CRITICAL PROCESS FILTRATION, INC.

Buying Guide

Filter Options for Plasma Products

Plasma Products

Blood fractionation processes create plasma-based products such as immunoglobulin, albumin and factor 8. These processes have some similarities to those used in cell-based production of biopharmaceuticals. Biopharmaceuticals are covered in a separate Selection Guide. In both cases, filters are used at almost every step to protect the processes and protect product quality.

The schematic below shows a simplified version of processes using cartridge or capsule filters to create, formulate and package plasma-based products. Some of these filtration steps may be repeated in support of individual processes or between processes, but the basic functions and types of filter media used are similar no matter where the filters are used in the facility.

Two processes are used in this industry. The traditional process uses diafiltration or ultrafiltration to physically separate the molecules in the plasma, then purify the fractions for packaging. More recently, chromatography processes have been developed and have shown higher efficiency and returned higher yields.

1 - Prefiltration
2 - Bioburden Reduction
3 - Sterilizing Filtration
4 - Process Air/Gas Filtration

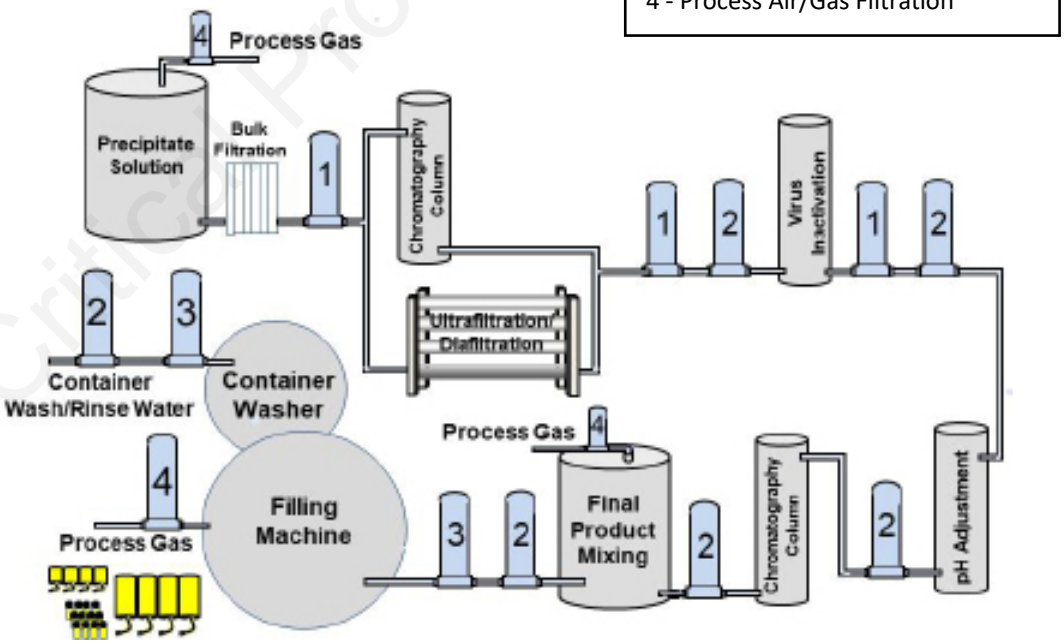


Figure 1: Filtration in Plasma Fractionation

Prefiltration

The goal of prefiltration is to protect downstream filters from premature fouling. It can also be to remove components that can interfere with other processes. Blood, whether from human or animal origin, contains so many proteins, cells, gels and particles that it requires multiple stages of filtration to remove substances that interfere with isolating and purifying the target molecules. Prefiltration, while represented as a single housing in the schematic (housings marked 1), is often a multi-stage process.

There are many possible prefilter configurations. It is possible that a single filter will suffice, with the filter only called upon to remove larger solids (larger than 3 to 5 microns). However, multi-stage prefiltration is more common, and uses filter with progressively smaller pore sizes to remove unwanted components.

Choosing the Right Filters

Larger components, those larger than 1 to 5 microns, are easily removed using depth filtration. Depth media in cartridge filters is available in two forms. Standard depth filters are self-supporting tubes made using a polymer, most often polypropylene, The tube is formed using the melt-blown or nano-spun process.

The other form of depth filter uses pleated flat sheet media, most often made with polypropylene or fiberglass. For blood plasma filtration, fiberglass media is most often used, because of its higher flow rates and throughput relative to polypropylene depth media.

Standard depth filters are rarely used for plasma applications because of the high loading of the plasma. While standard depth media will capture a range of particle sizes through the thickness of the media, the pleated media filters have the advantage of a large surface area that can hold a higher quantity of particles on their surface and have longer life in plasma filtration.

Bioburden Reduction

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 during processing and before they are packaged.

Depending on the nature and number of organisms, operators may choose to remove most of them before sterilizing filtration or remove all of them. The critical bioburden reduction filtration step (housings marked 2) protects processes, including the sterilizing filter, from being fouled by unwanted components, which could unnecessarily increase costs and potentially reduce product quality.

Choosing the Right Filters

Almost all bioburden reduction filtration is performed by membrane based filters, though some large environmental organisms like molds and yeasts may be removed by high efficiency pleated depth media filters.

Cartridge filters using pleated flat sheet media, most often made with fiberglass in plasma operations (as discussed above), can remove organisms as small as 1 micron in size. That can include most molds and yeasts as well as spores such as Bacillus subtilis. Fiberglass flat sheet depth media has better filter efficiency and generally allows higher flows than polypropylene depth media.

Membrane filters for bioburden reduction are available in a number materials with pore size ratings of anywhere from 0.85 microns to 0.22 microns. The nature of the fluid being filtered and the size and number of organisms will dictate the filter material and pore size. The filter material must exhibit low

protein binding characteristics to be effective in plasma fractionation.

It is important to identify the number and size of the organisms that are common in the operation. Then filters of the appropriate pore size can be chosen to assure that enough organisms will be removed to protect processes and the sterilizing filter from excessive loading and premature fouling.

Final Sterilizing Filtration

Bacteria removal, or sterilizing, is the most critical filter application in all life sciences operations (housings marked 3). It is the final filter most products see before packaging. However, sterilizing filtration may be used to protect any process that would be harmed by the presence of bacteria. In almost all systems, multiple filter steps are used to assure the reliable, successful performance of this critical function.

The filtration steps prior to the final, sterilizing filter are discussed above. The 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. The "final" filtration system often includes both prefilter(s) and a sterilizing filter.

Understanding Sterilizing Filters

When a filter is supplied as a "sterilizing grade" filter, it is expected to remove all bacteria, molds and yeasts so that the resulting fluid is "bacteria-free". In the plasma processing industry, this is considered "sterile". The filters are made to comply with industry standards. The most important of these is ASTM International Standard F838-05 - "Standard Test Method for Determining Bacterial Retention of Membrane Filters Utilized for Liquid Filtration". That test challenges the filter to remove at least 100,000 (106) bacteria per ml without any passing through to the product side of the filter. Filters supplied as sterilizing grade are almost always shipped with a "Certificate of Compliance" showing that the filter has been tested using a non-destructive method (integrity test) to assure its quality and state that it will retain bacteria as long as it is installed correctly and remains "integral". Most suppliers also provide a "Validation Guide" in support of the performance claim.

Choosing the Right Filters

All sterilizing grade filters are membrane-based filters with 0.22 or 0.1 micron pore size ratings. Many users install 0.22 micron filters that pass the ASTM test. However, a few organisms, such as mycoplasma and Acholeplasma laidlawii, have been found to pass through these filters under extreme circumstances. Filters with 0.1 micron membranes can be used to remove these smaller organisms, even though their occurrence in actual operating conditions is quite rare.

Membrane filters are available in a number of materials with different pore structures. The filters chosen should be tested rigorously to prove performance in the fluid being filtered under worst case conditions.

Process Air/Gas Filters

Process gas, whether air or inert gas or gas to displace oxygen (like nitrogen or CO2), may also carry particles and organisms. Filters (housings marked 4) are used to remove these potential contaminants from the gas stream and protect the quality of the plasma product.

Choosing the Right Filters

Virtually all gas and tank vent filters in plasma production are hydrophobic membrane with 0.22 micron pore size ratings. These filters are usually considered sterilizing grade, and are supplied with the same quality certification and validation support and filters for liquid applications.

An important note for filters used on tanks - tanks are not made to survive vacuum conditions. If the filter system creates an air flow restriction that results in too much vacuum as a tank is being emptied, then the tank could implode. Tanks have vacuum ratings, and most can, and should, be ordered with vacuum burst discs to prevent total tank failure. Advance planning can prevent burst disc activation or tank failure. Work

with the filter supplier to install the correct size filter system and avoid excessive vacuum.

Filter Options

The filters chosen must be compatible with the fluid being filtered. The particles and 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 Options for Plasma Product Applications

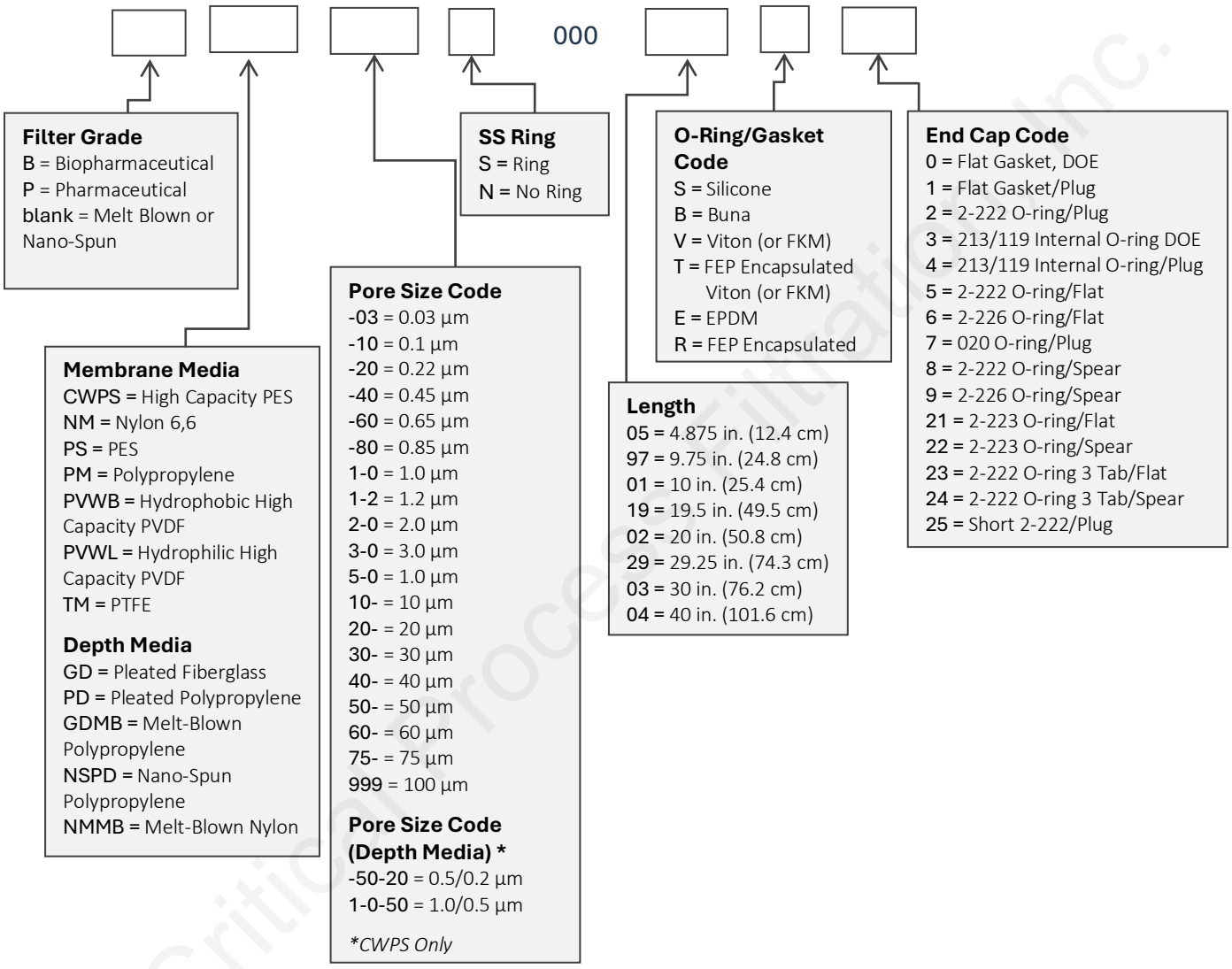
Process Area	Filter Application	Filtration Function	Media **
Ingredient Filtration	Particle Removal and Bioburden Reduction	Removal of larger particles and some larger organisms (molds, yeasts) to protect downstream processes and safeguard product quality	MB, NS, PD, GD
Small Particle and Bioburden Control	Small Particle Removal and Bacteria Reduction	Remove smaller particles (smaller than 1 micron) and reduce/remove organisms. Protect downstream processes. In final filtration systems, protect sterilizing filters from premature fouling by bacteria	PS, NM, PVWL, CWPS
Tank Vent and Process Gas Filtration	Particle and Organism Removal from Air and Process Gas	Prevent bacteria and fine particles in plant atmosphere from contaminating intermediates or product while being held in tanks. Block particles or organisms carried in process gases from reaching processes or product	TM, PM, PVWB
Sterilizing Filtration	Remove All Bacteria and Other Organisms	Remove all bacteria and other cell-based organisms from process fluids or product. May remove mycoplasma. May remove larger viruses.	PS, NM

**Media Codes

MB = Polypropylene Melt Blown Media
NS = Nano-Spun Polypropylene Media
GD = Fiberglass Pleated Depth Media
PD = Polypropylene Pleated Depth Media
CWPS = High-Capacity Polyethersulfone Membrane
PVWB = High Capacity Hydrophobic PVDF Membrane
PVWL = High Capacity Hydrophilic (PVDF) Membrane
PS = Polyethersulfone (PES) Membrane
NM = Nylon 6,6 Membrane
PM = Polypropylene Membrane
TM = PTFE Membrane

Ordering Information

Cartridge order numbers have several variables from grade to media and pore size to end cap type. For example, Pharmaceutical Grade, Polyethersulfone Membrane, 0.22 Micron Rating, with SS Support Ring, 20" Length, Silicone O-Rings, 2-226 O-Ring/Spear End Cap Configuration = PPS-20S00002S9.



Visit our website or contact us for more application information and to access data sheets on all of our products.

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