CRITICAL PROCESS FILTRATION, INC.

Application Summary

Ingredients in Small Molecule Drug Production Systems

Ingredients in Small Molecule Drug Production Systems

Ingredients used in the production of small molecule drugs are often from sources outside the direct control of plant operators. In general, system operators treat all ingredients as if they contain at least some form of contamination that might harm production processes and/or product quality.

The biggest issue with ingredients from outside sources is the unknown nature of the possible contamination. Even if the source of the ingredient has a reputation for quality and consistency, operators should guard against all possible scenarios. That means the possibility of unwanted particles, bacteria or other microorganisms and chemical contamination. While cartridge filters cannot address possible chemical issues, they are a cost effective method of controlling and removing unwanted particles and microorganisms. Assuring that the ingredients entering the production process are pure can only help process efficiency and improve product quality.

Filtration Goals

The abbreviated schematic in Figure 1 highlights the filters used for ingredient filtration before the ingredients enter the rest of the production process. These filters are designed to remove particles and microorganisms and also protect the ingredients from environmental contaminants while they are stored in tanks.

There are many possible filter configurations, and the actual filter systems used will be designed to remove the contaminats that are known to occur in specific ingredients. The ones shown perform the basic filtration functions needed to remove contaminants from any ingredients.

The filters highlighted in Figure 1 perform three functions, particle control (filter 1), microorganism and small particle control (filter 2), and tank contents protection (filter 3). A fourth filter may also be used, if ingredient sterilization is desired before a particular process.

Filters for Particle Control

The unwanted particles in any ingredients could be almost any size. Larger particles, those larger than 1 to 5 microns, are easily removed using depth filtration.

Depth media in cartridge filters is found in two forms. The standard depth filter is a self-supporting tube made using a polymer, most often polypropylene, though Nylon is also available from some suppliers. 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 most 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.

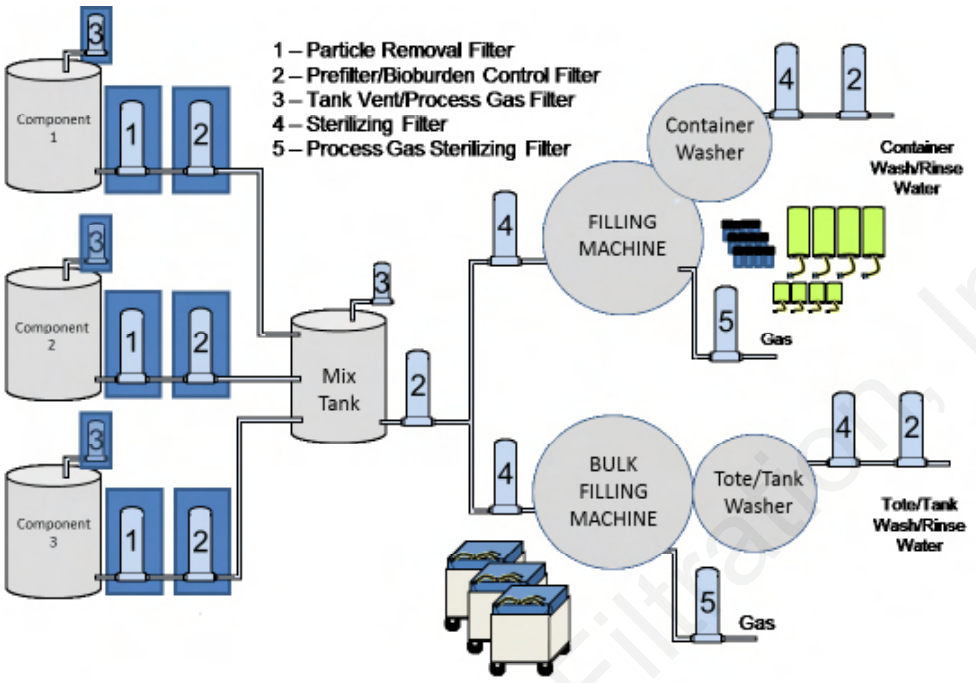

Figure 1: Ingredient Filters in Small Molecule Drug Production Systems

Filters for Bioburden and Small Particle Control

The next level of filtration used for ingredients is to remove smaller particles and some bacteria or other microorganisms. Most of these "bioburden control" filters are based on membranes. The performance requirements for the filters is determined by the level of particle and microorganism purity required by the rest of the process. If the process requires only a reduced bioburden load, then a filter with pore size rating of 0.45, 0.65 or even 0.85 microns might be used, based on the expected level of contamination. However, if a process requires that an ingredient be "bacteria-free", then the filter pore size will probably be 0.22 microns or perhaps 0.10 microns, if mycoplasma control is a requirement.

Tank Vent Filters

The tanks used in production systems, even the tanks made of stainless steel, are not designed to be operated at elevated pressure or under a vacuum. Doing so would cause structural bulging or tank implosion. Therefore, air is allowed to flow into and out of the tank to avoid pressurizing the tank or causing a vacuum condition. As a tank is filled, the air inside is allowed to escape. When the tank is emptied, air (or a process gas such as nitrogen) is allowed to enter the tank to replace lost liquid volume. The air or gas entering the tank is filtered to remove particle and bacterial contamination.

Figure 1 on the previous page shows the tank vent filters (filter 3) on the tops of tanks. These filters, as shown, are used to filter the air directly in contact with ingredients in the tanks. The filters protect those ingredients from microorganisms and particulates in surrounding air.

Filters used for liquid applications are usually made of materials that attract water – are 'hydrophilic' – and allow the easy flow of liquids through the media or membrane with low resistance. For air filtration, it is critical that the media remain dry. If the media

becomes wet and the pores are filled with liquid, then the required air flow is restricted and the pressure or vacuum inside the tank can reach critical levels and cause tank failure. The various media used for air filters are 'hydrophobic' – they repel water – and resist wetting from water vapor.

As with the bioburden control filters, vent filter performance targets are determined by process requirements. Most vent filters are designed to prevent bacteria, molds and wild yeasts from entering the tanks, so the pore sizes are usually 0.22 microns.

Filter Options

The filters chosen must be compatible with the fluid being filtered. The particle sizes 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 Small Molecule Drug Ingredient Filtration

Process Area	Filter Application	Filtration Function	Media **
Particle Control	Remove Larger Particles (1 to 5 micron)	Protect downstream processes and filters from fouling by large particles	MB, NS, NMMB, GD, PD
Bioburden Control	Large Organisms Removal	Remove particles and larger organisms like yeasts and molds	GD, PD
	Bioburden Reduction	Remove most bacteria from the water stream to help meet water quality requirements	CWPS, PVWL, NC, NM, PS
	Bacteria Removal (Sterilizing)	Remove all bacteria from the water stream	PS, NM
Vent Filtration	Particle and Bacteria Removal	Prevent airborne contaminants from reach tank contents	PVWB, TM

**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 Membrane
TM = PTFE Membrane
PVWB = High Capacity Hydrophobic PVDF Membrane
PVWL = High Capacity Hydrophilic PVDF Membrane

CRITICAL PROCESS FILTRATION, INC.
One Chestnut Street
Nashua, NH 03060
603.880.4420
FAX: 603.880.4536
CriticalProcess.com