CRITICAL PROCESS FILTRATION, INC.

Application Summary

Reducing the Bioburden Load in Downstream Biopharmaceutical Processes

Reducing the Bioburden Load in Downstream Biopharmaceutical Processes

While the final, sterilizing filters are considered the most critical filters in the process, the filtration steps that protect them are equally critical. All of the filters in the system must work together to produce a safe, high quality product.

This summary focuses on reducing the number of microorganisms that are in downstream biopharmaceutical process. The filters used do not necessarily remove all microorganisms but must remove at least some to protect either downstream processes or the final, sterilizing filters from contamination.

Every biopharmaceutical operation must deal with a different bioburden load. Because the process itself is based on microorganisms, one of the first upstream process filtration steps is the harvesting of the cells or the removal of the cells from the process stream. There are also upstream processes such as growth media preparation that use filters to reduce or remove microorganisms that might contaminate those solutions. See the companion Application Guide, "Filtration in Preparation of Cell Culture Media and Buffers" for more information on those applications.

In downstream processes, the focus may be on removing organisms that are endemic to the plant environment, like molds and yeasts. They may enter the production system during mixing processes or be carried into the facility by personnel and introduced through normal handling of ingredients and equipment. Depending on the nature and number of organisms, operators may choose to remove most of them before the sterilizing filter or remove all of them. This critical filtration step protects the final, sterilizing filter from premature fouling by organisms that would disrupt batch processing. Process disruption will unnecessarily increase costs and potentially reduce product quality.

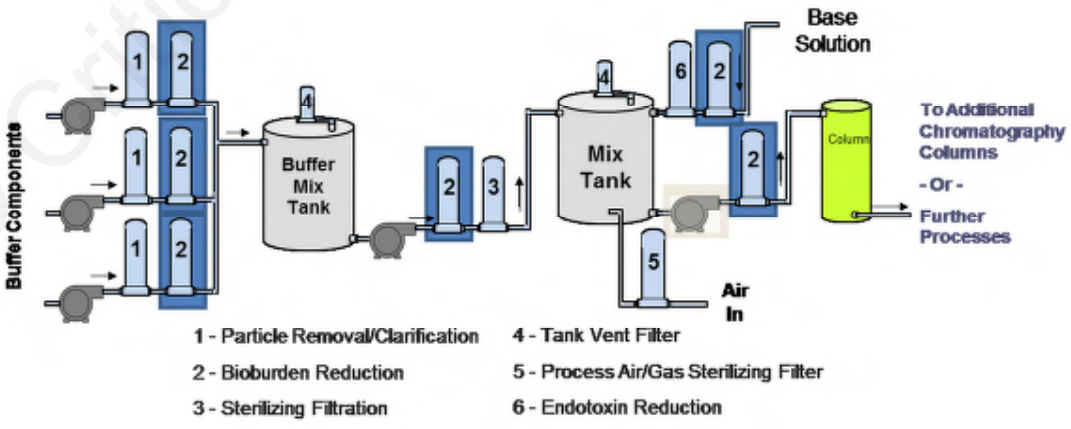

Figure 1: Bioburden Reduction Filters in Downstream Biopharmaceutical Processes

The possible locations of bioburden reduction filters are highlighted in the schematic in Figure 1. There are many other possible filter configurations, but these show the basic functions of bioburden reduction - protecting downstream processes and the preventing excess bioburden from reach and fouling the sterilizing grade filters. This simplified diagram also shows a prefiltration step, usually for larger particle removal, before some bioburden reduction filters, though the two may be combined in some systems.

Choosing the Right Filters

Almost all bioburden reduction filtration is performed by membrane based filters, though some large 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 polypropylene or fiberglass, 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, though polypropylene may be a better choice in some chemical filtration applications.

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. In biopharmaceutical operations, the product itself is usually a form of protein, so filter media with low protein binding properties are best. That usually means polyethersulfone (PES) or polyvinylidene fluoride (PVDF) membranes. Materials like nylon, by their nature, attract and bind proteins, so they are not used in most biopharmaceutical processes.

Generally, a stream with a high load of molds and yeasts will be filtered using pleated depth media. If the fluid contains more bacteria, then a sub-micron rated membrane filter with either a 0.65 micron or 0.45 micron pore size will remove most of the organisms. It is important to identify the number and size of the organisms to be sure that enough will be removed to protect the sterilzing filter from excessive loading and premature fouling.

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 Reduction in Biopharmaceuticals

Process Area	Filter Application	Filtration Function	Media **
Bioburden Reduction	Large Organism Reduction (molds, yeasts)	Reduce the number of large organisms that might foul downstream filters, including sterilizing filters	PD, GD
	Bacteria Reduction	Reduce the number of bacteria in the fluid stream - protect final filters from excessive contaminant loads	CWPS, PS, PVWL

**Media Codes

GD = Pleated fiberglass Depth Media PD = Pleated Polypropylene Depth Media CWPS = High Capacity Polyethersulfone (PES) Membrane
PS = Polyethersulfone Membrane PVWL = High Capacity Hydrophilic PVDF Membrane

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