

Reducing the Bioburden Load in Drug Formulation & Filling

Reducing the Bioburden Load in Drug Formulation & Filling

All of the filtration steps prior to the final, sterilizing filters are considered 'prefiltration'. As discussed in another Application Summary on 'Prefiltration in Small Molecule Drug Formulation and Filling', the prefiltration steps may focus only on particle removal, but that is not usually the case. This summary discusses the use of filters to remove some, but not necessarily all, of the bacteria in a stream before the sterilizing filters.

Every operation has to deal with a different bioburden load. Organisms can be brought into the process with

outside ingredients. Other organisms that may be endemic to the plant environment, like molds and yeasts, may enter the process during the mixing process 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 sterilizing filter from being prematurely fouled by organisms and disrupting batch processing, which would unnecessarily increase costs and potentially reduce product quality.

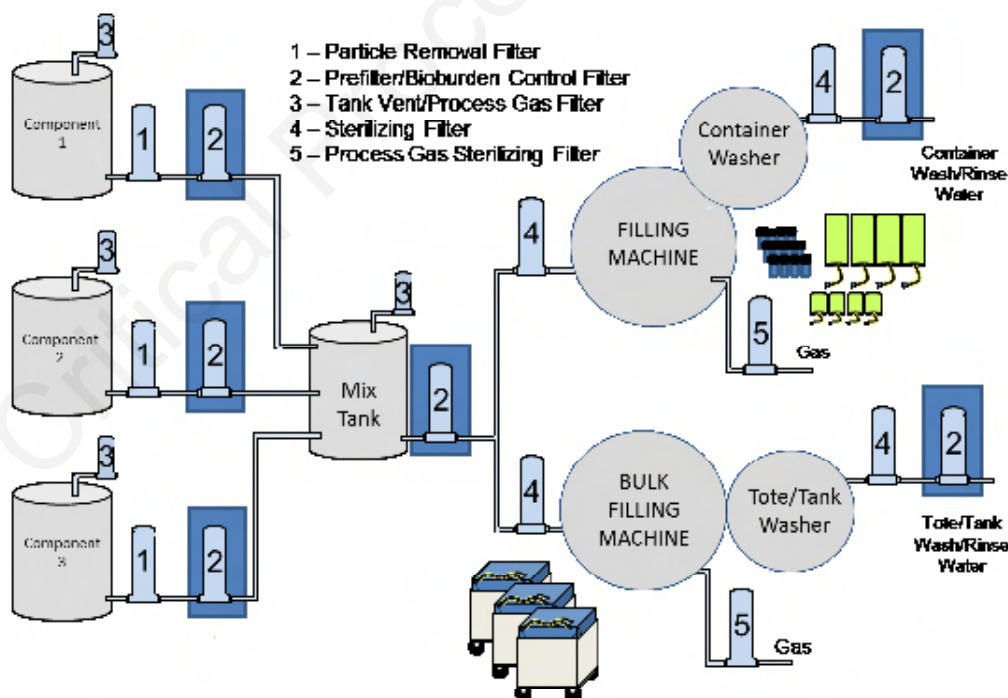


Figure 1: Bioburden Reduction Filters in Small Molecule Drug Formulation & Filling

The abbreviated schematic in Figure 1 shows a few examples of locations for bioburden reduction filters in small molecule drug formulation and filling. There are many other possible filter configurations, but these show the basic function of bioburden reduction - protecting the sterilizing grade filters. This simplified version also shows a prefiltration step before bioburden reduction, though the two may be combined in some systems.

No matter the system configuration, removing at least some of the organisms present is a critical process that protects the critical sterilizing filters downstream. In the example in Figure 1, bioburden reduction is also a possible step just before product mixing, which will improve process efficiency and protect the quality of the final product.

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.

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 sterilizing 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 as in flat disc form for laboratory scale testing.

Filter Media Options for Bioburden Reduction in Small Molecule Drug Formulation & Filling

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, NM, PS, PVWL

**Media Codes

GD = Pleated fiberglass Depth Media PD = Pleated Polypropylene Depth Media CWPS = High Capacity Polyethersulfone (PES) Membrane
 NM = Nylon 6,6 Membrane PS = Polyethersulfone (PES) Membrane PVWL = High Capacity Polyvinylidene (PVDF) Membrane



One Chestnut Street
 Nashua, NH 03060
 603.880.4420
 FAX: 603.880.4536

CriticalProcess.com

The information contained herein is subject to change without notice. The Critical Process Filtration logo is a trademark of Critical Process Filtration, Inc. Viton is a trademark of DuPont Performance Elastomers L.L.C.

© 2025 Critical Process Filtration, Inc. • All Rights Reserved

Application Summary • Reducing the Bioburden Load in Drug Formulation & Filling Rev -