



## session 6: NOVEL technologies deployed in Biomanufacturing

**Closed Processing: A Key Enabler for Next  
Generation Biomanufacturing**

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**MERCK**

who is Merck?

# Three High-tech Businesses Competing in Attractive Markets

## Healthcare

As One for Patients



Leading among  
**SPECIALTY PHARMA**  
markets

- Biologics and small-molecule **prescription medicines** against cancer, multiple sclerosis, infertility
- **Research** focus: Oncology, Immunology & Immuno-Oncology

## Life Science

Impacting Life and  
Health with Science



A leading  
**LIFE SCIENCE**  
business

- Tools and services for **biotech research and production**
- **Tools and laboratory supply** for academic research and industrial testing

## Electronics

Advancing Digital Living



A leading business in  
**HIGH-TECH SOLUTIONS**

- High-tech solutions and materials for **electronics**
- Broad portfolio of **decorative and functional solutions**

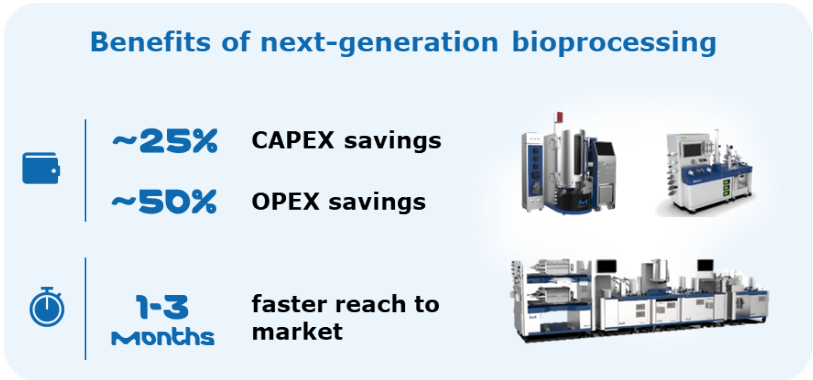
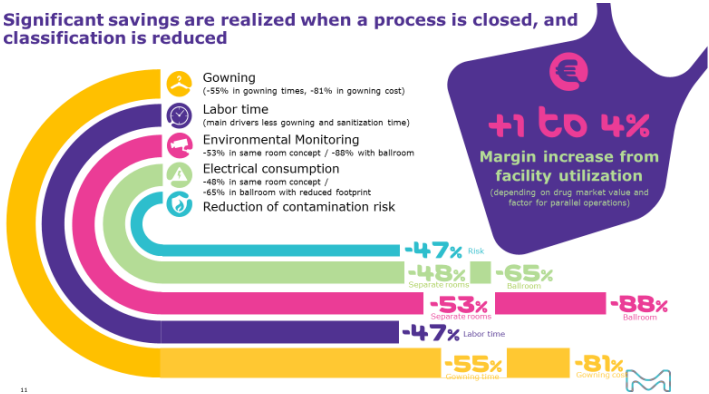
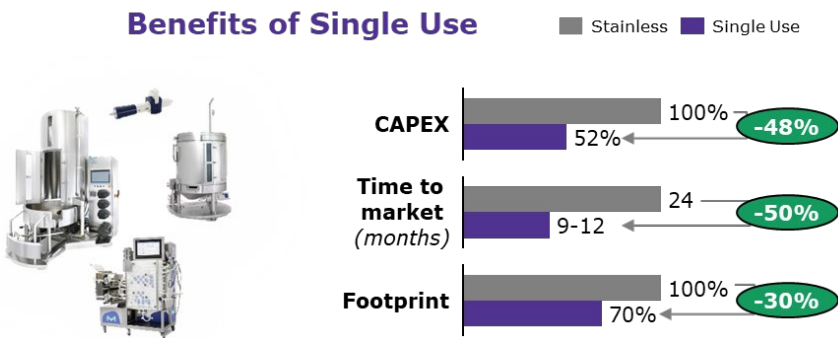
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# closed processing overview



# Single use, closed, and next-generation processing are critical to meeting market aspirations

 <b>Trends</b>	<b>Smaller batches, flexible multi-product facilities</b>	<b>Need for speed, without quality compromises</b>	<b>Cost consciousness</b>	
 <b>Aspiration</b>	 <b>-90%</b> changeover time	 <b>-70%</b> build time	 <b>10X</b> quality robustness	 <b>-90%</b> CAPEX and OPEX



Source: Cytiva report on Single use, BioC deck, Fisher et al., International Journal of Pharmaceutics, 2022

# terminology and concepts

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Closed processing

## There are different ways of achieving closed processing

"A process step (or system) in which the product and product contact surfaces are not exposed to the immediate room environment"

### Functionally closed system

- **May be opened** but rendered closed through a **sanitization or sterilization step prior to processing**
- Once system is rendered closed, transfer into or out of the system must be done in a closed manner (e.g., aseptic connection, filter, etc.)

### Fully closed system

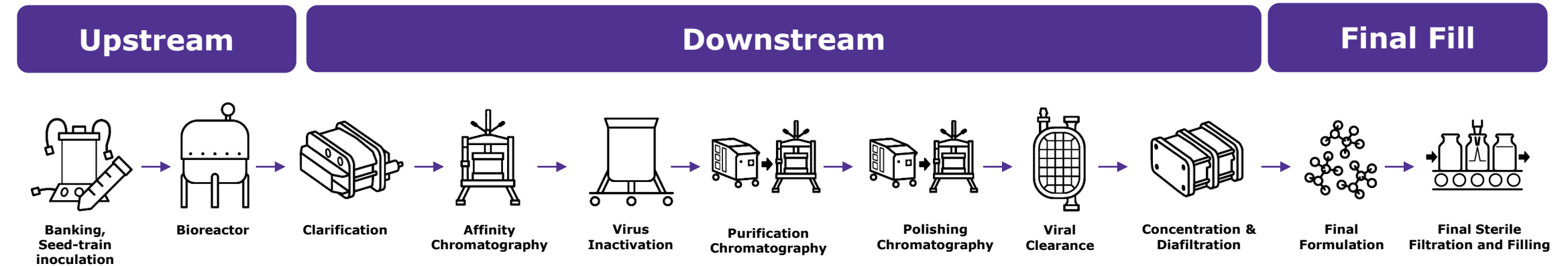
- **Never opened or exposed to the environment**
- Materials added or removed from the system must be done in a closed manner (e.g., aseptic connection, filter, etc.)
- Some processes may require closed and contained disconnection & disassembly



***Closed Processing does not mean sterile***

**System closure =  
f (bioburden, cleanliness, integrity)**

# Closed processing is a powerful measure to prevent contamination and maximize facility utilization



**Closed processing** well established to mitigate contaminations

In many cases, equipment and technologies used for downstream bioprocessing requires **open manipulations** that could allow particulates and/or bioburden to enter the system boundary

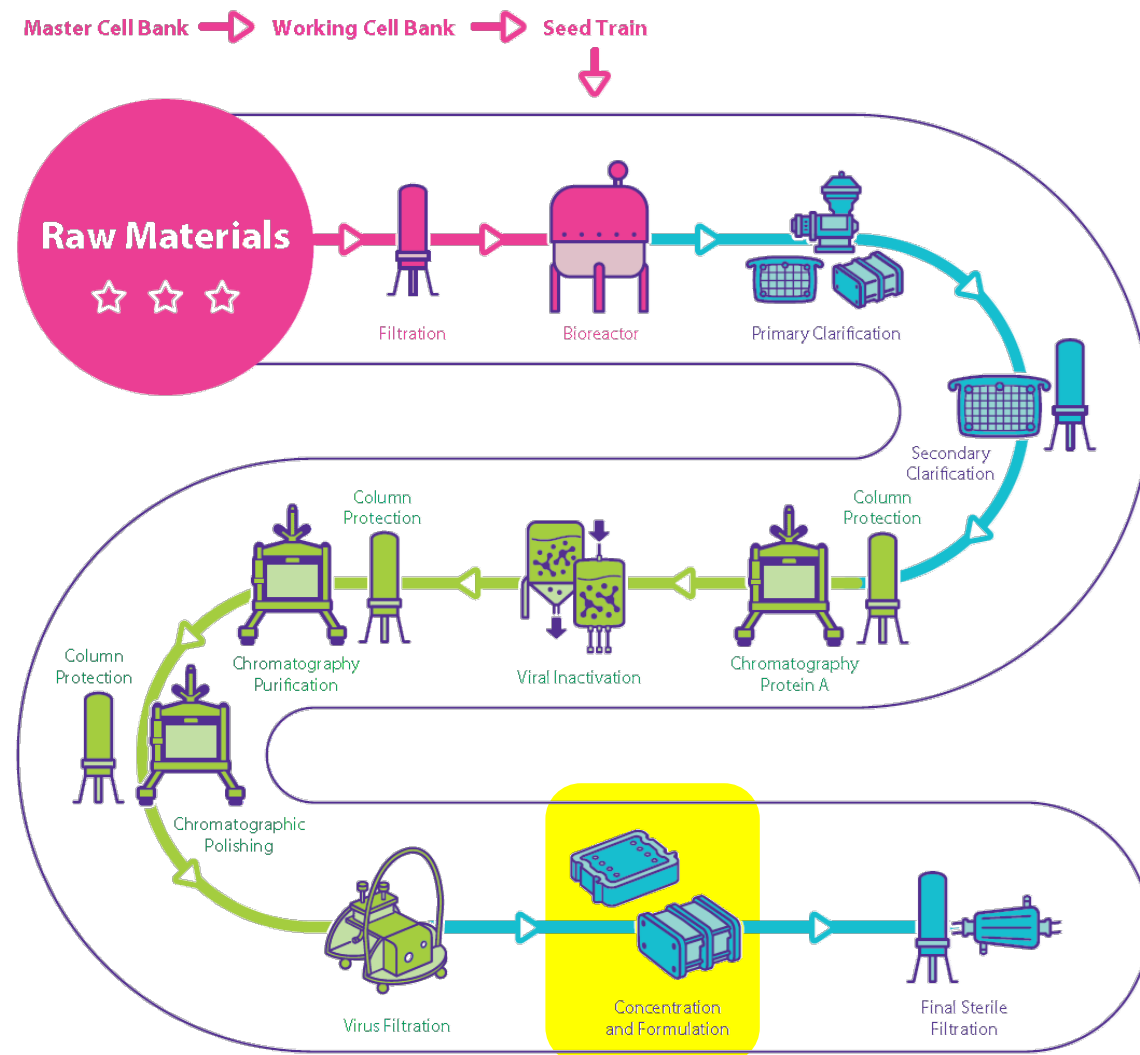
**Aseptic processing** to achieve sterility of the end-product

**Moving downstream steps to single use and closed is a natural next step in the evolution of biomanufacturing**



# Introduction

## Challenges and opportunities in TFF



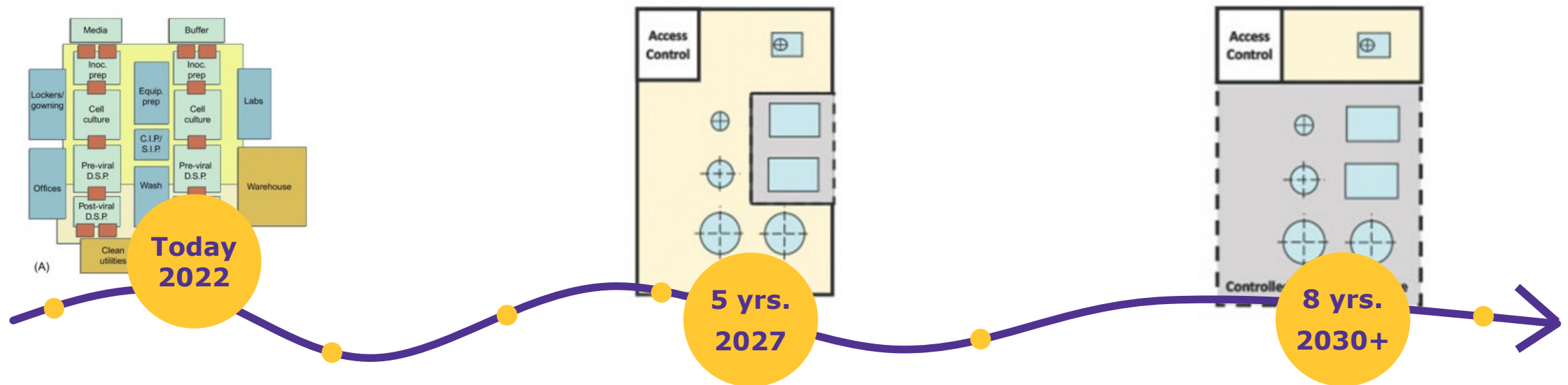
- 1 Significant time/labor spent on
  - Device preparation
  - Post-use cleaning
  - Sampling and validation
- 2 Stainless steel equipment restricts scaling scope and platform movability

# Pellicon® Capsules & Manifolds

- **User friendly:** Self-contained design that is delivered pre-assembled and pre-sterilized for hassle-free installation via genderless AseptiQuik® connectors
- **Ready to use in minutes:** Supplied gamma sterilized and preservative-free, skip cleaning and sanitization! Just run your buffer flush equilibration
- **Reduce risks, increase flexibility:** Operate in closed mode with specifically designed Flexware® assemblies and Mobius® TFF systems to reduce contamination risks while improving process efficiency
- **Linear scalability:** Consistent high flux performance across all scales that further enables customers to reliably switch from/to our industry leading Pellicon® 3 cassettes



# Closed processing will be an evolutionary journey for drug manufacturers



## Critical steps closed; most unit ops briefly open or functionally closed

- **SU technologies** used to close critical steps
- Contamination **risk mitigation** is driver
- **Separate rooms** with traditional clean room classification and environmental controls
- **Campaign** strategy for multi-product mfg.

## Functionally closed process with some fully closed unit ops

- Adapted technologies **and aseptic connectors** used to close steps
- Reduced cleanroom requirements is driver
- **Ballroom concept** cleanroom with **fully closed unit ops in CNC space**
- **Multi-product mfg.** is the norm; labor intensive product changeover still required

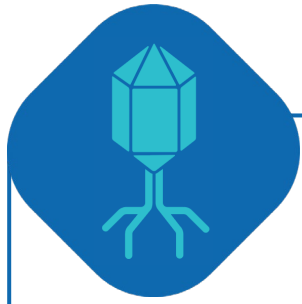
## Fully closed process with closed disconnection and disassembly

- **Fit for purpose** closed processing technologies
- **Multi-product and platform mfg.** is driver
- **Majority of unit ops in CNC space** with very limited cleanroom footprint
- **Concurrent** multi-product and/or multi-platform mfg. is possible

# value drivers and benefits

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# Closed processing drivers differ by modality, but benefits are universally realized



## Viral vector & live viruses

- Filtration not possible
- Biosafety
- Animal vaccine never sterile filtered

Future state:

- Multi-platform solutions
- Ballroom concept



## mAbs & Recombinant proteins

- Reduce human interferences
- Reduce environmental control requirements

*"The flowpaths used in closed mode help increase process safety and enable easier, faster, and reduced environmental controls."*



## Cell therapy

- Manufacturing at 'point of use'
- Small, fast set-up capabilities
- Safety of product and patient

*"The main objective is the assurance of an uncompromised product using a processing mode which doesn't have potentially harmful steps."*

**Closed processing mitigates contamination and safety risks, and enables multi-modal manufacturing**



## Closed Processing

### Key benefits and value drivers



1

Mitigates contamination and safety risks

2

Significant cost reductions and energy savings for both new and existing facilities

3

Reduction in time to market, cycle time, and product changeover

4

Reduced footprint and infrastructure requirements

5

Enables multi-product and multi-platform manufacturing within the same facility



**THANK  
YOU**