Application Summary

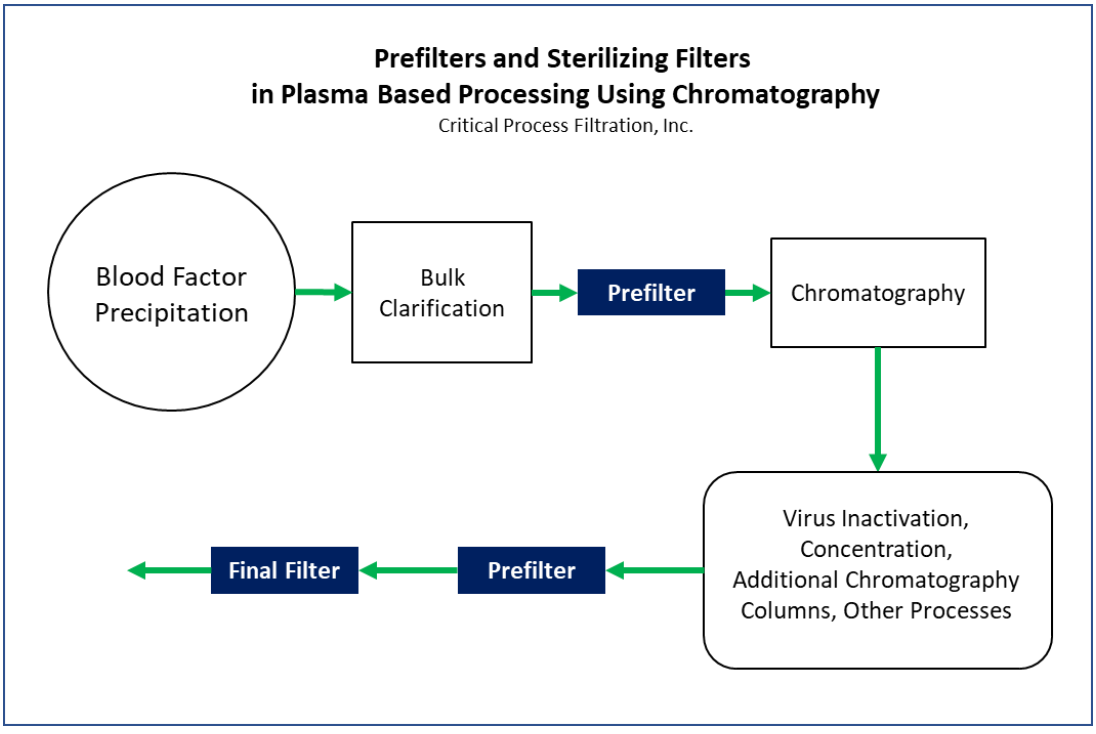
Prefiltration and Sterilizing Filtration of Plasma-Based Products

Ensuring product sterility is the most critical filter application in all biopharmaceutical operations. The final filter is the last chance for sterile filtrate before most products are packaged. In almost all systems, multiple filtration steps are used to provide reliable, successful performance of this critical function.

All filtration steps prior to the final, sterilizing filter are considered 'prefiltration' steps. The exact filtration goals of these steps vary according to the product and process, but the most critical function of prefilters is to protect the sterilizing filters from premature fouling by bacteria or other particles in the plasma product. This extends the life of the sterilizing filters, and can reduce the overall cost of filtration.

Sources of Bacteria

Every plasma fractionation operation has to deal with different bacteria. The blood plasma used in the process will contain any number of different microorganisms. Numerous organisms also exist in every environment and surround every facility. Facilities try to prevent them from entering the processes by operating in a clean room environment, appropriate protective clothing worn by plant personnel, and robust cleaning procedures. Filters may be employed to block microorganisms from entering any storage tanks used during processes. These measures are rarely, if ever, 100% effective, so operators use steps, including filters, to remove microorganisms from the products before they are packaged.

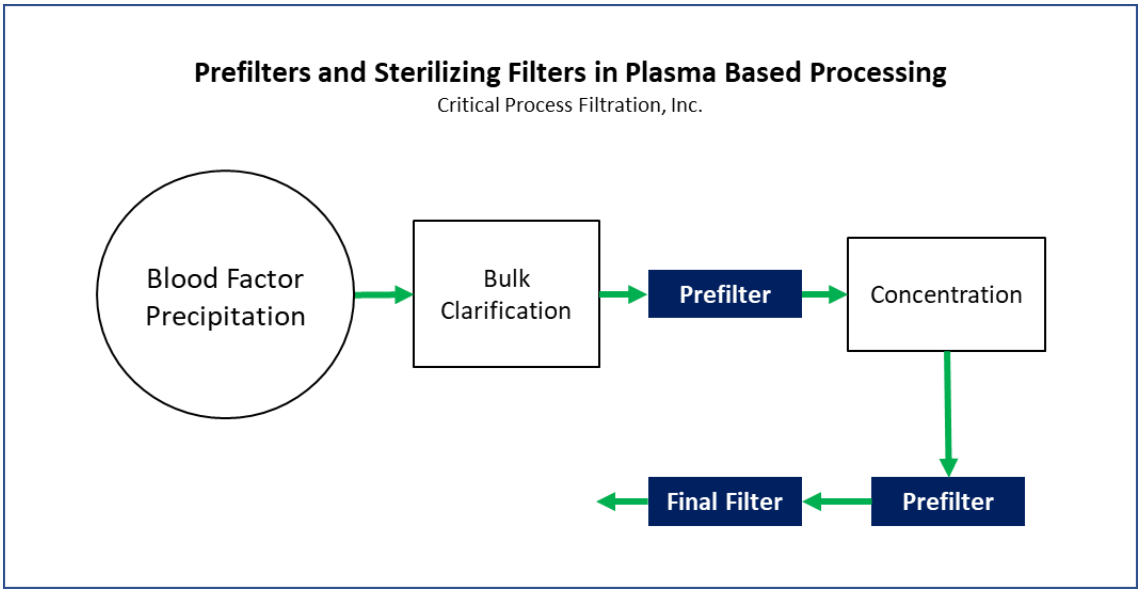


Filter Functions

The abbreviated schematics below show a 'classic' plasma fractionation process based on concentrating the target factors, and a more modern, chromatography-based process. The blue boxes show the locations for the filters that are critical to the removal of bacteria from plasma-based products. There are many possible filter configurations, but these show the two basic functions of prefiltration and sterilizing filtration.

The prefiltration step protects sterilizing filters from being prematurely fouled by microorganisms or particles carried by the fluid stream. If sterilizing filters are fouled, the batch process will be disrupted, which will unnecessarily increase costs and reduce product quality. Depending on the nature and number of particles and microorganisms in the product, operators may choose prefilters based on their ability to remove particles alone, particles and some microorganisms, or particles and most microorganisms before the sterilizing filter.

Removing both particles, and most or all of the microorganisms before the sterilizing filter, may require multiple prefiltration steps. If there are only a few large organisms in the fluid stream (molds, yeasts or other organisms from the environment), then using a depth filter with a larger micron pore size rating will reduce the particle load and capture a sizable portion of the organisms, protecting the final filter. If the microorganisms expected in the fluid stream are smaller or more numerous, then membrane filters with a pore size rating of 0.85 - 0.45 microns may be used.



Choosing the Best Filtration Scenario

Each clarifying or prefiltration application can present unique requirements. Some are as simple as a single step to remove particles. Others can require multiple steps to sequentially filter the process stream to achieve optimal performance and throughput. Another consideration is to incorporate multiple layers into a single pleated module, acting as a built in prefilter. Scenarios are shown on next page.

Single Step Prefiltration

If the filtration goal is to remove particles larger than a specified size, a single filter could be employed as shown below.

Particle removal or clarification is typically accomplished with an appropriately rated depth filter. For larger particles and moderate loading, a melt blown polypropylene or nylon cartridge could be used. Removal of smaller particles and/or fluids with a higher particle load might require a pleated depth filtration media, typically made from polypropylene or fiberglass. The final choice should be based on material compatibility, target flow rate and desired filter life.

Multiple Step Prefiltration

For streams with higher particle loading and a broad range of particle size, multiple prefilter steps may be required. Too large a pore size may allow enough particles through to prematurely foul a downstream filter. Too tight a pore size may lead to the prefilter itself fouling. Installing different filters in series allows each one to handle a portion of the load, resulting in longer run times, improved process efficiency and lower overall cost.

The schematic above shows three prefiltration steps. Some cases may only require two, while some may require even more. Here again it is common to use melt blown or pleated depth filters. Pore size and material will depend on fluid compatibility, particle size distribution, flow rate and expected filter life. The Critical Process Filtration Applications Lab can assist with testing to identify the optimum combination of filters for your process.

Bioburden Reduction

There are two ways bioburden reduction can be incorporated in the prefiltration line. One is to install separate prefilters, and bioburden reduction filters as shown below.

The other is to utilize a bioburden reduction filter with a prefilter layer built into the cartridge.

The main considerations in choosing between the two possibilities are space (there may only be room to install one filter in a process line) and the relative fouling rates of the two layers. If the prefilter fouls before the bioburden reduction layer, it may be more economical to install separate filters so the less expensive prefilter can be replaced independent from the more expensive bioburden reduction filter.

In some cases, it may be sufficient to replace the final sterilizing filter with one incorporating a prefilter layer. This can extend the life of the final filter without the need for installing additional filter housings in an existing line.

Here again consideration must be given to the relative fouling rates of the two filtration layers, and the expected filtration life of the combination.

Choosing the Right Filters

The Critical Process Filtration Technical Services team can assist in evaluating your Prefiltration and Sterilizing Filtration needs, and conduct testing as necessary to identify the optimal solution for your process. Filter recommendations will be made based on fluid compatibility, flow rate requirements, process sanitation/sterilization methods, removal requirements and test data from our Applications Lab.

Conclusion and Summary

There are many opportunities for process optimization by installing the appropriate Prefiltration or Bioburden Reduction filters to extend processing times and reduce the load on expensive final filters. Critical Process Filtration supplies a wide range of filter materials and configurations allowing optimization of your filtration process while minimizing filtration costs. For more information, please contact the Critical Process Filtration Technical Service team.

Cartridge, Capsule & Laboratory Filter Options for Prefiltration and Sterilizing of Plasma-based Products

Prefilter Options

- GDMB (polypropylene spun bond depth filter)
- NSPD (nano-spun polypropylene depth filter)
- PPD (polypropylene pleated depth filter)
- PGD (fiberglass pleated depth filter)
- BCWPS (high capacity PES)

Bioburden Reduction Options

- BPS (PES membrane)
- BNM (Nylon 6,6 membrane)
- BPVWL (hydrophilic PVDF membrane)

Bioburden Reduction with Built in Prefilter

- BPS (PES membrane with High capacity PES prefilter layer)

Sterilizing Filter Options Prefilter (validated for >7-log bacteria removal)

- PPS (Dual layer PES membrane)
- SPS (Single layer PES membrane)
- PNM (Nylon 6,6 membrane)

Sterilizing Filter with Built in Prefilter (validated for >7-log bacteria removal)

- HPPS (PES membrane with High Capacity PES prefilter layer)

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