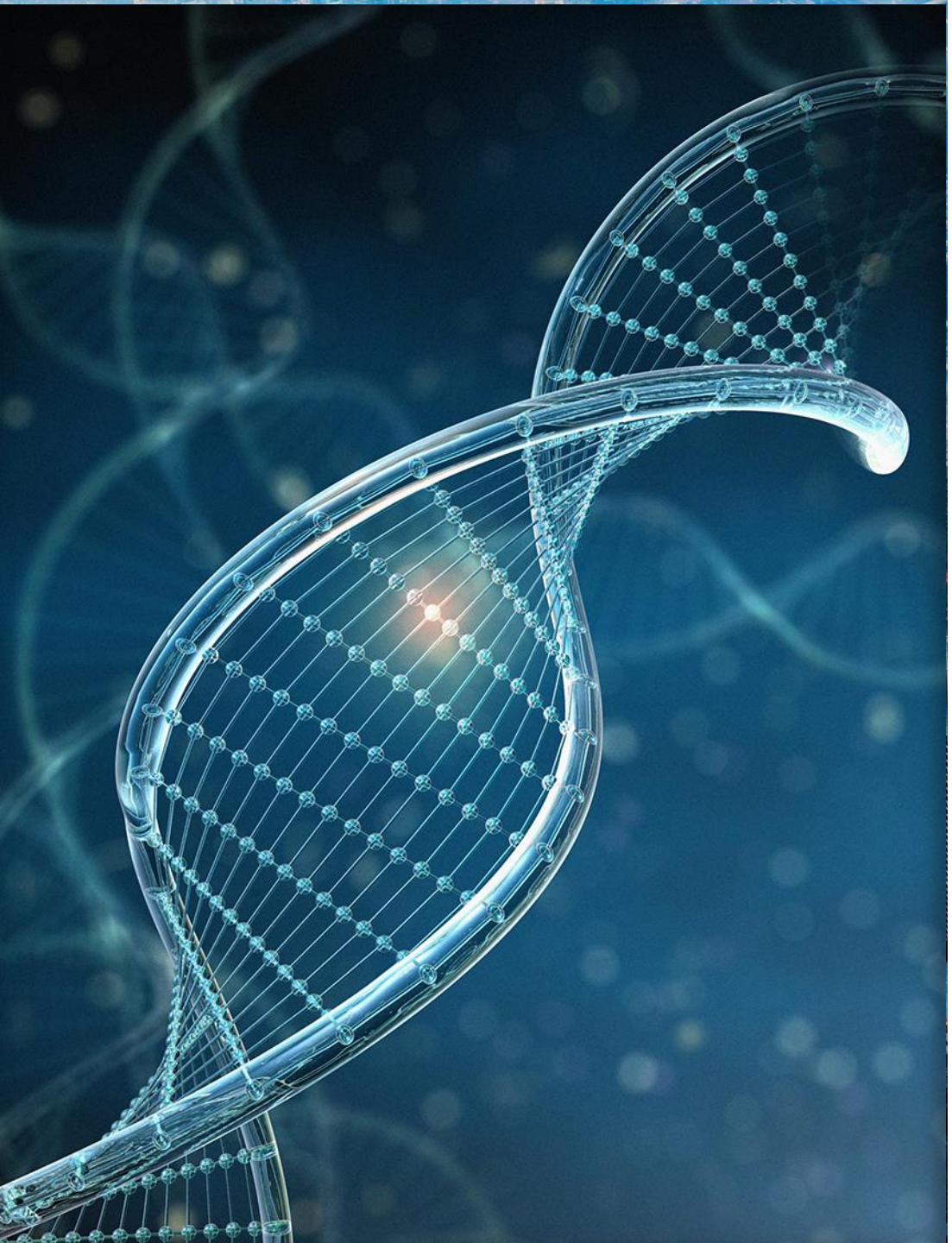


Life Sciences

Sterile Filtration: Filter Sizing for Process Optimization

2024 Entegris at a Glance

A global leader in electronic materials and process solutions for the semiconductor, life sciences, and other high-tech industries

FOUNDED	HEADQUARTERS	EMPLOYEES	2022E REVENUE	PATENTS
1966	Billerica, MA	8,800+	>$4B[1]	~4,250

Business Divisions

- Advanced Materials Handling (AMH)
- Microcontamination Control (MC)
- Specialty Chemicals and Engineered Materials (SCEM)
- Advanced Planarization Solutions (APS)

Our Mission

To help our customers improve their productivity, performance and technology by providing enhancing materials and process solutions for the most advanced manufacturing environments

[1] Based on proforma guidance for 2022 (provided on 8/2/22).

Life Sciences:
Normal Flow Filtration

Entegris

NFF: Sterile Filtration Introduction

Sterile filtration is the process of removing microorganisms from a fluid stream without adversely affecting product

Bacterial retention, per ASTM F838-20, for liquid sterile filtration is required

[1]**Membrane thickness:** 65–130 µm

Rating range: 0.2 µm*

Retention rating: Absolute

Absorption: Low to medium

Filter design parameters are critical for LS filtration applications:

- Membrane design
- Device design

Device Design

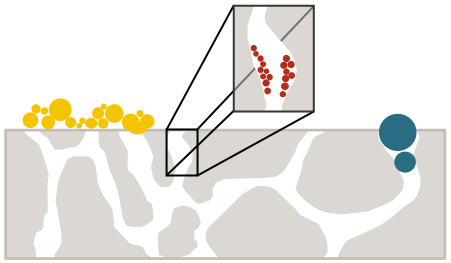
1. Connectivity

3. Geometry

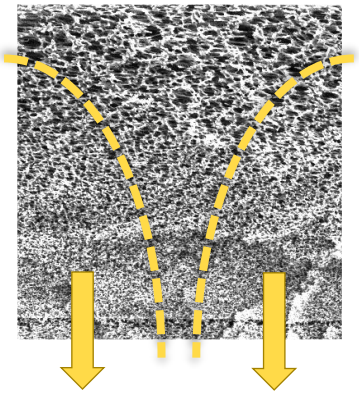
2. Form Factor

Membrane Design

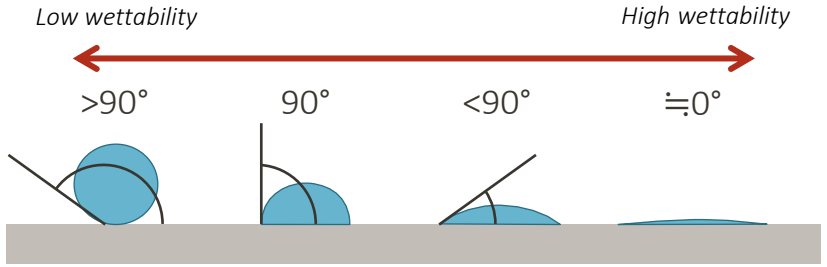
1. Retention Mechanisms



2. Pore Morphology



3. Hydrophilicity



[1]Range can vary per membrane type and porosity.

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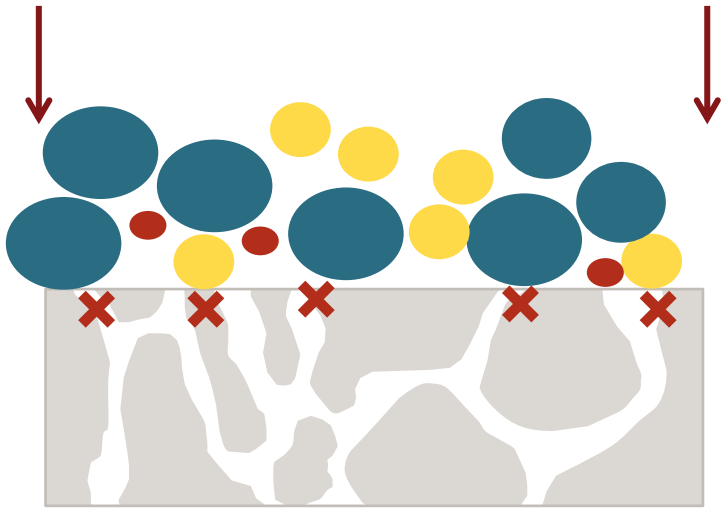
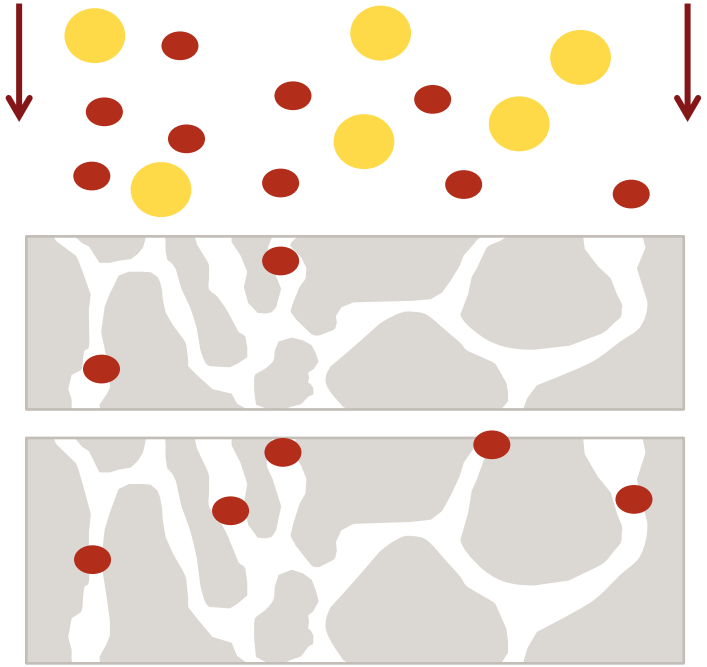
Membrane Retention Mechanism

How a filter plugs



Complete Pore Plugging

Cake Layering Plugging



Gradual Pore Plugging

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NFF: Depth Filtration Introduction

Depth filtration, typically made of multiple porous layers with depth, is used to capture the solid contaminants from the liquid phase

[1]**Media thickness:** mm – inch

Rating range: 0.1–100's µm

Retention rating: Nominal

Absorption: Medium to high

Filter design parameters are critical for LS filtration applications:

- Media design
- Device design

Device Design

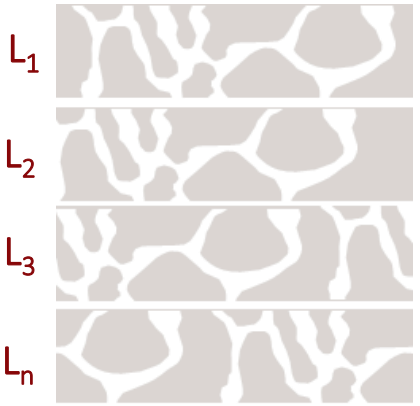
1. Connectivity

3. Geometry

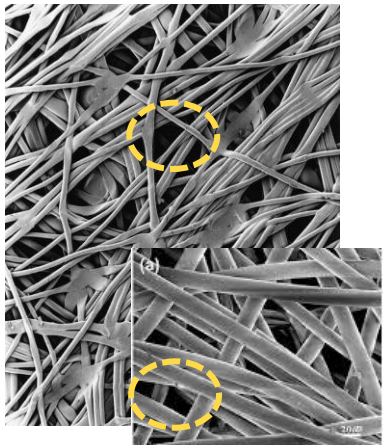
2. Form Factor

Media Design

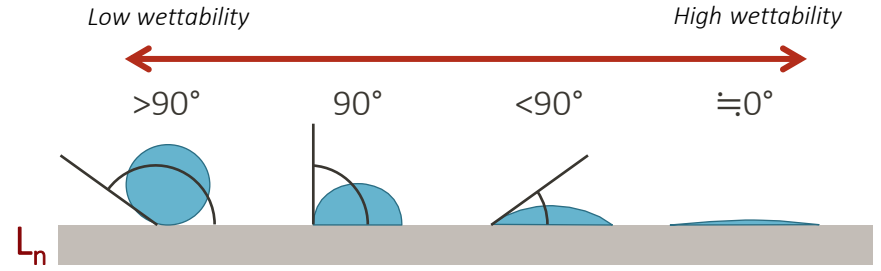
1. Media Layering



2. Pore Rating



3. Hydrophilicity



[1]Range can vary per media type, layering, and porosity.

Source: https://www.researchgate.net/figure/a-SEM-images-of-as-received-base-non-woven-polypropylene-fabric-b-PA-11-electrosprayed_fig1_227107761

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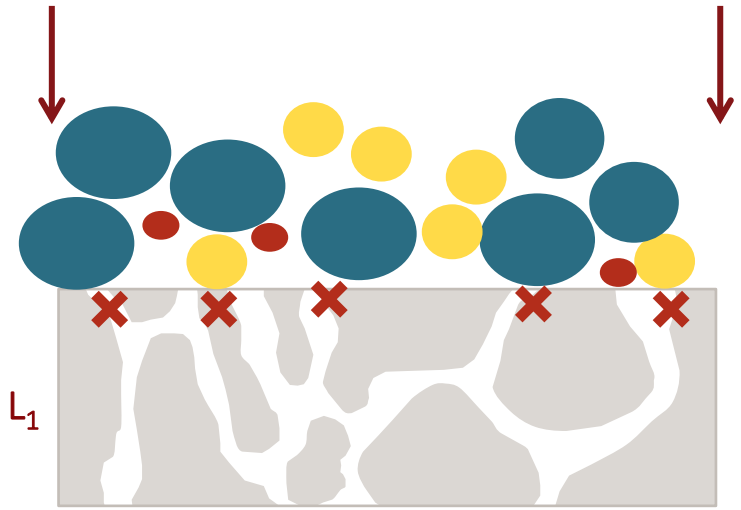
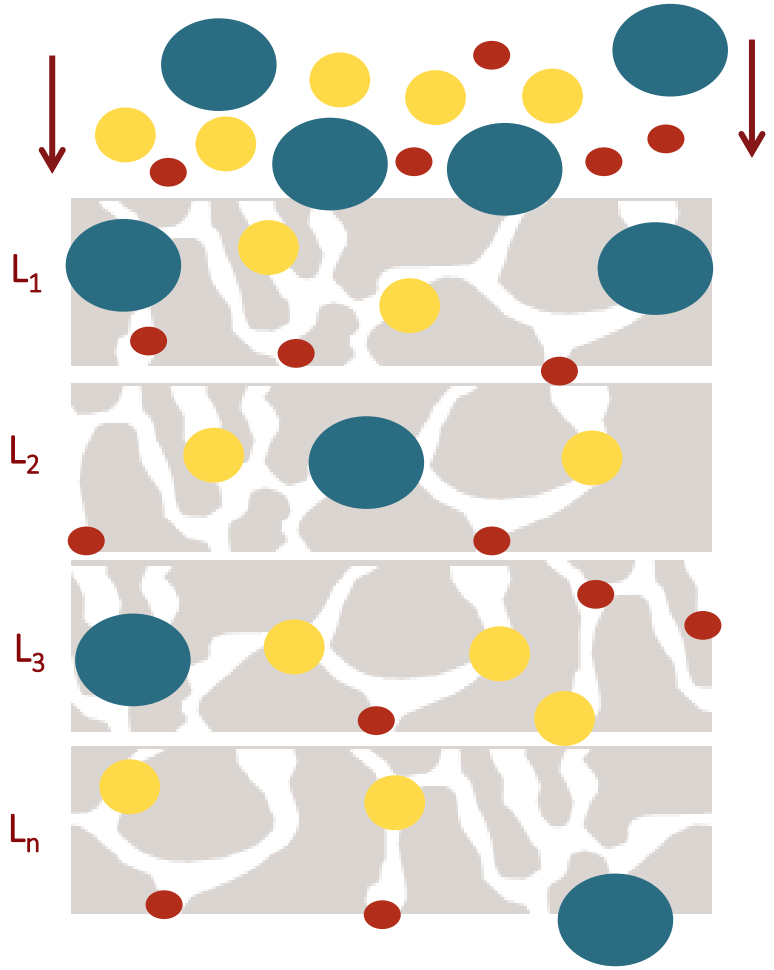
Media Retention Mechanism

How a filter plugs



Complete Pore Plugging

Cake Layering Plugging



Gradual Pore Plugging

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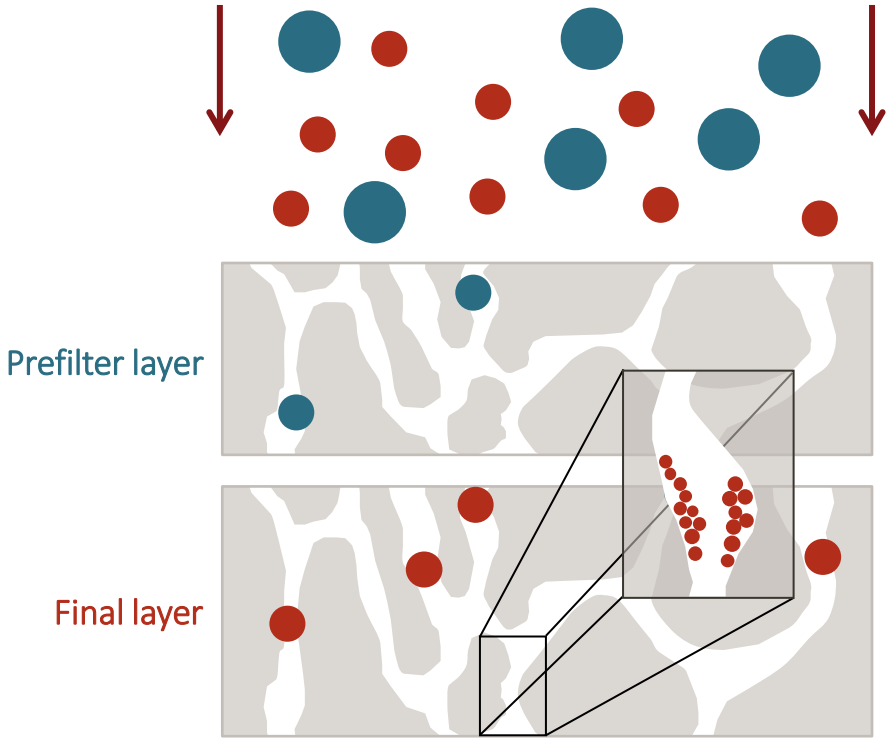
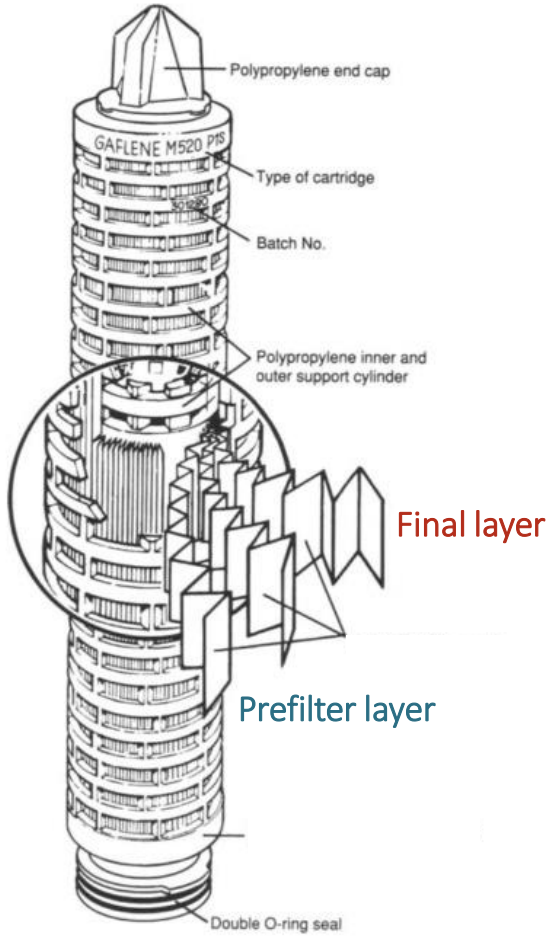
Membrane and Media Optimization

Layering

- **Prefilters** can be defined as membrane or media filters that are used to **remove larger particles** than a sterilizing grade filter
- Can maximize **throughput capacity**, enhance **retention efficiency**, and extend **filtration lifespan**
- The membranes and/or media have a combination of symmetric or asymmetric membranes to maximize filtration performance





Source: https://www.sciencedirect.com/topics/engineering/liquid-filtration

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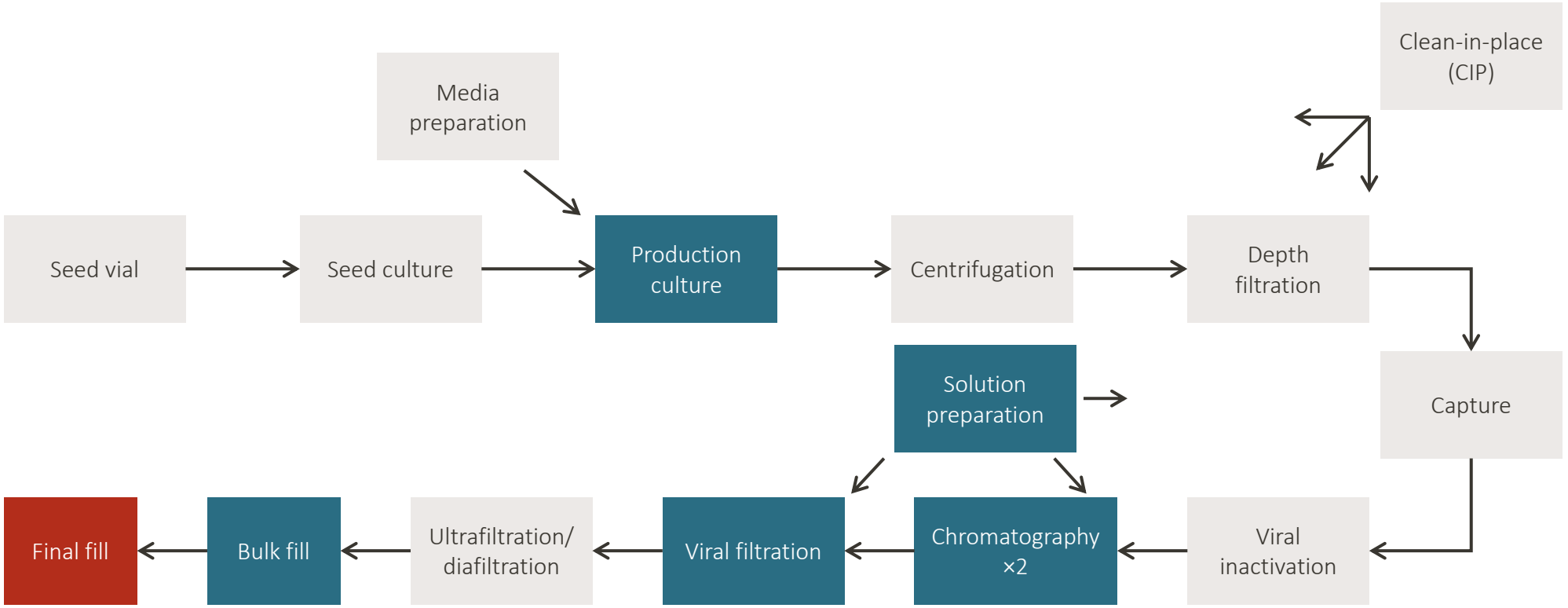
Sterile Filtration Introduction

Example: mAbs bioprocess



Sterile filtration steps

Filter Sizing: What is it?

Filter*ability* testing: a bench-scale test that takes full-scale process parameters and tests a filter's capacity to determine what is the optimal filtration solution

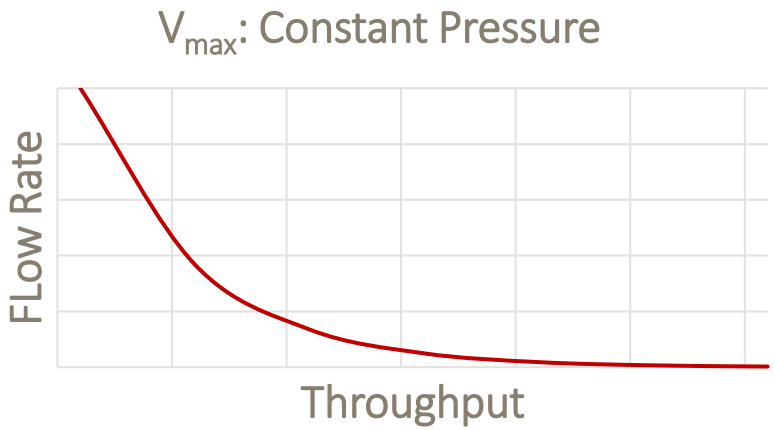
Parameters:

- ☐ Pressure drop
- ☐ Flow rate
- ☐ Flow/flux decay
- ☐ Flow resistance
- ☐ Turbidity
- ☐ Mixing
- ☐ pH
- ☐ Filtrate quality

Testing Methodologies:

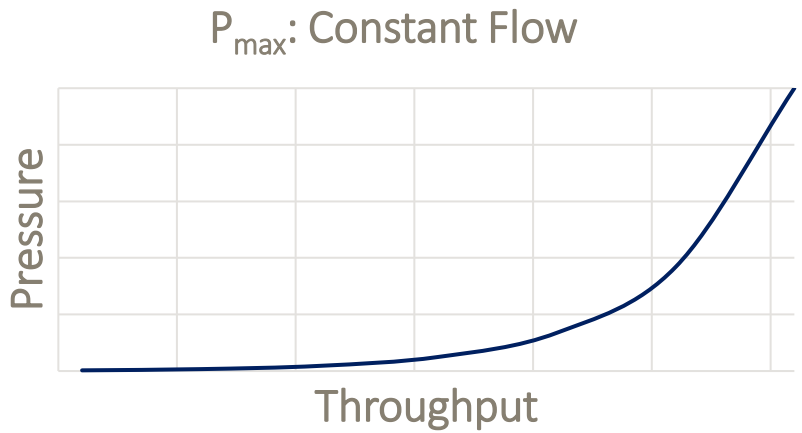
V_{max} – Constant pressure

- Throughput test that measures ***flow rate changes*** over time
- Sizing based on gradual pore plugging model



P_{max} – Constant flow

- Throughput test that measures ***pressure changes*** over time
- Sizing based on gradual pore plugging model



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V_{max}: Constant Pressure Methodology

V_{max}: Constant pressure

- Throughput test that measures flow rate changes over time
- Gas source is used to drive fluid
- Can mimic process conditions

Benefits:

- Requires limited amount of fluid and/or time
- Sizing based on gradual pore plugging model

Limitations:

- May not be appropriate for all solutions
- May required additional intermediate testing

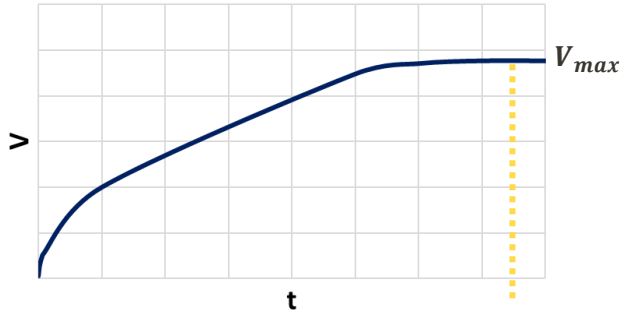
A = Min. effective filtration area (m^2)
V = Batch volume (L)
V_{max} = Maximum filter capacity (L/m^2)
Q_i = Initial flux (LMH)
T_b = Process time (min)

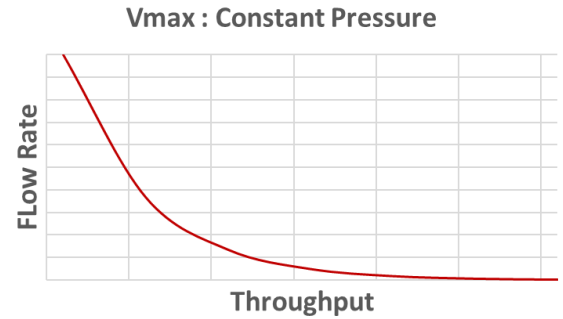
(1) $\frac{t_b}{V} = \frac{t_b}{V_{max} \cdot A} + \frac{1}{Q_i \cdot A}$

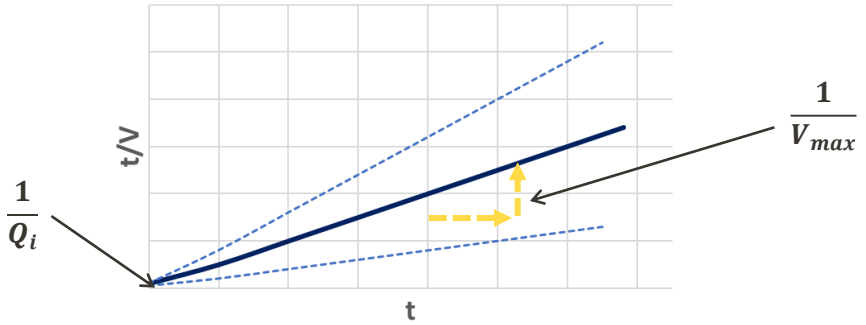
(2) $\frac{A}{V} = \frac{1}{V_{max}} + \frac{1}{Q_i \cdot t_b}$

(3) $\frac{A}{V} = \frac{1}{V_{max}}$

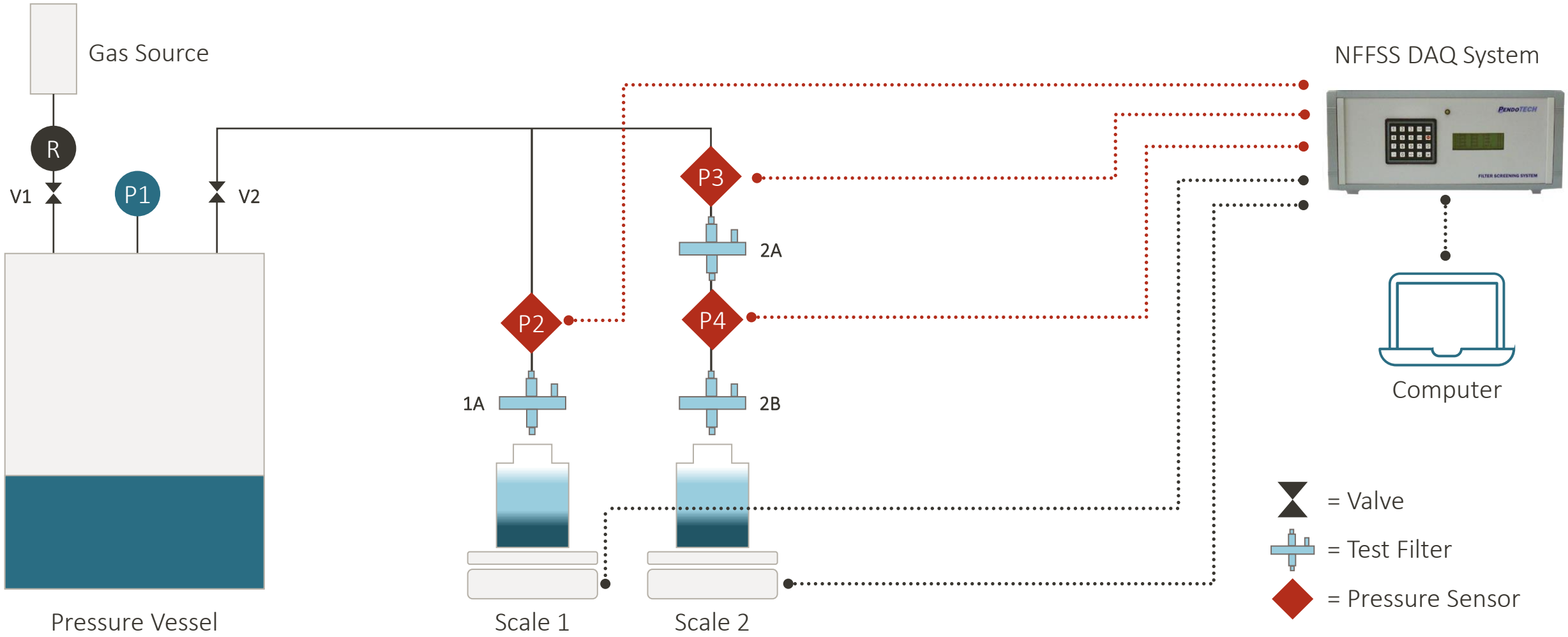
(4) $\frac{A}{V} = \frac{1}{Q_i \cdot t_b}$







V_{max} – Constant Pressure System Methodology



Source: https://pendotech.com/pendotech-products/control-systems/filter-screening-system-nff/

Entegris

P_{max}: Constant Flow Methodology

P_{max}: Constant flow

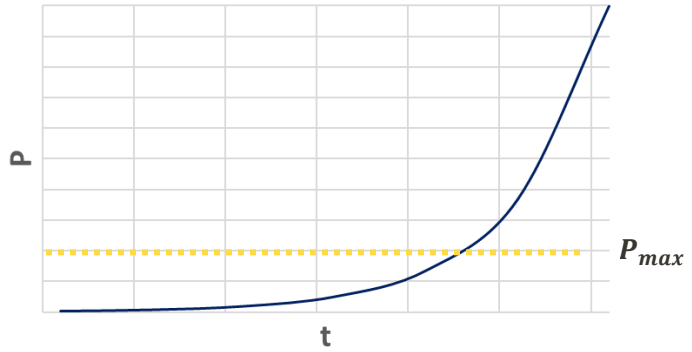
- Throughput test that measures pressure changes over time
- Pump is used to drive fluid
- Can mimic process conditions

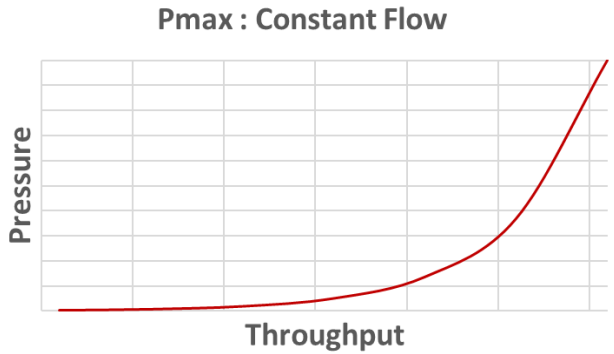
Benefits:

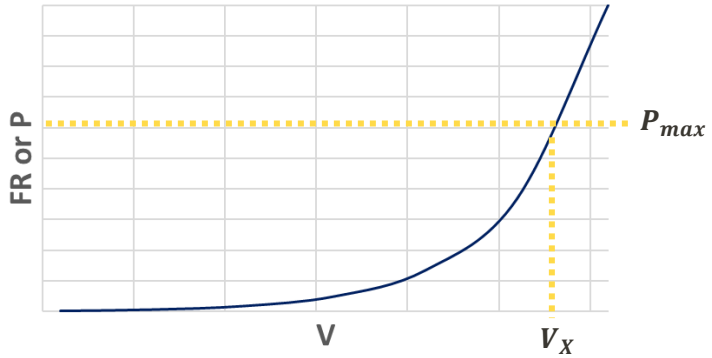
- Requires limited amount of fluid and/or time
- Sizing based on gradual pore plugging model

Limitations:

- May not be appropriate for all solutions
- May required additional intermediate testing
- May require longer testing durations







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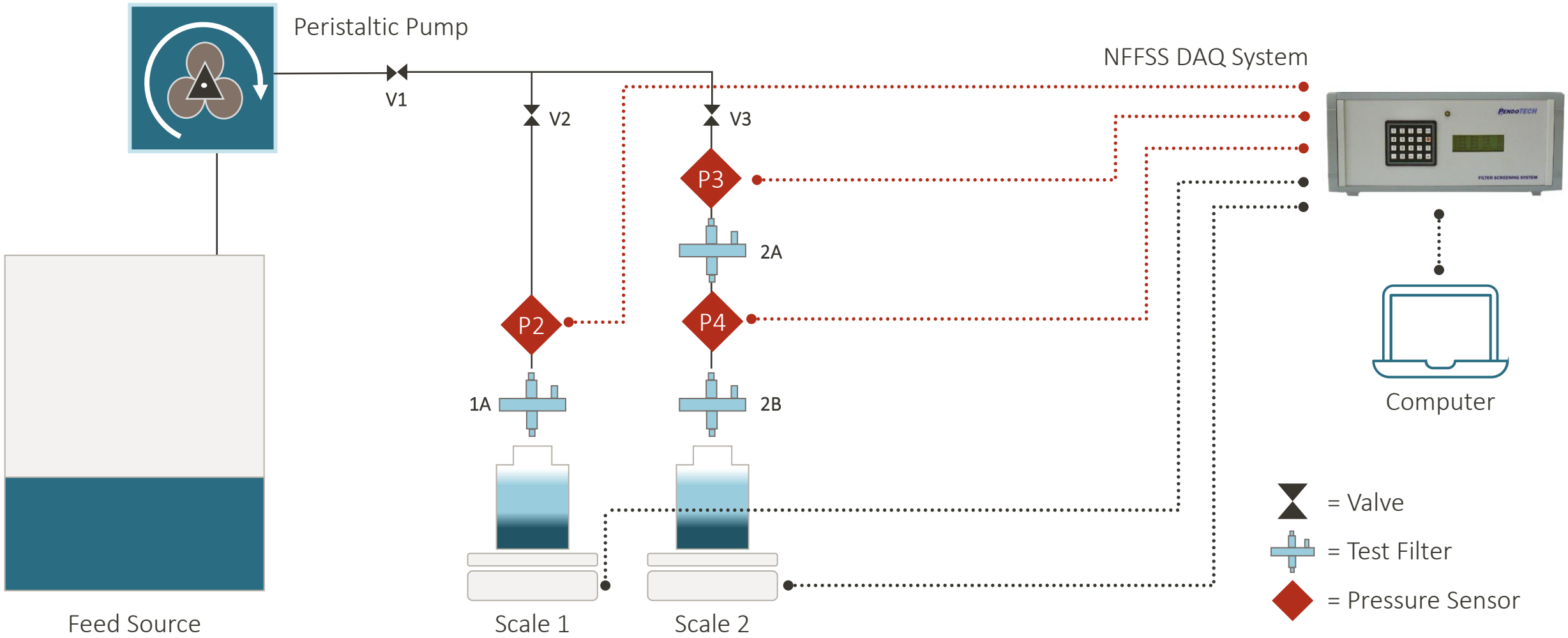
Pmax – Constant Flow



Source: https://pendotech.com/pendotech-products/control-systems/filter-screening-system-nff/

Case Study 1.1: Sterilizing Grade PES Assessment

Purpose:

- Impacts of single layer vs. dual-layer sterilizing grade filters

Test Design:

- **Test mode:** Constant flow
- **Solution:** mAbs analog solution
- **Filters evaluated:**
  - Single-layer: 0.2 µm PES
  - Dual-layer: 0.45/0.2 µm PES
    0.65/0.2 µm PES
- **Filter size:** 47 mm disc
- **Number of samples:** 5

Analysis:

- **Batch size:** 10 L – 100 L

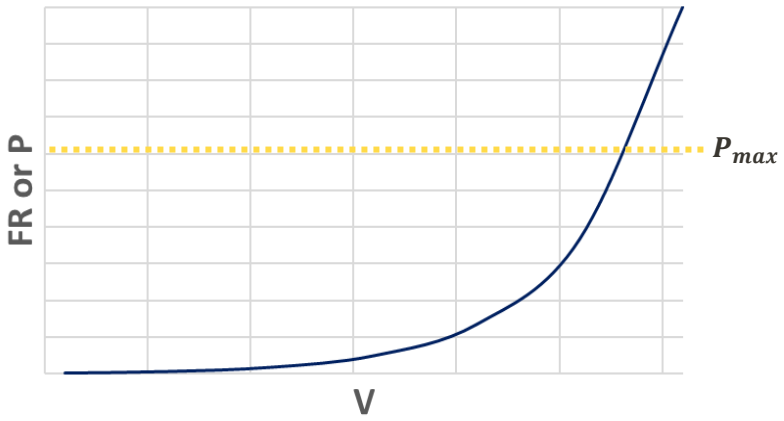


Image 1 source: https://midsci.com/item/ASFILTHOLD47/Pall-47-mm-In-line-Filter-Holders/
Image 2 source: https://www.dscbalances.com/products/pall-60539-wwptfe-membrane-disc-filter-0-2-um-47-mm-50-pkg

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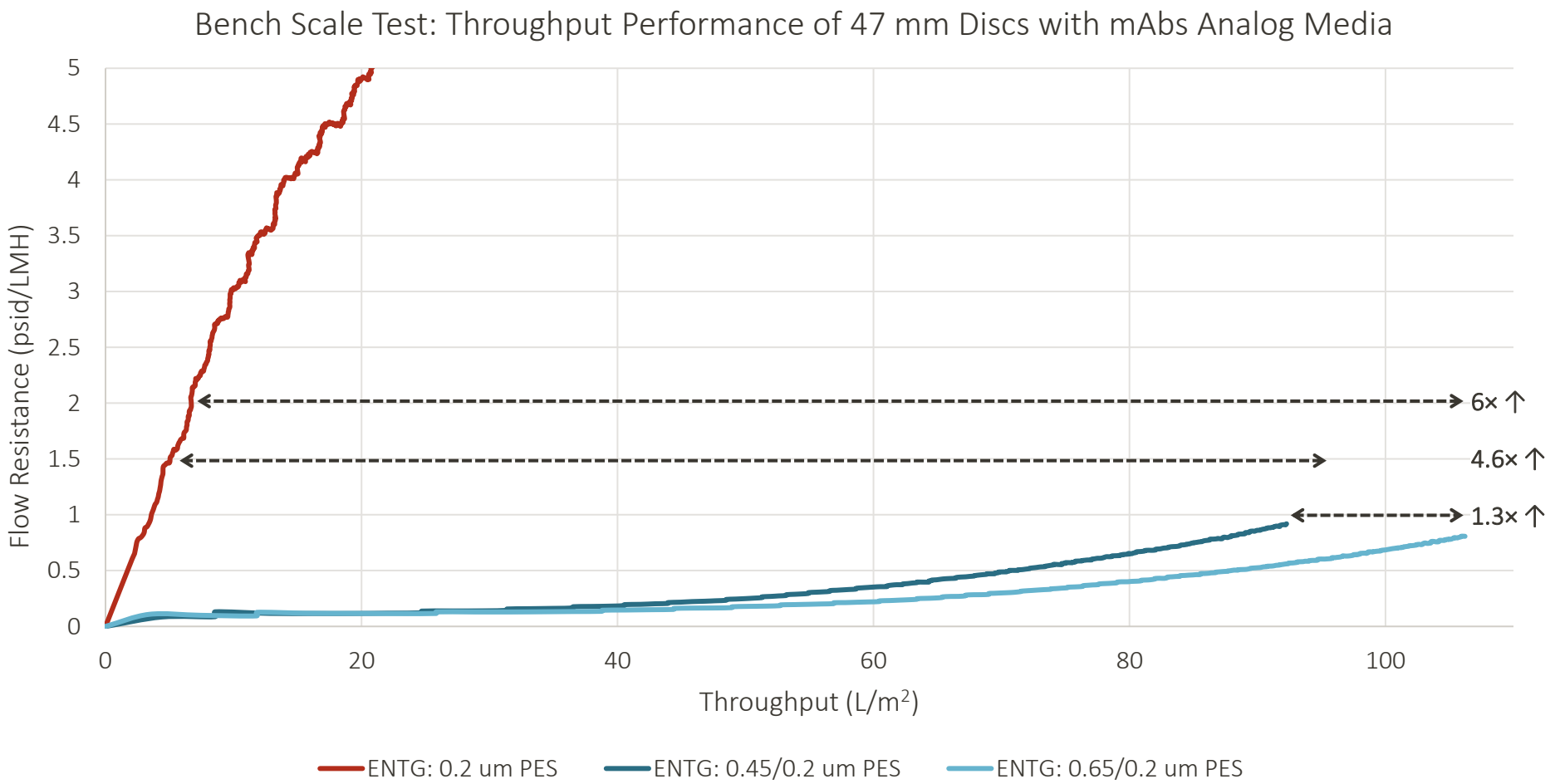
Case Study 1.2: Sterilizing Grade PES Assessment



Dual-layer has significant more throughput

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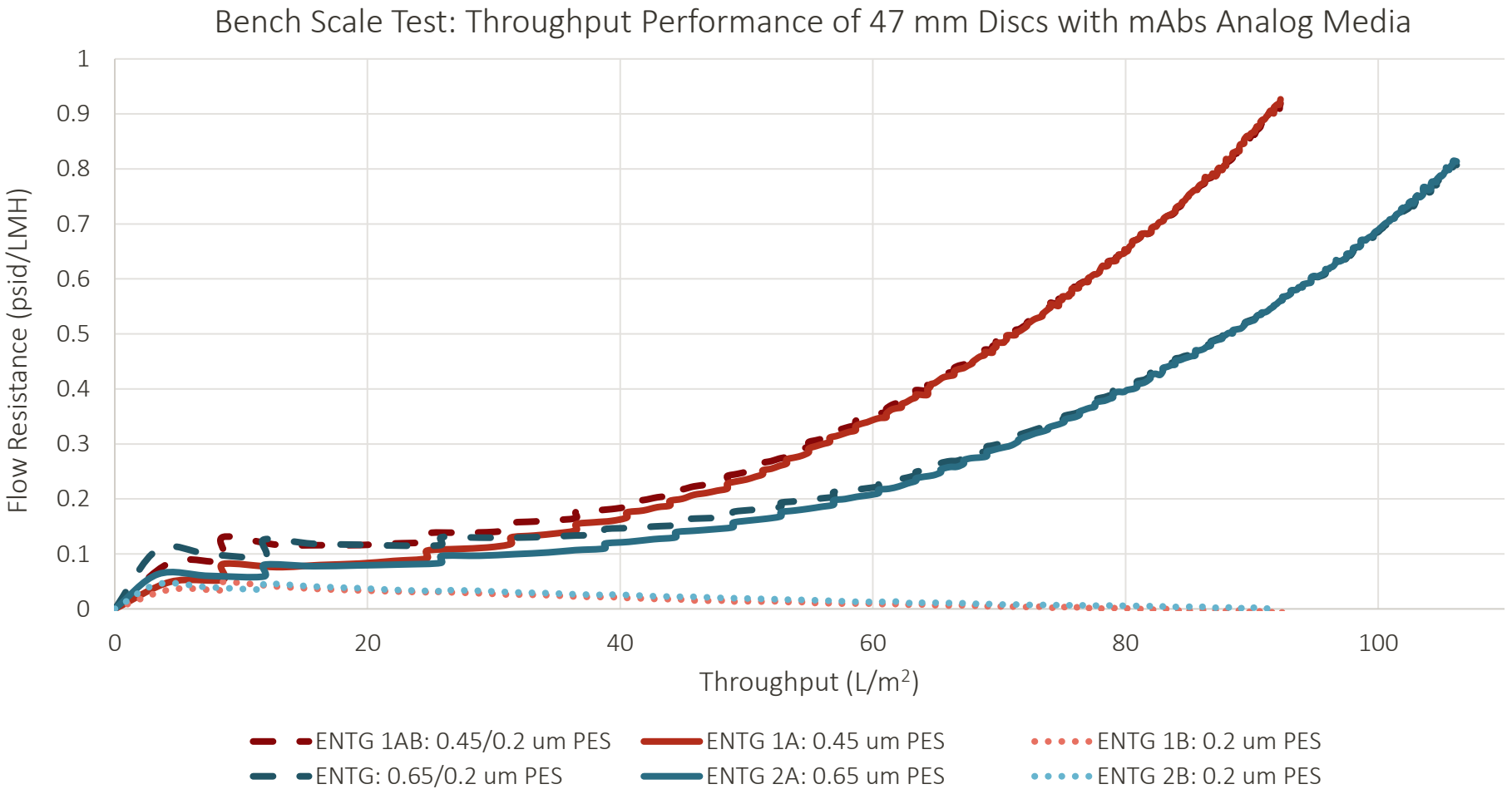
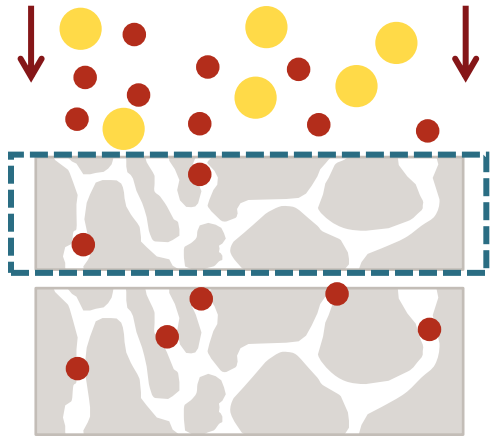
Case Study 1.3: Sterilizing Grade PES Assessment





Gradual pore plugging

Pre-filter layer primarily plugs

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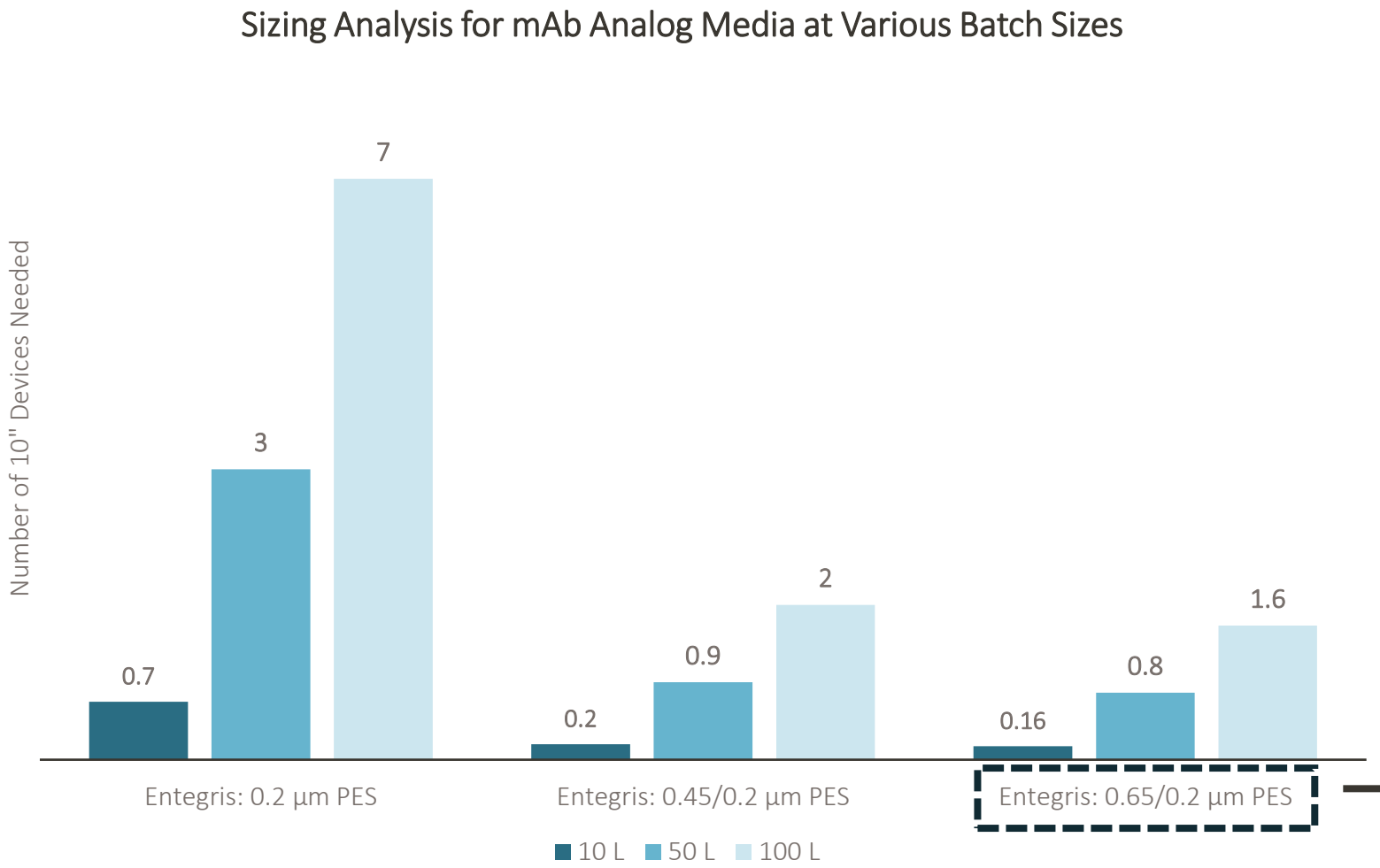
Case Study 1.4: Sterilizing Grade PES Assessment



- Dual-layer PES provides more **efficient scaling** advantages
- More **cost efficient** ⟶ ~4.4× at full-scale

Case Study 2.1: Membrane Impact on Upstream Media Processing

Purpose:

- Impacts of different manufacturer PES and PVDF membranes on performance

Test Design:

- **Test mode:** Constant pressure
- **Solution:** CHO media/CHO media with glucose
- **Filters evaluated:**
  - Dual-layer T1: 0.45/0.2 µm PES/PVDF
  - Dual-layer T2/T3: 0.45/0.2 µm PES
    0.8/0.2 µm PES
- **Filter size:** 47 mm disc
- **Number of samples:** 5

Analysis:

- **Batch size:** 100 L – 1000 L

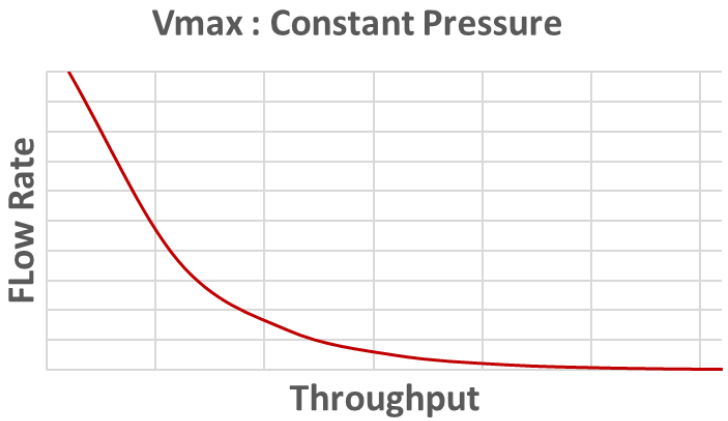


Image 1 source: https://midsci.com/item/ASFILTHOLD47/Pall-47-mm-In-line-Filter-Holders/
Image 2 source: https://www.dscbalances.com/products/pall-60539-wwptfe-membrane-disc-filter-0-2-um-47-mm-50-pkg

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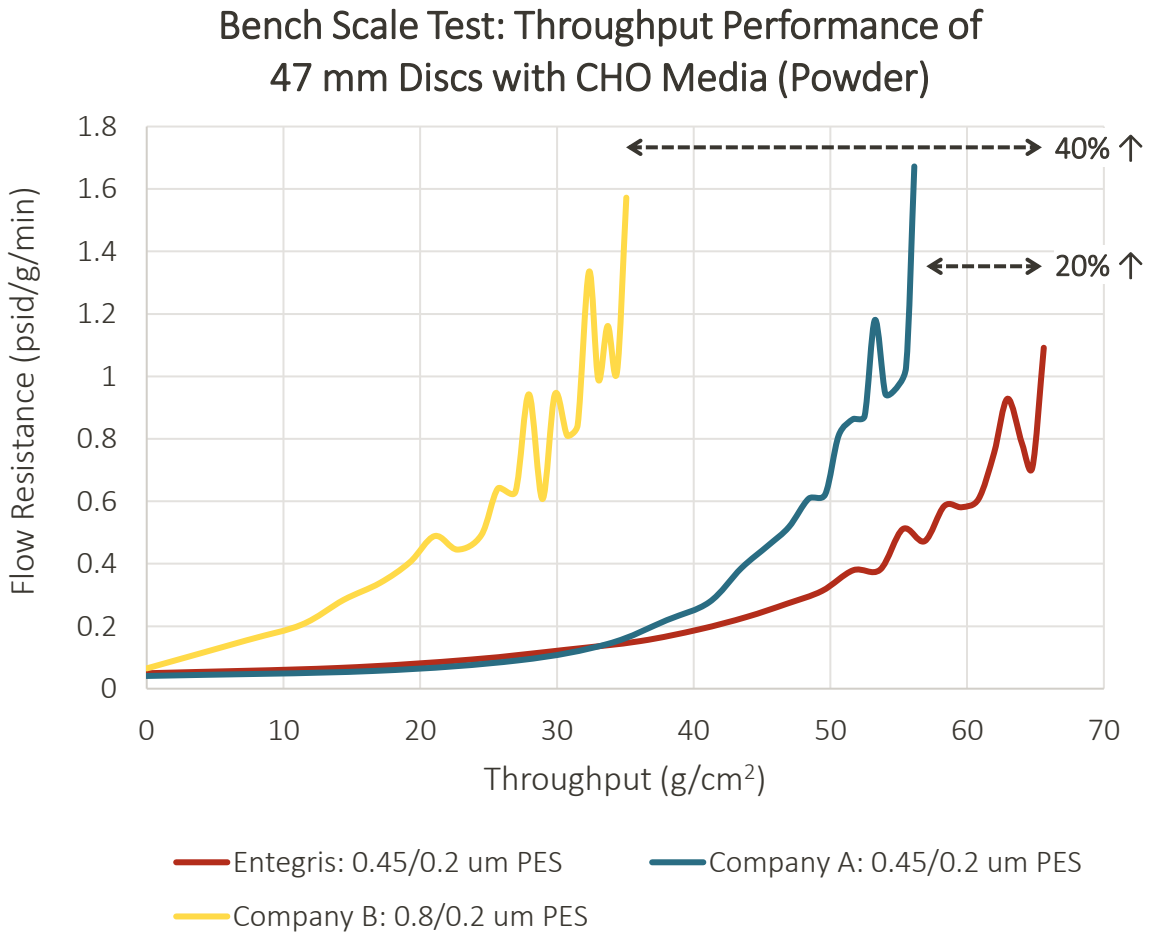
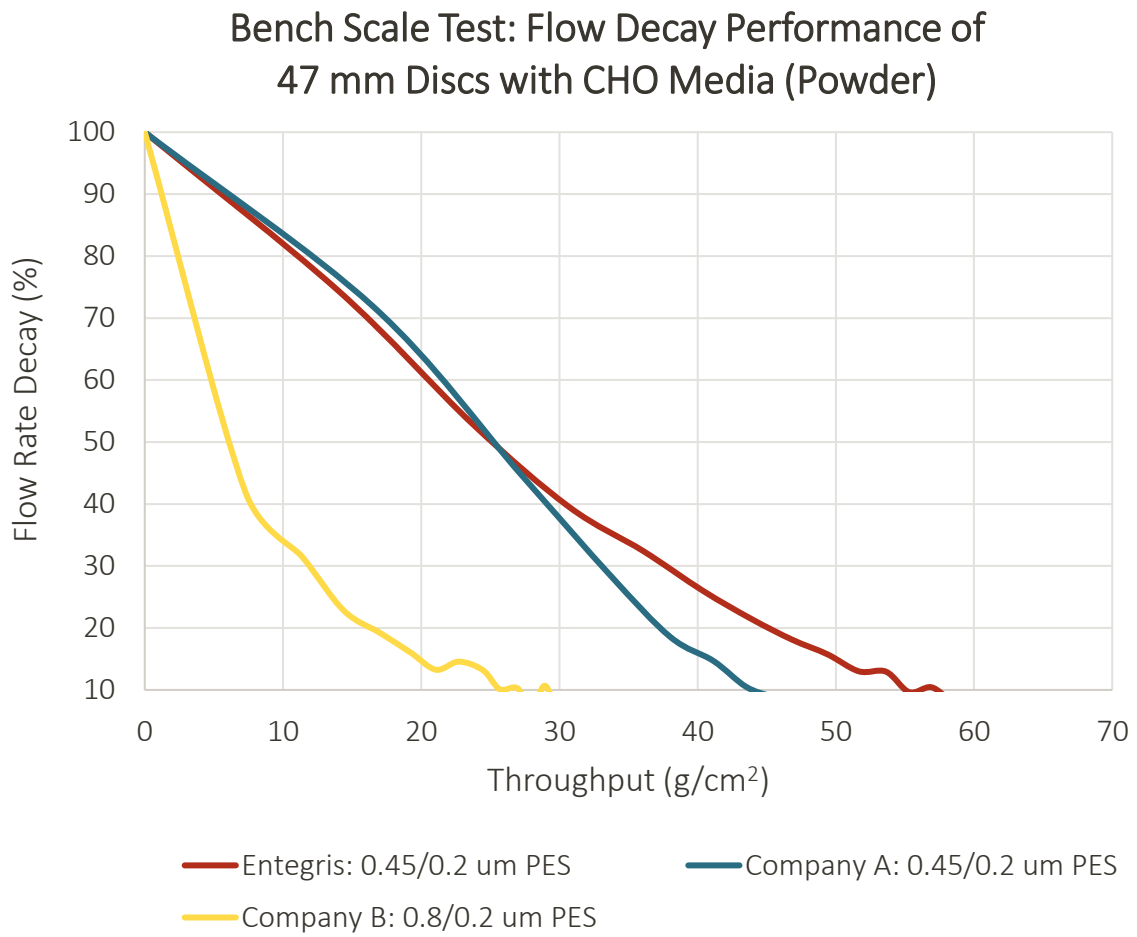
Case Study 2.2: Membrane Impact

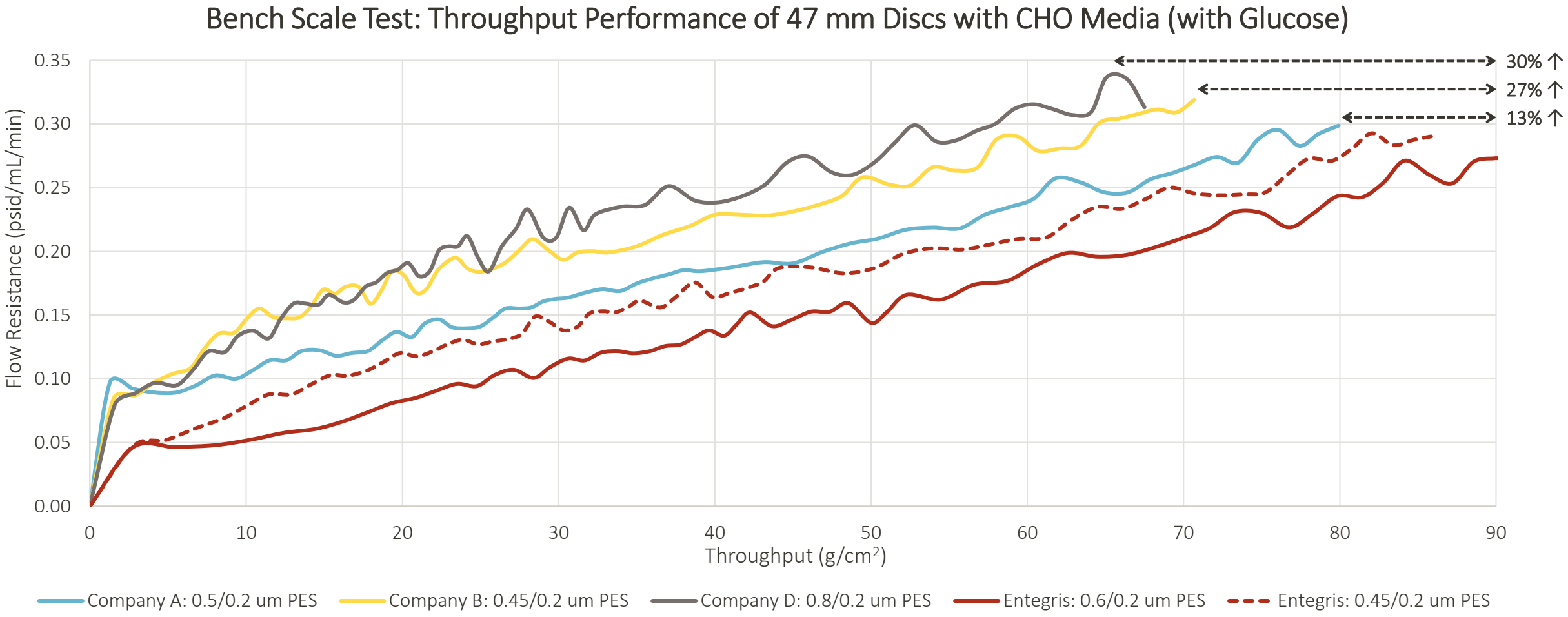
Dual-layer PES analysis



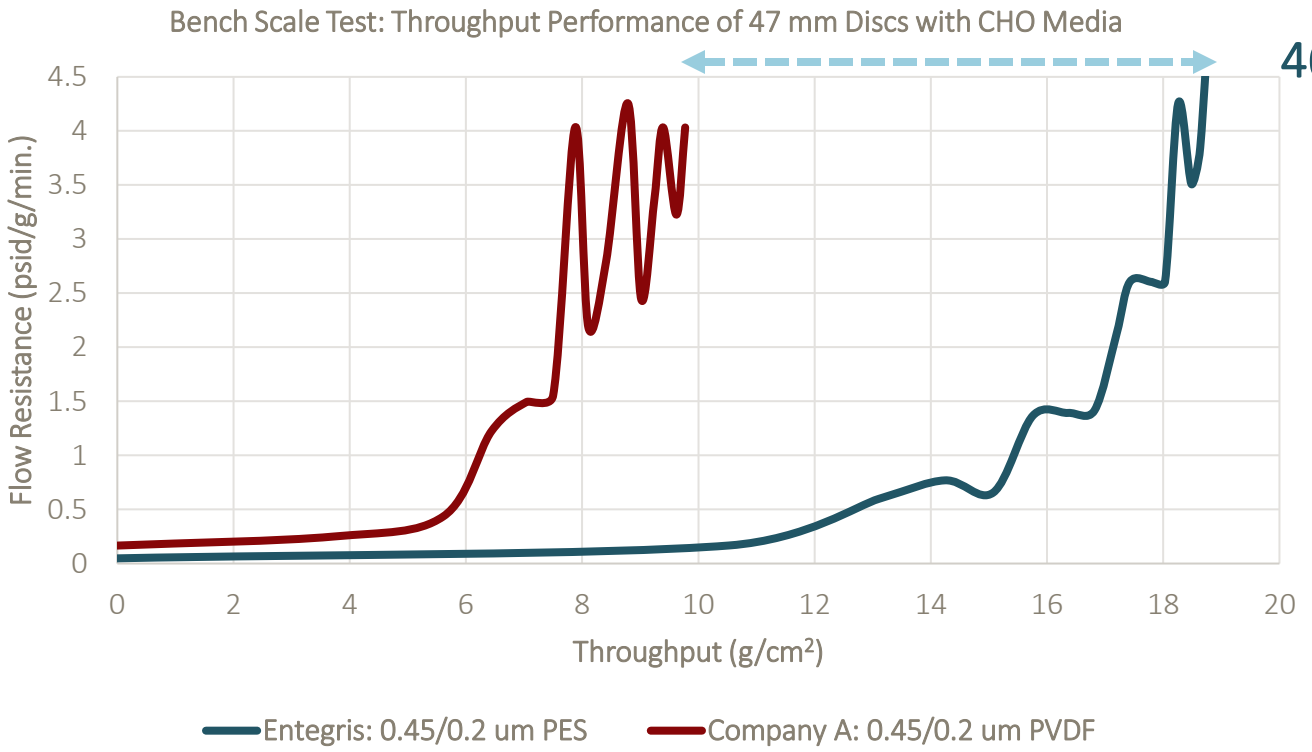


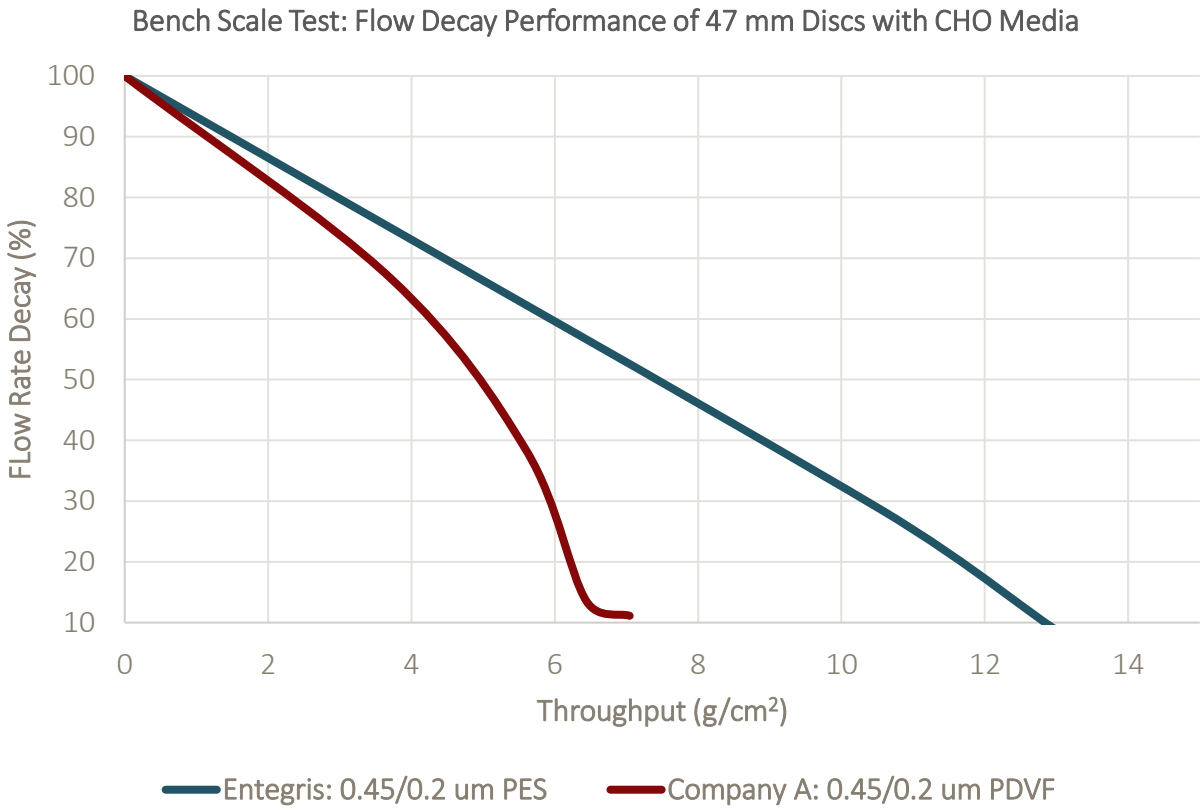
Case Study 2.3: Membrane Impact

Dual-layer PES analysis



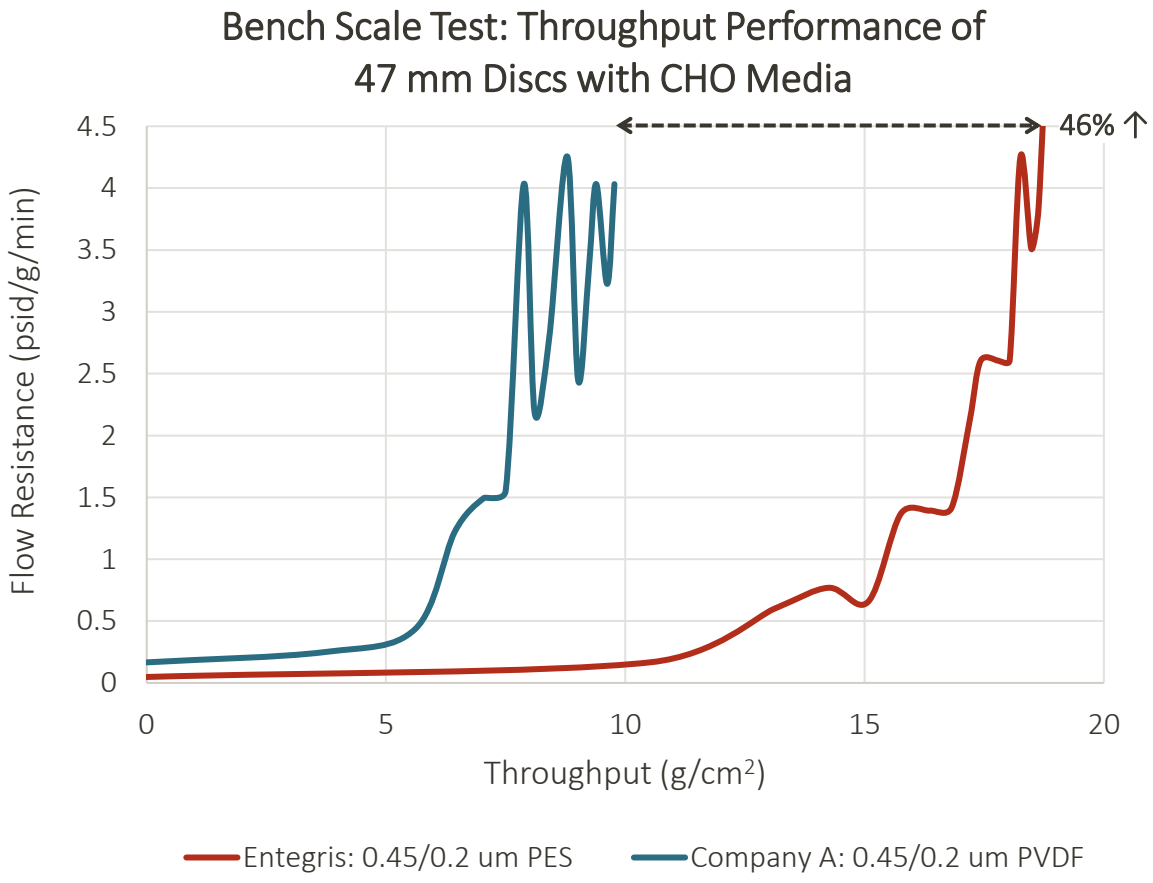
Case Study (2.4): Membrane Impact – Dual Layer PVDF Analysis

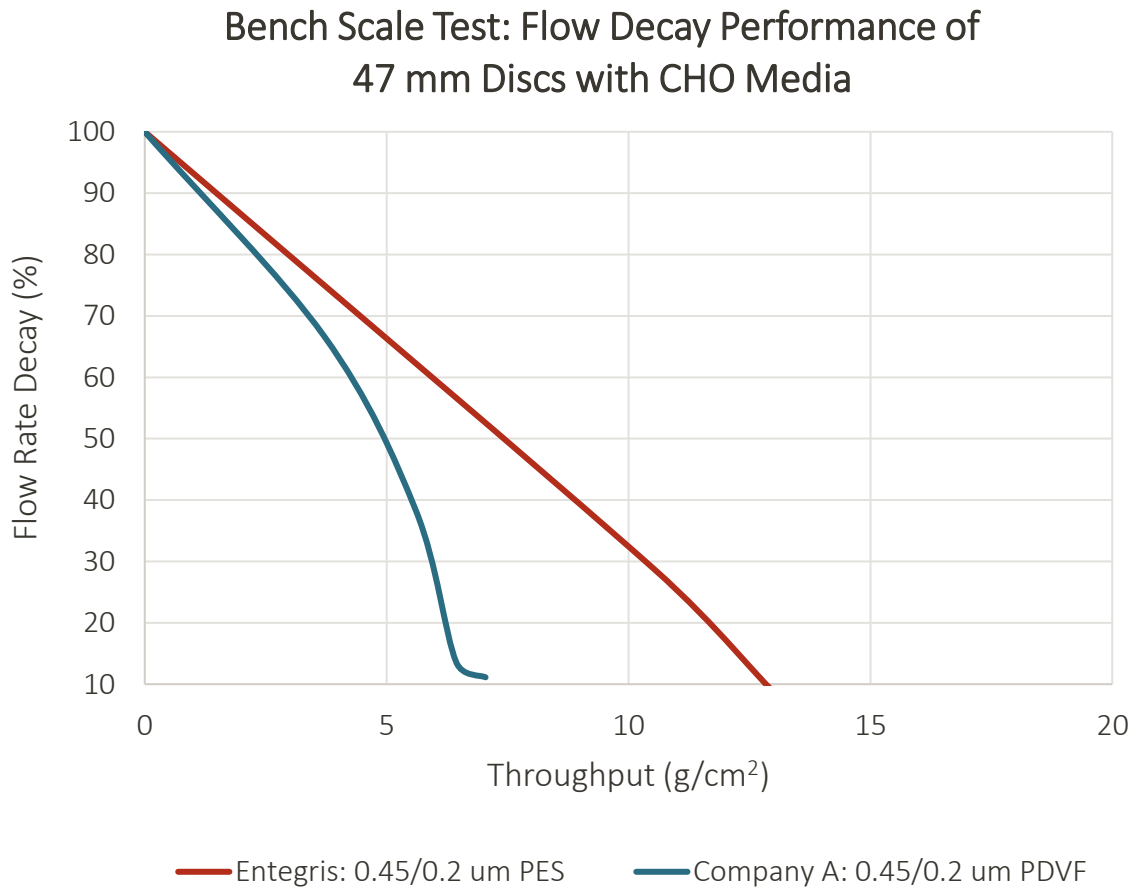




Case Study 2.4: Membrane Impact

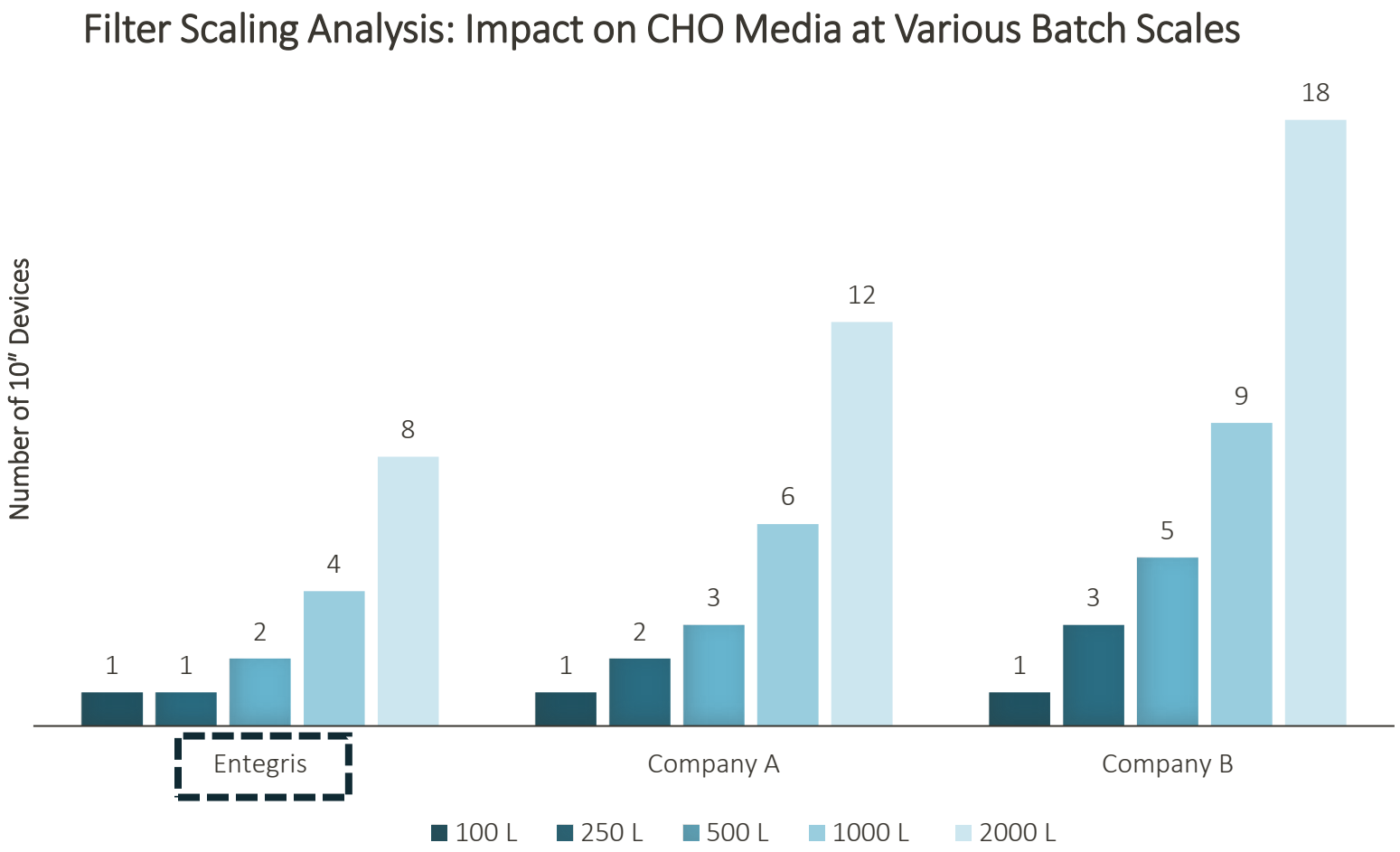
Dual-layer PVDF analysis





Case Study 2.5: Membrane Impact

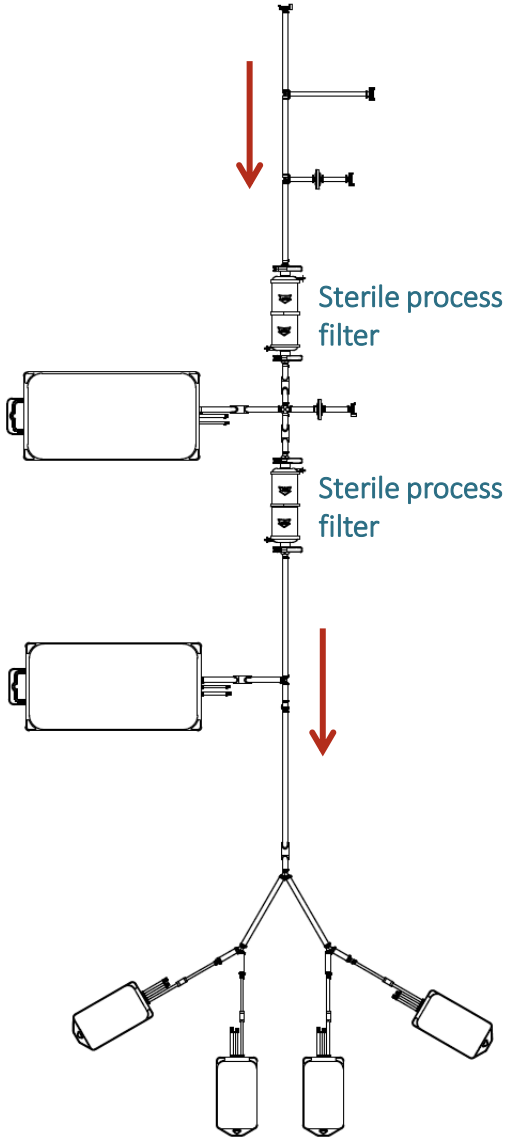
Sizing analysis

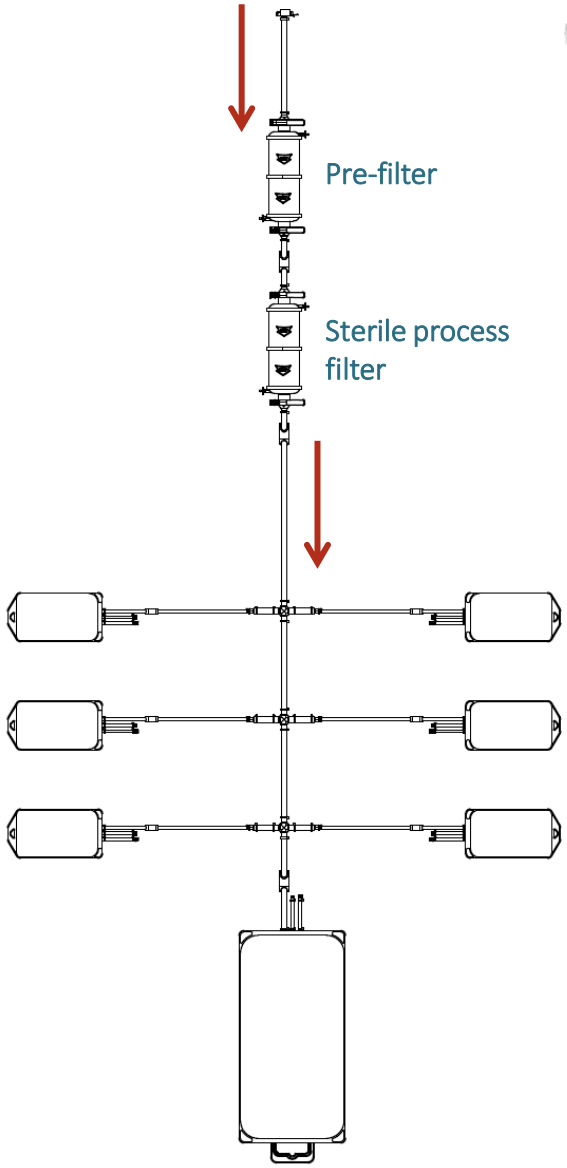


- Entegris PES provides more **efficient scaling** advantages
- Advantage in providing more efficient single-use designs
- More **cost efficient** ⟶ ~2.1× at full-scale

Filter Optimization for Single-Use Integration

- Selecting the correct **size** filter, **connectivity**, and **rating** will be critical
- Selecting appropriate single-use components, e.g., sterile connectors, tubing, bag volumes, etc.
- Selecting correct **pre-filter** and **sterilizing grade filter** for process
- **Design for optimal product performance, ease of assembly, and operator efficiency**





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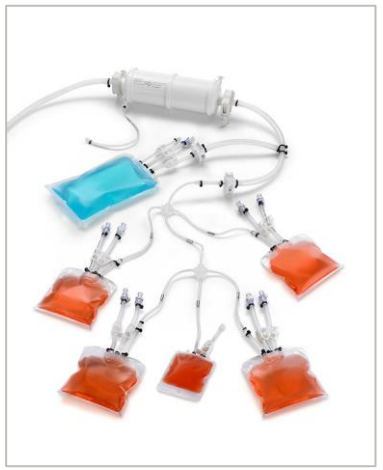
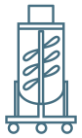
Entegris: A Single-Use and Filtration Solutions Partner

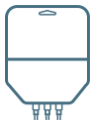
- Entegris **standard sterile filtration solutions** can be adapted into a wide variety of bioprocessing steps
- **Standard** and **custom single-use solutions** for integration with filtration
- Entegris is committed to providing engineered solutions and quality-by-design products into the life sciences market



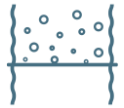
Fluid handling



Bioreactors and mixing

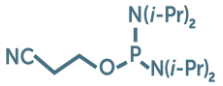


Single-use assemblies



Filtration and purification

Clean chemical storage



Organophosphorus and specialty chemicals

Particulates and automated testing

Entegris

QUESTIONS?

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