CRITICAL PROCESS FILTRATION, INC.

Application Summary

Sterilizing Filtration During Small Molecule Drug Formulation & Filling

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All pharmaceutical processes use both "prevention" and "remediation" to control system contamination. Barriers, typically filters, are used to "prevent" bacteria from entering the process, but there are still means by which contamination may occur – system maintenance, raw material addition, etc. This requires additional filters to "remediate" any potential bacterial contamination, removing any organisms and protecting product quality and patient safety. Bacteria removal, or sterilizing, is the most critical filter application in small molecule drug production as it is the final filter most products see before packaging.

In almost all processes, multiple filters are used to both block bacteria from entering ("prevention") and to remove any bacteria that manage to enter the process ("remediation").

Sources of Bacteria

Ingredients brought into a facility may contain bacteria. If a water system is used, the source water (usually a municipality) will almost always carry some bacteria. The plant air itself, even in cleanrooms, will have airborne bacteria. Since each location has different environmental conditions, every pharmaceutical operation has to deal with different bacteria. Most small molecule drug production processes are based on chemistry, so the environment for bacteria may be harsh. That sounds like a good thing, but there are many examples of bacteria adapting and even thriving in harsh environments, so operators will act as though bacteria are present in every fluid.

Measures taken to prevent bacteria from entering the process include the garb worn by plant personnel and cleaning procedures like hand washing. Those preventive measures also include filters to block bacteria from entering storage and mix tanks (housings marked "3" in the diagram) or being carried into the system by process gases (housings marked "5"). However, as mentioned above, preventive measures are rarely, if ever, 100% effective, so operators wisely use remediation steps, including filters, to remove microorganisms from the production stream. The most critical of these filters are the sterilizing filters used just before packaging.

Sterilizing Filters

The abbreviated schematic in Figure 1 shows the most common locations for sterilizing filters (housings marked "4"). There are other possible filter locations. For example, sterilizing filters might be placed just before mix tanks or other processing steps if the operators determine that the process should be bacteria free.

Depending on the nature and number of organisms, operators may choose to remove most or all of them before the sterilizing filter. The critical bioburden control filtration step (housings marked 2) protects processes as well as protecting sterilizing filters from being prematurely fouled by organisms. Fouled sterilizing filters will disrupt batch processing, unnecessarily reduce process efficiency and increasing costs. Read more about bioburden control in the Application Summary "Reducing the Bioburden Load in Drug Formulation & Filling".

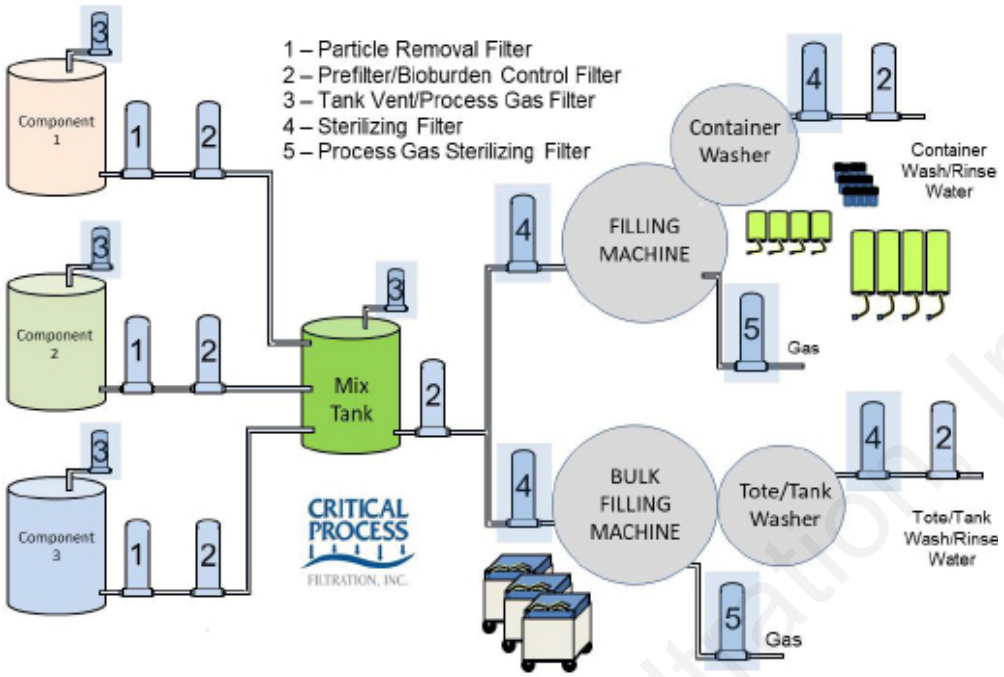

Figure 1: Sterilizing Filters in Small Molecule Drug Formulation & Filling

Choosing the Right Filters

All sterilizing filtration is performed by membrane based filters with pore size ratings of either 0.22 microns or 0.10 microns. The 0.10 micron filters are used in applications where the liquid may contain mycoplasma or organisms smaller than almost all bacteria.

Filters chosen for sterilizing must pass the ASTM F-838-05 test for retention of bacteria. The test challenges the filters to retain bacterial loads far more than any that will be found in pharmaceutical manufacturing operations. The extra margin of safety demonstrated by the filters gives operators confidence in the performance of the filters, as long as they remain "integral" during operation, meaning that their use does not damage them and create gaps through which bacteria can pass.

All filter manufacturers provide "validation guides" for sterilizing filters that show test results and other information regarding filter construction, biosafety and performance.

Filter Options

The filters chosen must be compatible with the fluid being filtered. The organisms targeted for removal also need to be considered. Filters must be designed to function after whatever disinfection or sterilization process will be used.

Critical Process Filtration provides multiple 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 Sterilizing Filtration During Small Molecule Drug Formulation & Filling

Process Area	Filter Application	Filtration Function	Media **
Bioburden Control and Sterilizing	Bioburden Reduction	Remove most bacteria from the fluid stream to help meet water quality requirements	CWPS, PVWL, PS
	Bacteria Removal (Sterilizing)	Remove all bacteria from the fluid stream	PS, NM
	Tank Vent Filtration	Prevent bacteria from entering tanks when liquid is drawn from them. Remove bacteria from process gas.	PVWB, TM

**Media Codes

CWPS = High Capacity PES Membrane NM = Nylon 6,6 Membrane PS = Polyethersulfone Membrane

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

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