble detector to enable automating filter venting

**Pressure Transmitter:**
Transmitter connected to single-use pressure sensor part of the Single-Use filtration assembly.Up to 75psi +/-3 psi

**Pneumatic Valve:**
Automated valve for tubing from shore 55 to 80

**Load Cells:**
Weight monitoring of flush up to 50 kg with accuracy ± 10 g. Locking mechanism when system is moved.

## Automated System Features and Benefits

- Eliminates complex manual operations
- Customizable recipes to fit process requirements
- Process reliability enhanced through recipe edition
- Controlled and fully recorded operation

## System Option List

**Filtration Setup:**

- Single or redundant filtration assembly

**Feed Line:**

- Product peristaltic pump flowrate (0–3.5 L/min or 0–16 L/min)
- WFI peristaltic pump flowrate (0–3.5 L/min or 0–16 L/min)
- Inlet pinch valve manifold (x3)
- Inlet line equipped with flow meter (0–3.5 L/min or 0–16 L/min)
- WFI flush container and load cell
- Dedicated product flush container and load cell

**Integrity Test:**

- Integritest® 5 instrument (including OPCUA licence)

**Automation & Controls:**

- Configurable input/output signal exchange via multiconnector (x1)
- External pump control (e.g; from filling machine)
- Remote electrical enclosure

**Additional Options & Safety:**

- Additional manual sampling valve
- Additional pressure sensor
- Additional transparent, foldable protection door
- Additional compressed $N_2$/air supply standard
- Mirrored flow path system configuration

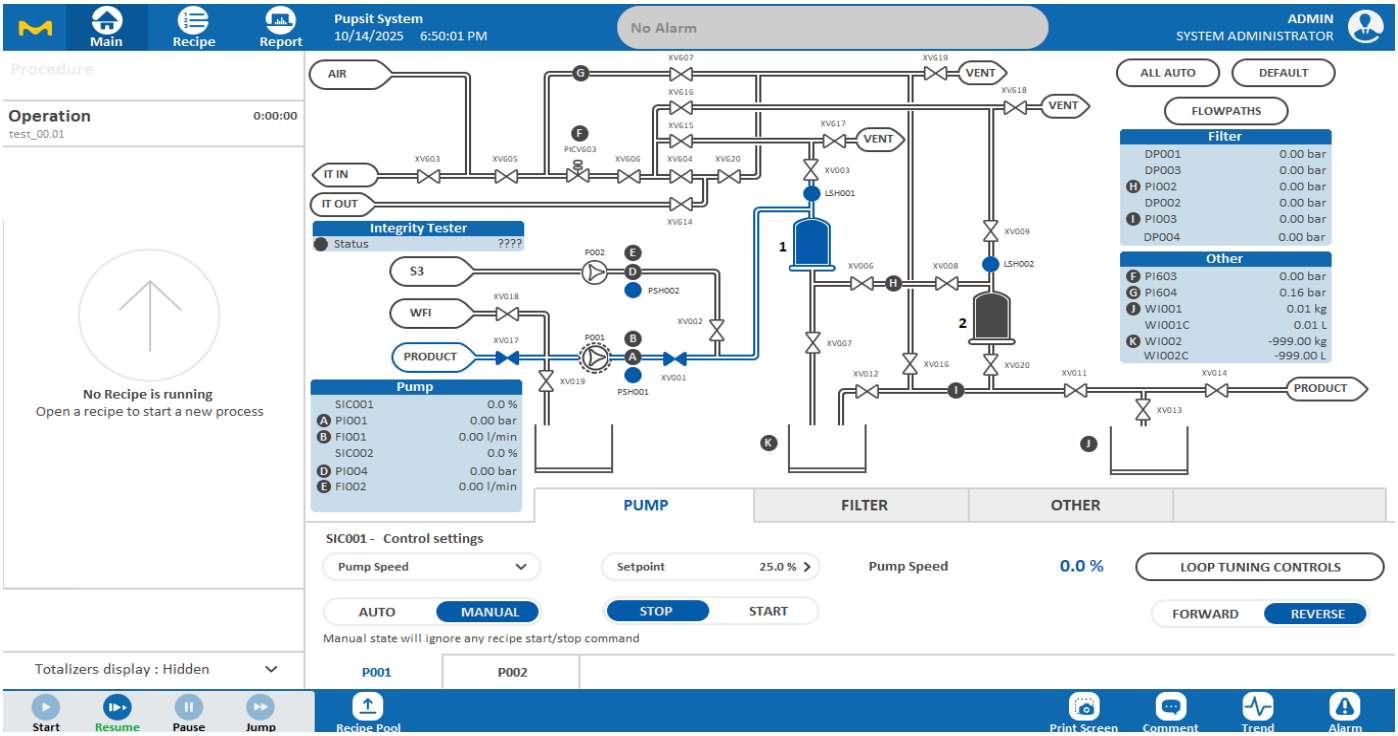
# Automated System Features Option List

## CCP6 HMI

The CCP® software provides a single control platform across our portfolio of automated systems for a familiar look and feel at each step of your process that helps reduce training time for operators.

The software offers recipe-driven processing that eliminates manual operation, reduces process variability, and minimizes the risk of errors. Process operations are easily created and managed using the recipe editor, each aspect of your process is monitored from the HMI, and the report generator allows you to create state-of-the-art batch reports.

The software is designed for GMP facilities and fulfills FDA guidelines 21 CFR Part 11 requirements for electronic records and signatures.




## Integritest® 5 Filter Integrity Test Instrument:

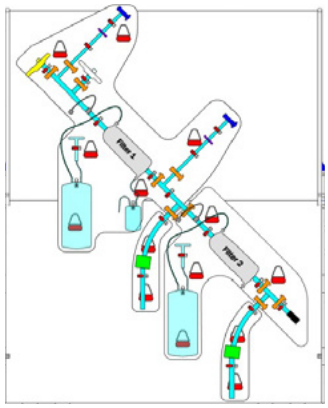
The automated Integritest® 5 Filter Integrity Test Instrument accurately and reliably verifies the integrity of your filters and processing equipment. It is portable, easy to implement, and delivers a simple and intuitive user experience, while providing optional flexibility to fit your process. The instrument is designed to support diffusion, bubble point and HydroCorr test methods.

## Mobius® Filtration System Portfolio

Our portfolio covers the full suite of system setups ranging from shadow boards that can be designed for either single or redundant filtration systems in either vertical or horizontal designs tailored for training and process development (PD) purposes, up to fully functional, fit-for-purpose manual and automated systems.

Depending on your process and facility needs, our technical specialists will assist you in building a tailor-made solution.

### Shadow Board



### Manual System

### Automated System

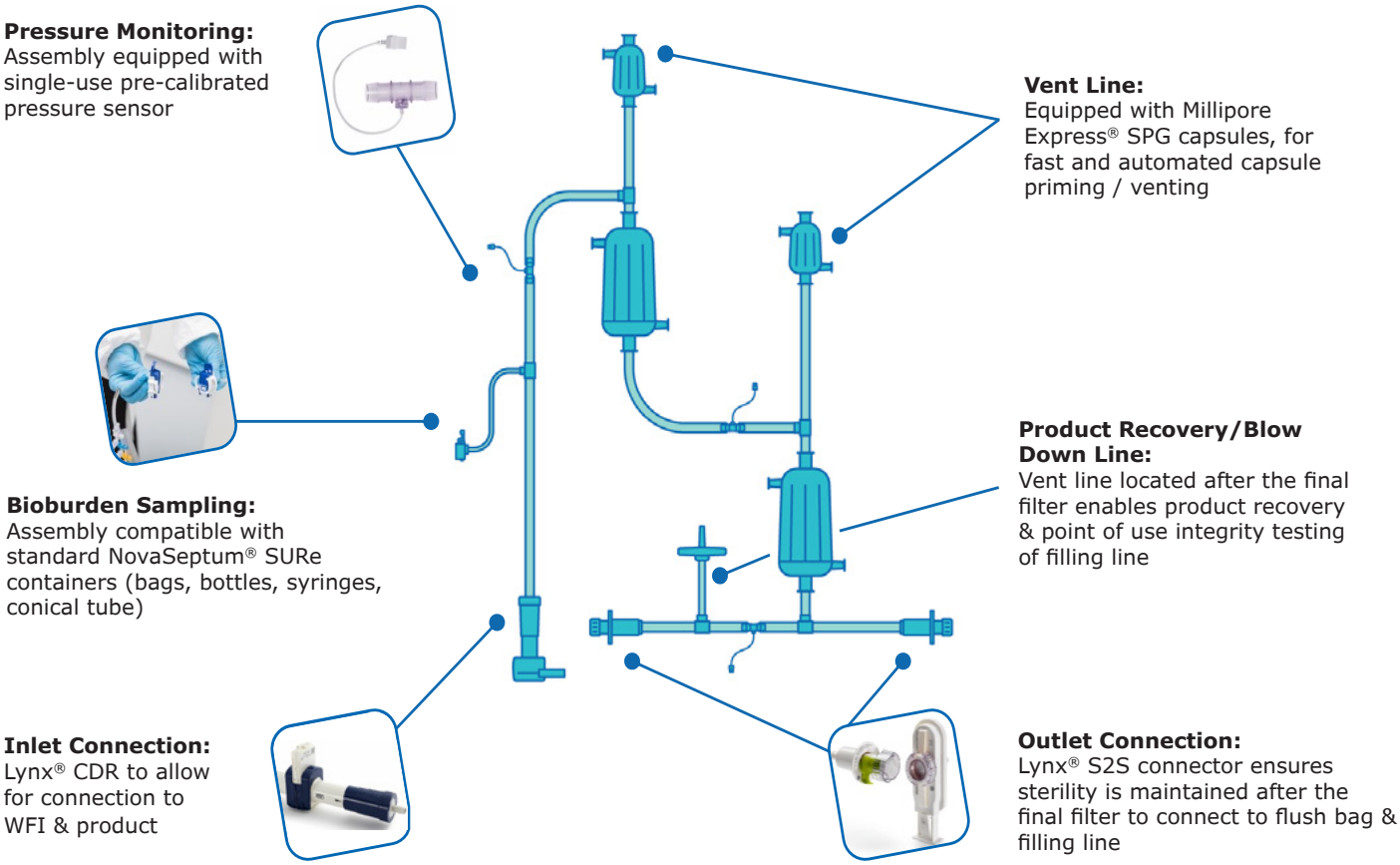
| System Type | Filtration Sequence | In-line Pressure Sensing Technology | Design Compatibility | Footprint* | In-line Feed Pump | Process Monitoring | Batch Reporting | Recipe Development | IT5 Commu-nication |
|---|---|---|---|---|---|---|---|---|---|
| **Shadow Board** | Single / Redundant | Yes | Horizontal Vertical | Cost-efficient, easy-to-use magnetic board for training and PD purposes | | | | | |
| **Manual System** | Single / Redundant | Yes | Horizontal Vertical | L: 1300 mm W: 800 mm H: 2000 mm | ✓ | ✓ | ✓ | | |
| **Automated System** | Single / Redundant | Yes | Vertical | L: 1600 mm W: 1070 mm H: 2000 mm | ✓ | ✓ | ✓ | ✓ | ✓ |

*Example dimensions for redundant vertical 10" system design

# Mobius® Single-Use Assembly Design & Features

## Automation Compatible 'Vertical' Design Features

The single-use filtration assembly has been pre-engineered and optimized to easily & safely enable PUPSIT and check integrity of the assembly at point of use, while also minimizing product loss & dilution of the final drug product. Pre-engineered assemblies are designed with the following features.




*Alternative design: inlet manifold or separate WFI inlet*

Pre-engineered design including :

- **Millipak® Final Fill** capsule filters with Durapore® membrane (PVDF) for filtration of small volume, high value solutions or **Opticap® XL capsules** containing Durapore® or Millipore Express® membranes for larger volume processing, both providing maximum sterility assurance
- **Millipore Express®** SPG vent filters maintain flowpath sterility during capsule filter priming and venting
- **Millipak®** Barrier capsule filters that maintain sterility while allowing the flow of gas and liquid for easier integrity testing
- **Lynx® CDR** connectors enable up to 6 sterile connections, disconnections, and reconnections wet & under pressure
- **Lynx® S2S** connectors provide the highest level of security for critical connections
- Single-use **pressure sensors** for safety & monitoring of the filtration process
- **NovaSeptum® SURe** standard sampling systems to ensure representative sterile sampling

## Sterilizing Grade Filter Membranes:

Choosing the right filter and filtration device format for your final sterile filtration is critical to building a robust final filtration assembly.

Our membranes for aqueous sterile liquid filtration include Durapore® filters, made with polyvinylidene fluoride (PVDF) membrane providing high throughput and superior robustness and hydrophilic polyethersulfone (PES) Millipore Express® membrane filters which provide a non-PFAS filter option that deliver high flux and capacity.

To apply pressure and enable venting during integrity testing we recommend our Millipore Express® SPG filters. These irradiation-compatible capsule filters contain super hydrophobic membrane and provide optimal gas filtration and venting in single-use applications.

| | Modality / Application | | | | | Functionality | | |
|---|---|---|---|---|---|---|---|---|
| | mAb, Plasma, R-Protein | Vaccines & Viral Vectors | Ophthalmics | Small Vol. Parenterals | Large Vol. Parenterals | Final Filtration | Gas | Integrity Testing |
| **Millipore Express® SHC filters** | ■ | ■ | | ■ | ■ | ✓ | | |
| **Millipore Express® SHF filters** | ■ | ■ | ■ | ■ | ■ | ✓ | | |
| **Durapore® 0.22 µm filters** | ■ | ■ | ■ | ■ | ■ | ✓ | | |
| **Aervent® and Aerex® filters** | | | | | | | ✓ | |
| **Millipore Express® SPG filters** | | | | | | | ✓ | |
| **Millipak® Barrier filters** | | | | | | | | ✓ |

■ Recommended for specified modality
✓ Recommended for specified functionality
□ Recommended with Mobius® iPUPSIT Filtration system

## Sterilizing Grade Filter Format:

**Opticap® XL Capsule Filters** with Millipore Express® or Durapore® Membranes
Opticap® XL capsules are designed to meet the **filtration needs for larger drug product batches**. Opticap® XL capsule filters are available in a wide range of media, surface areas, pore sizes, and inlet/outlet connections to meet your application needs.

**Millipak® Final Fill Capsule Filters** with Durapore® Membrane
Millipak® Final Fill capsule filters **maximize product recovery** with a stacked disc design that decreases hold-up volume, while offering additional security for critical filtration operations. Design features reduce the risk of operator error, improve process monitoring, and enable easy integration into single use assemblies. These capsule filters contain the proven and trusted Durapore® membrane in multiple pore sizes offering flexibility for your specific process needs.

**Millipak® Barrier Filters**
Millipak® Barrier filters contain both hydrophilic and hydrophobic sterilizing-grade Durapore® membranes, **allowing the flow of both liquid and gas**. These filters simplify PUPSIT by maintaining the sterility of the system while removing the constrains of a flush bag or a can.

Each Opticap® XL and Millipak® capsule filter is integrity tested during manufacturing and is supported with an Emprove® documentation package or validation guide. For traceability and easy identification, each device is marked with the product name and identifying characteristics.

## Lynx® S2S Sterile Connection

Lynx® S2S (Sterile to Sterile) is a single actuation connector for joining two sterilized fluid paths. Compatible with pre-use sterilization by autoclave and irradiation methods, the flow path remains **completely closed** during Lynx® S2S actuation, eliminating contamination risk and enabling sterile connection in classified and non-classified areas.

Each Lynx® S2S connector is **100% air-integrity tested** in manufacturing. To ensure a sterile connection can be made in non-classified areas, connector sets have been validated utilizing an aerosolized bacterial challenge method with greater than $10^6$ Colony Forming Units (cfu) of *Brevundimonas diminuta* and a direct bacterial soiling method with greater than $10^6$ cfu of *B. diminuta*.

## Lynx® CDR Sterile Connection

Lynx® CDR (Connect, Disconnect and Reconnect) device provides a **reliable and validated connection** for multiple transfers of sterile fluids. Compatible with pre-use sterilization by autoclave and irradiation methods, the unique product design provides flexibility in single-use bioprocessing by enabling up to six connect/disconnect/reconnect cycles of multiple flow paths, while remaining sterile and leak free.


Each Lynx® CDR connector is 100% **air-integrity tested** in manufacturing. To ensure a sterile connection can be made in non-classified areas, validation studies for Lynx® CDR devices included using CFU fluxes from 5000x to 500,000x higher than maximum ISO 8:2019 conditions, and a failure risk model developed from device prototypes, to demonstrate Lynx® CDR devices are fully capable of maintaining multiple sterile connections in ISO 8 environments with greater than 3 log (1,000x) safety margin.

## NovaSeptum® SURe

NovaSeptum® SURe single-use **sterile sampling assemblies** are designed to protect your single-use process from potential cross-contamination ensuring representative samples. These sampling assemblies can be easily adapted and integrated to your final filtration assembly via standard **AseptiQuik® S** connectors.

Because NovaSeptum® SURe assemblies will ensure your sample will be isolated from point of sample to analysis, they are ideally suited to enable **closed bioburden sampling**. These standard assemblies come as single or manifold designs leveraging **various popular containers**: bag, bottles, syringes or conical tubes. They can also be customized to better fit your sampling requirements.

## Certification Levels

Mobius® assemblies are available in several levels of certification. Certification of an assembly is based on the qualification of the components in the assembly, the level of leak testing performed during manufacturing, and the testing performed on the assembly lot after manufacturing. The certification level also impacts the shelf life and sterility claims that are made for the assembly.

| Certification Level | Shelf Life | Sterility | USP <85> Endotoxins USP <788> Sub-visible Particulates | Leak/Intergrity Testing | *Biological Reactivity*[3] *USP <665> *Extractables* |
|---|---|---|---|---|---|
| **Gold + HIT**[1] **and/or RPIT**[2] | 2 Years | Sterile (Quarterly dose audit) | One assembly per lot tested | 100% assembly integrity tested | *Post Irradiation |
| **Gold** | 2 Years | Sterile (Quarterly dose audit) | One assembly per lot tested | 100% assembly leak tested | *Post Irradiation |
| **Silver** | 2 Years | Sterile (Quarterly dose audit) | Quarterly review of results | Lot sample tested | *Post Irradiation |
| **Bronze** | No claim | No claim | No testing performed | No testing performed | Post Irradiation |
| **Basic** | No claim | Non-sterile | No testing performed | Lot sample tested | Post Irradiation |

1 HIT = Helium Integrity Test

2 RPIT = Restrained Plate Integrity Test

3 Family component materials were tested post-irradiation and all materials meet the criteria for Biological Reactivity Testing. These tests can be one or a combination of the following test methods USP <88> Class VI (*In Vivo*), USP <87> (In Vitro), ISO 10993-5 (*In Vitro*).

## The Emprove® Program. The Smart Way to Master Compliance and Control.

Ensuring the compliance of your pharma and biopharma products involves the compilation of a vast amount of data, which can be time- and resource-intensive. To help facilitate and accelerate your risk assessment continuum, we have developed the Emprove® Program, offering convenient access to reliable information for a broad portfolio of products.

Each product in the portfolio is complemented with different types of dossiers: Material Qualification Dossier, Quality Management Dossier, Operational Excellence Dossier, Component Extractables Reports and Advanced Qualification Dossier. They provide information on the manufacturing process, shelf-life, regulatory statements, extractables, validation tests and much more.

Specifically for single-use assemblies, the Emprove® Advanced Qualification Dossier (AQD) is the first-of-its-kind “On-Demand” Emprove® Dossier to address qualification needs for custom and configurable Mobius® assemblies. From assembly general information, component information, specification to extractable data, find all the information you need for your assembly in one place.

For more information, please visit:
**SigmaAldrich.com/emprove-FandSU**

## Services

Our Mobius® iPUPSIT Filtration System is supported by the following services:

- Factory Acceptance Test (FAT)
- Site Acceptance Test (SAT) / Installation Qualification/Operational Qualification (IQ/OQ)
- Preventive maintenance
- Training
- Common Control Platform® CCP6 / Recipe creation support & training

## Millipore® Validation Services

Complementing our product and system portfolio, our Millipore® Validation Services assist you in demonstrating that your single-use assemblies and sterilizing-grade filters used in manufacturing produce safe drugs.

We offer comprehensive **Standard services** to ensure your success in regulatory alignment, including:

- Bacterial retention testing
- Product-specific integrity testing
- Compatibility evaluation
- Extractables & leachables
- Patient safety evaluation

Additionally, we provide a **Custom proposition** to support your unique needs, such as:

- Assembly-specific point-of-use leak test
- Sensitivity & diffusion limit
- Product recovery optimization
- TOC flush study and
- Dilution flush curve

With dedicated support from our validation specialists across all continents, we have the expertise you need to navigate validation challenges.

Contact us to discuss how we can support:
**SigmaAldrich.com/sufiltervalidation**

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For additional information, please visit
**SigmaAldrich.com/final-sterile-filtration**
To place an order or receive technical assistance, please visit **SigmaAldrich.com/support/customer-support**



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