Application Summary

Prefiltration & Sterilizing Filtration of Plasma Based Products

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Bacteria removal, or sterilizing, is the most critical filter application in all biopharmaceutical operations. It is the final filter most products see before packaging. However, in almost all systems, multiple filter steps are used to assure the reliable, successful performance of this critical function.

All filtration steps prior to the final, sterilizing filter are '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.

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 use barriers to try to prevent them from entering the processes, like the garb worn by plant personnel and cleaning procedures like hand washing. These barriers may also include filters to block microorganisms from entering any storage tanks used during processes. However, the barriers are rarely, if ever, 100% effective, so operators wisely use steps, including filters, to remove microorganisms from the products before they are packaged.

Filter Functions

The abbreviated schematics in Figure 1 show a 'classic' plasma fractionation process based on concentrating the target factors, and a more modern, chromatography based process. The filter housings 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 the microorganisms before the sterilizing filter may require multiple filtration steps.

If there are only a few large organisms in the fluid stream (molds, yeasts or other organisms from the environment), then using a 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 microns, 0.65 microns or 0.45 microns may be used.

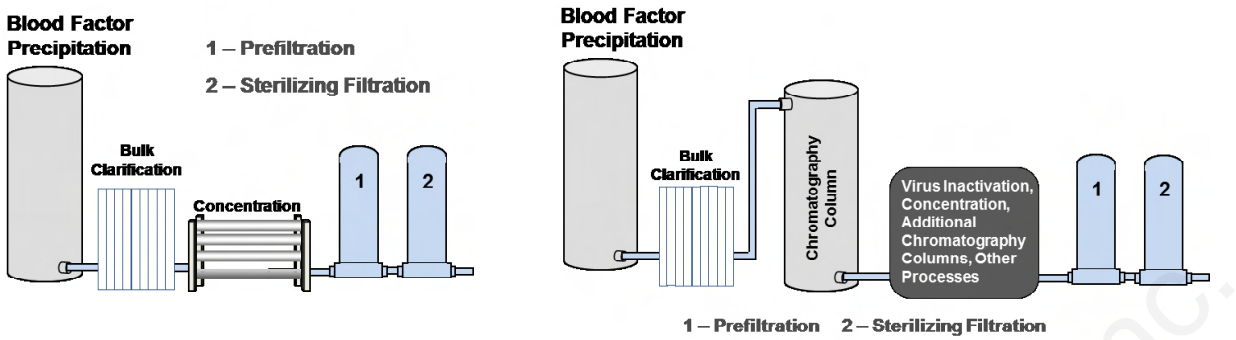

Figure 1: Prefilters & Sterilizing Filters in Blood Fractionation

Sterilizing filters, as the name suggests, remove all bacteria from the fluid stream. They must be validated to do so in the process under worst-case operating conditions. In most cases, the filters are designed to remove bacteria as small as 0.22 microns. In some cases, if smaller organisms like mycoplasma have been detected, filters with smaller pore size ratings will be used.

Choosing the Right Filters

Filters designed primarily for particle removal are usually made using depth media. Pleated depth filters using either polypropylene or fiberglass media are usually used in plasma processing. Filters with a pore size rating of 1 micron or smaller are most often used in these applications. Fiberglass media is preferred for plasma processing because of the high flow rates and low protein binding, plus it is generally more efficient at particle removal than polypropylene media.

Almost all filtration for removing bacteria or other microorganisms is performed by membrane based filters, though some large organisms like molds and yeasts may be removed by high efficiency pleated depth media filters. Membrane filters with low protein binding characteristics and pore size ratings of 0.65 or 0.45 microns are commonly used. Membrane filters are available in materials such as polyethersulfone (PES) or polyvinylidene fluoride (PVDF). These materials have low protein binding characteristics. The nature of the fluid being filtered and the size and number of organisms will dictate the filter material and pore size.

Sterilizing filters all have pore size ratings of either 0.22 microns or 0.10 microns. The 0.10 micron filters are used in applications where the liquid may contain mycoplasma or organisms smaller than almost all bacteria. Polyethersulfone (PES) membrane is low protein binding. Using the PES filter with asymmetric pore structure allows for high flows and minimal effect on product yield.

Filter Options

The filters chosen must be compatible with the fluid being filtered. The organisms targeted for removal also need to be considered. Finally, assure that the filters are designed to function after whatever disinfection or sterilization process will be used.

Critical Process Filtration has several filter options, as shown in the table below. These filters are available as cartridge filters and disposable capsule filters as well is in flat disc form for laboratory scale testing.

Filter Media Options for Bioburden Control and Sterilizing Filtration in API Formulation & Filling

Process Area	Filter Application	Filtration Function	Media **
Prefiltration and Sterilizing	Particle and Large Organism Removal	Remove particles and larger organisms like yeasts and molds	GD, PD
	Bioburden Reduction	Remove most bacteria from the product stream to assure product quality and safety	CWPS, PVWL, PS
	Bacteria Removal (Sterilizing)	Remove all bacteria from the stream	PS

**Media Codes

MB = Melt-Blown Polypropylene Depth Media NS = Nano-Spun Polypropylene Depth Media GD = Pleated Fiberglass Depth Media
PD = Pleated Polypropylene Depth Media CWPS = High Capacity Polyethersulfone (PES) Membrane PS = Polyethersulfone (PES) Membrane
PVWL = High Capacity Polyvinylidene Fluoride (PVDF) Membrane

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