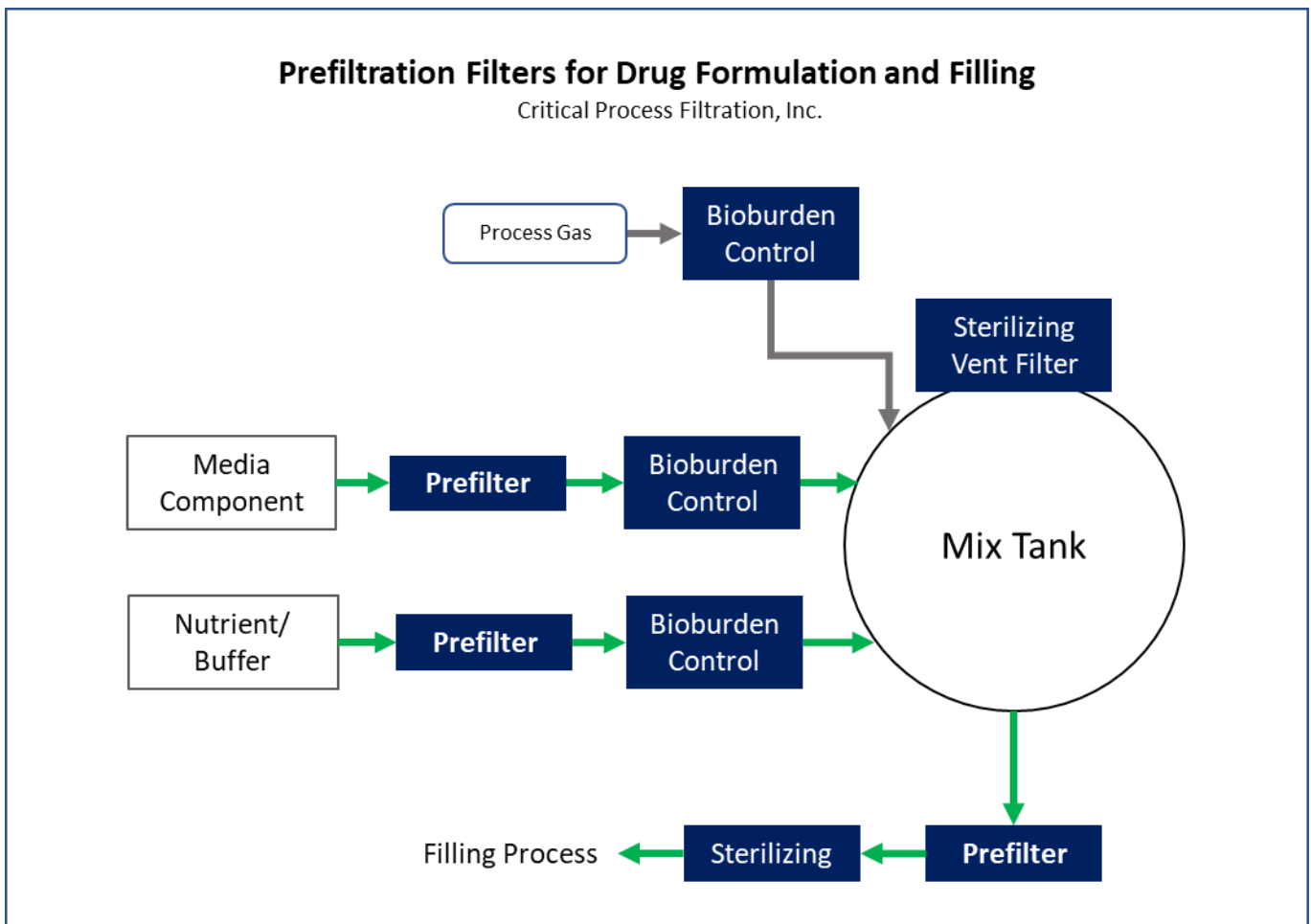


Prefiltration in Drug Formulation and Filling

When it comes to filtration, the final formulation and filling steps for both pharmaceutical and biopharmaceutical drug manufacturing processes are similar. Multiple filters are used to ensure cleanliness and sterility of the process. The diagram below shows typical filtration steps in a formulation and filling process. In a biopharmaceutical process the purified

product from the bioreactor is one of the media components. This report focuses on the proper selection of Prefiltration filters to ensure optimized process performance. While the schematic shows two component streams feeding the mix tank, many processes require additional feed streams, each with potentially unique filtration requirements.



What is Prefiltration?

The act of improving the efficiency of primary function filters by placing a prefilter before them. The prefilter removes contaminants that clog the function filter and render it less efficient. By incorporating less expensive prefilters the function filters last longer and [overall costs are reduced](#). Types of prefilters vary based on the primary function, size and type of contaminants, fluid quantity, required throughput, and sterilization & sanitization process.

Clarification Prefilter – removes contaminants (1 micron or even less) and visual elements that cause haze in the fluids that could affect process efficiency or product quality.

Particulate Prefilter – removes larger particles (> 5 micron) that may be present in raw material streams.

Bioburden Control Prefilter – more critical steps could require Prefiltration that also acts as bioburden reduction - removing most, but not necessarily all bacteria.

Sterilizing Prefilter – can be a Clarification or Bioburden Control Prefilter depending on what is being filtered just before the final filters (endotoxins or bacteria).

The primary functions that benefit from Prefiltration are Bioburden Control and Sterilizing.

Why Use Prefilters?

The main goal of filtration in these processes is to ensure that all unwanted contaminants are removed from the product - especially bacteria. Prefilters are the work horses that protect expensive final filters from fouling, extending their life and minimizing overall filtration costs. A robust process risk assessment will help identify process steps where appropriately placed prefilters can increase process efficiency and lower overall cost of filtration.

Clarification & Particle Removal Prefiltration

Each prefiltration application can present unique requirements. Some are as simple as a single step to remove particles. Others can require multiple steps to sequentially filter the process stream to achieve optimal performance and throughput. Another consideration is to incorporate multiple layers into a single pleated module, acting as a built in prefilter.

Single Step Prefiltration

If the filtration goal is to remove particles larger than a specified size, a single filter could be employed as shown below.



Particle removal or clarification is typically accomplished with an appropriately rated depth filter. For larger particles and moderate loading, a melt blown polypropylene or nylon cartridge could be used. Removal of smaller particles and/or fluids with a higher particle load might require a pleated depth filtration media, typically made from polypropylene or fiberglass. The final choice should be based on material compatibility, target flow rate and desired filter life.

Multiple Step Prefiltration

For streams with higher particle loading and a broad range of particle size, multiple prefilter steps may be required. Too large a pore size may allow enough particles through to prematurely foul a downstream filter. Too tight a pore size may lead to the prefilter itself fouling. Installing different filters in series allows each one to handle a portion of the load, resulting in longer run times, improved process efficiency and lower overall cost.



The schematic above shows three prefiltration steps. Some cases may only require two, while some may require even more. Here again it is common to use melt blown or pleated depth filters. Pore size and material will depend on fluid compatibility, particle size distribution, flow rate and expected filter life. The Critical Process Filtration Applications Lab can assist with testing to identify the optimum combination of filters for your process.

Bioburden Reduction & Sterilizing Prefiltration

There are two ways prefilters can be incorporated in the process line. One is to install separate prefilters, the other is to integrate a prefilter layer into the filter.



Integrated Prefilter Options

The main considerations in choosing between the two possibilities are space (there may only be room to install one filter in a process line) and the relative fouling rates of the two layers. If the prefilter fouls before the bioburden reduction layer, it may be more economical to install separate filters so the less expensive prefilter can be replaced independent from the more expensive bioburden reduction filter.



In some cases, it may be sufficient to replace the final sterilizing filter with one incorporating a prefilter layer. This can extend the life of the final filter without the need for installing additional filter housings in an existing line.



Here again consideration must be given to the relative fouling rates of the two filtration layers, and the expected filtration life of the combination.

Choosing the Right Filters

The Critical Process Filtration Technical Services team can assist in evaluating your Prefiltration needs, and conduct testing as necessary to identify the optimal solution for your process. Filter recommendations will be made based on fluid compatibility, flow rate requirements, process sanitation/sterilization methods, removal requirements and test data from our Applications Lab.

Conclusion and Summary

There are many opportunities for process optimization by installing the appropriate Clarification, Prefiltration or Bioburden Reduction filters to extend processing times and reduce the load on expensive final filters. Critical Process Filtration supplies a wide range of filter materials and configurations allowing optimization of your filtration process while minimizing filtration costs. For more information, please contact the Critical Process Filtration Technical Service team.

Cartridge, Capsule & Laboratory Filter Options for Prefiltration in Formulation and Filling

Clarifying and Particle Removal Options

- GDMB (polypropylene spun bond depth filter)
- NSPD (Nano-spun polypropylene depth filter)
- PPD (polypropylene pleated depth filter)
- PGD (fiberglass pleated depth filter)
- BCWPS (high capacity PES)

Bioburden Reduction Options

- BPS (PES membrane)
- BNM (Nylon 6,6 membrane)
- BPVWL (PVDF membrane)

Bioburden Reduction with Built-in Prefilter

- BPS (PES membrane with High capacity PES prefilter layer)

Sterilizing Filter with Built in Prefilter (validated for >7-log bacteria removal)

- HPPS (PES membrane with High Capacity PES prefilter layer)

Additional Application Summaries on Filtration in Pharmaceutical & Biopharmaceutical Processes

- [Sterilizing and Bioburden Reduction Filtration in Biopharmaceutical Processes](#)
- [Filter Use for Bioburden Reduction and Sterilization in Drug Formulation and Filling](#)
- [Tank Vent and Process Gas Filters for Pharmaceutical and Biopharmaceutical Production](#)



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