CRITICAL PROCESS FILTRATION, INC.

Application Summary

Prefiltration in Small Molecule Drug Formulation and Filling

Prefiltration in Small Molecule Drug Formulation and Filling

Prefiltration includes the filtration steps just before 'final' or sterilizing filtration in the formulation and filling process for small molecule pharmaceutical production. In most cases, prefiltration is focused on removing solid contaminants. Some operators also include the removal of larger microorganisms, such as molds or yeasts, in the prefiltration process. All prefiltration steps are designed to protect the final filters from excessive amounts of contaminants that could foul the final filters and disrupt batch processing, causing both quality and cost issues.

Each chemical component or raw material used in production has its own unique characteristics. The same is true for mixed solutions, whether intermediates or the final product. Prefilters are chosen based on chemical compatibility and used to assure that the ingredients and intermediates do not contain harmful particulates that could harm downstream processes, including further filtration steps.

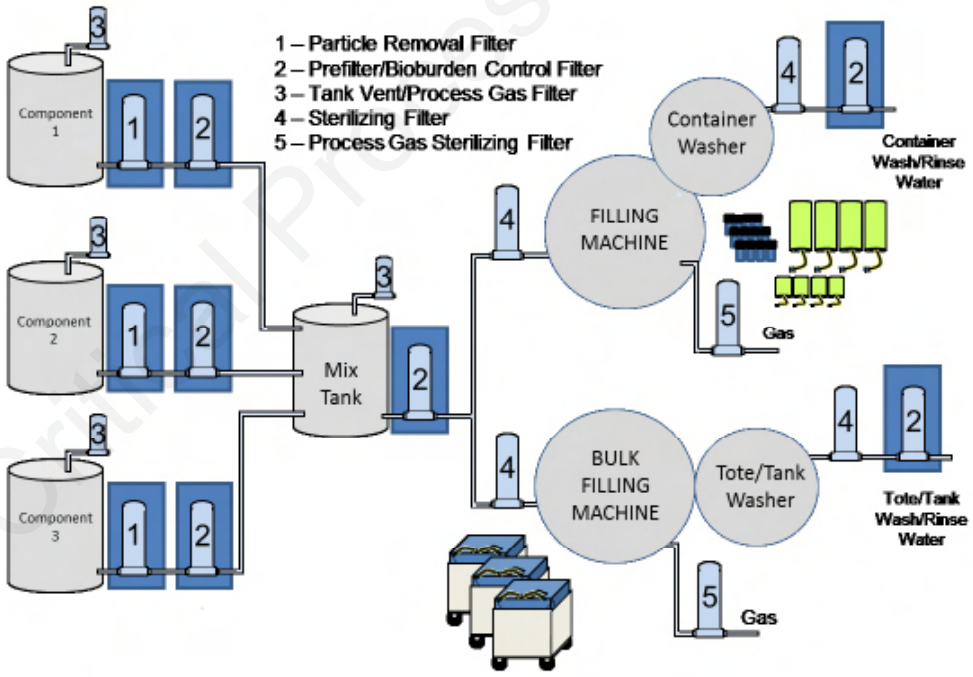

Figure 1: Prefilters in a Small Molecule Drug Production

The filters highlighted in Figure 1 are examples of the possible locations for prefilters in drug production. There are other possible filter system configurations, including systems that include sterilizing grade filters before the final mix tank. This simplified version indicates a 2 stage prefiltration process before the final mix tank, then a single prefilter downstream of the mix tank to protect the final filters used during the filling process.

As discussed in a companion Application Summary on "Choosing the Right Filters for Particle Removal...", particles can be introduced to the process with ingredients from outside sources. Bacteria can also be brought into the process with outside ingredients. Airborne organisms, 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.

Removing these particles and organisms, no matter the source, is a critical process that improves protects downstream filters, improves process efficiency and protects the quality of your final product.

Choosing the Right Filters

Almost all particle removal filtration applications are done using depth filtration media. Cartridge filters use two forms of depth media. The standard depth filter is a self-supporting tube made using a polymer, most often polypropylene. The tube is formed using the melt-blown or nano-spun process.

The other form of cartridge depth filter uses pleated flat sheet media, most often made with polypropylene or fiberglass. Polypropylene is the most widely used material for water and chemical filtration, but fiberglass has better filter efficiency and generally allows higher flows and throughput than polypropylene in prefiltration applications.

Standard depth filters will capture a range of particle sizes through the thickness of the media. Pleated media filters have the advantage of a large surface area that can hold a higher quantity of particles on that surface than the standard depth filters.

If a prefiltration process is also expected to remove at least some bacteria or other organisms, then membrane filters may be used. Pleated membrane filters with pore size ratings of anywhere from 1.0 microns to 0.22 microns have been used as prefilters, depending on the sizes of the particles and organisms that are targeted for removal.

Filter Options

Depth filtration products such as Critical Process Filtration Melt-Blown Polypropylene or Nano-Spun Polypropylene cartridges are commonly used for particulate removal. These products will hold a large quantity of particulates before requiring replacement. Yarn wound filters are another depth filter technology, but seldom utilized in pharmaceutical application due to extractables and particle shedding. Additionally, the superior construction of Critical Process Filtration's Melt-Blown or Nano-Spun filters ensures consistent particle removal unmatched by yarn wound filters.

Depending on the type of particles in the fluid streams, an economical alternative to standard depth filters may pleated media filters. Pleated filtration products, such as pleated polypropylene depth filters, have several times more surface area than melt-blown or nano-spun depth filters and will hold a much higher quantity of particles. Pleated filters do generally cost more, but the increased life in high-particle-load applications and capital savings from reduced number of cartridges required for batch processes may make pleated filters economically advantageous.

Filter Media Options for Prefiltration in Small Molecule Drug Production

Process Area	Filter Application	Filtration Function	Media **
Prefiltration	Particle Reduction	Reduce particulate load to protect performance of downstream water treatment processes	MB, NMMB, NS, PD, GD
	Bacteria Removal (Sterilizing)	Reduce the number of bacteria in the fluid stream - protect final filters from excessive contaminant loads	CWPS, NM, PS, PVWL

**Media Codes

MB = Melt-Blown Polypropylene Depth Media NS = Nano-Spun Polypropylene Depth Media NMMB = Melt-Blown Nylon Depth Media
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 Fluoride (PVDF) Membrane

CRITICAL PROCESS FILTRATION, INC.

One Chestnut Street
Nashua, NH 03060
603.880.4420
FAX: 603.880.4536

CriticalProcess.com