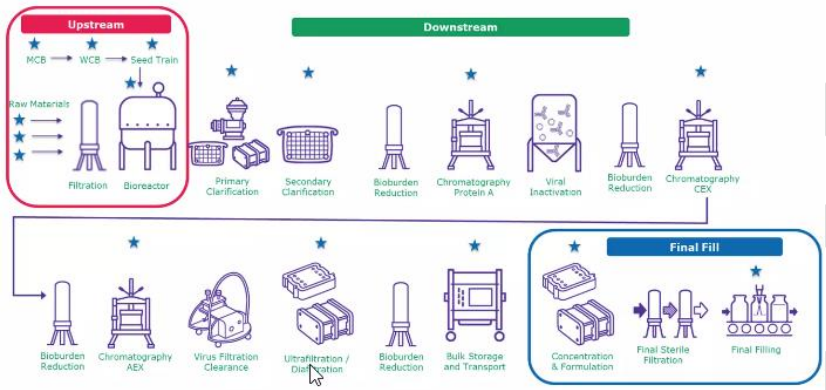
Non-Confidential information

We use PVDF to produce our Durapore® membranes that are critical in almost any steps of the discovery, development, and production of pharmaceutical and biopharmaceutical medications and therapies.
There are different considerations at different process steps, requiring risk-based filter selection.



Upstream Process
- Bioreactor protection
- Drug supply continuity
- Business risk mitigation

Downstream Process
- Bioburden Reduction
- Assure drug substance purity

Final Fill
- Regulatory requirements
- Drug product sterility assurance
- Assure patient safety

Here are some critical applications in which the membranes cannot be readily/ easily substituted:

1. Buffer filtration

Biomanufacturing requires large volumes of buffers for different steps in downstream processing, with filter selection highly dependent on the needs of the specific process step. It must be mentioned that such filters must be fully scalable from lab-scale process development tools to pilot and production scale manufacturing. 0.22 µm Durapore® filters contain a single layer of 0.22 µm polyvinylidene fluoride (PVDF) membrane and are low-binding, non fiber releasing with low extractables.

2. Media Filtration

Upstream bioburden control focuses on preventing microorganisms from entering cell culture processes. Sterile filtration is routinely implemented to protect the bioreactor and upstream processes from contamination. There are multiple media filtration options that deliver sterility assurance and high performance at every step. Filter selection is guided by risk analysis to identify the level of bioburden control required, the efficiency (throughput) of cell culture media processing, and the filter formats available. Durapore® 0.1 µm and 0.22 µm filters contain one layer of polyvinylidene fluoride (PVDF) membrane and provide high flow rates and throughputs. These filters offer sterilizing-grade performance.

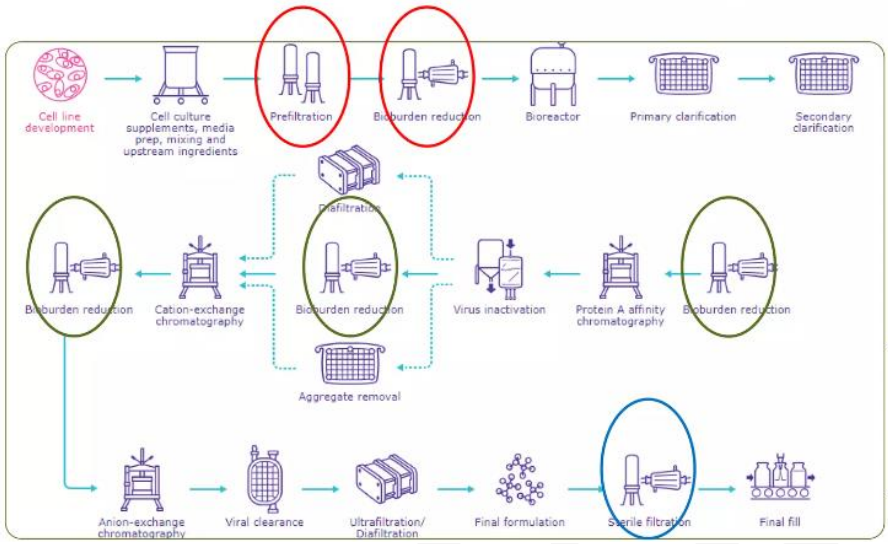
3. Gas or vent filters

Gas or vent filters containing hydrophobic membrane are commonly used as air vents throughout biomanufacturing to maintain near-ambient pressure in processing tanks and closed systems. These filters act as a barrier, preventing both the entry of adventitious microorganisms and the release of product aerosols.

Generally, the main considerations for gas filtration include filter position, sizing, sterilization processes, and integrity testing practices. There are stringent regulatory expectations for critical gas or vent filters, which include confirming the integrity of filters on sterile holding tanks and filling machines, and after steam-in-place sterilization or use.

- Sterilizing-grade 0.2 µm hydrophobic polytetrafluoroethylene (PTFE) membrane are used in bioprocessing applications where it is critical to use a phobic filter with validated bacterial and viral retention capabilities.
- 0.22 µm hydrophobic sterilizing-grade polyvinylidene fluoride (PVDF) membrane provide reliable removal of contaminants and microorganisms from gases.
- 0.2 µm polytetrafluoroethylene (PTFE) membrane are used for the removal of bacteria and viruses from moist gas streams in moderately- or non-critical applications.
- Hydrophilic and hydrophobic sterilizing-grade 0.22 µm Durapore® PVDF membrane allows the flow of both liquid and gas. These filters simplify Pre-Use Post Sterilisation Integrity Testing (PUPSIT) in final filtration assemblies by maintaining sterility while removing the constraints of a flush bag or a can.

The use of our products generally occurs within highly regulated industry sectors where a swift and rapid transformation is impossible. As today membranes and devices are highly optimized for each individual process/application. Due to the extended time required for re-validation, re-qualification as well as in some cases re-authorisation procedures, it is critical we enable a smooth transition without supply interruption.

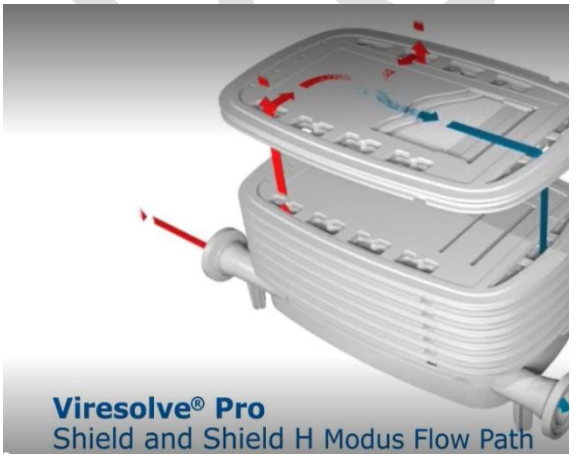


Bioburden reduction filters and sterilizing-grade filters are used in multiple biopharmaceutical applications.

- Cell culture media
- Buffer and Prep
- Product intermediates
- Drug product, final fill

4. Viral Filtration

In brief, our products containing PVDF either as membranes or as housings for other membranes are used by thousands of companies globally (see confidential answer). The use sectors are in the areas Healthcare, manufacture of monoclonal antibodies, vaccines and recombinant proteins just to name a few.



Question 6

Sub-question f) and g)

Step	Objective	Supply chain position	Cost Estimates (K Euro)	
			Low estimate	High estimate
Process Development	Design of alternative process for new device	Customer/ Manufacturer	**See Confidential attachment**	
Scale-up / Pilot comparability	Identification of impacts across on the whole process; and Demonstrate filter efficiency nor impurity profile are adversely impacted	Customer/ Manufacturer		
Hardware				
Re- validation, e.g., impurity or virus spiking trial		External contractor		
Cost of filing to FDA or other regional authority	Filing new product	Customer/ Manufacturer		
Cost of changing SOP	Implementation	Customer		
People/Resources and training		Customer		
		Total		