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Preparation, Separation,
Filtration & Monitoring Products

Tech Note

Improved Product Recovery using Blow-down and Millipak® Final Fill Filters

Summary

For manufacturers of parenteral products, maximizing product recovery during final sterile filtration is key to achieving process efficiency as loss of even a few milliliters of formulated product can translate to thousands of dollars in lost revenue. The objective of this study was to compare hold-up volumes of sterilizing-grade pleated membrane filters with those of Millipak® Final Fill stacked disc filters following filter drain by gravity and air blow-down.

Implementation of a filter blow-down was shown to reduce hold-up volume for both pleated and stacked disc filters, but for any given filter membrane area, the stacked disc format of Millipak® Final Fill filters resulted in lowest hold-up volume and highest product recovery. This combination of stacked disc filter format and blow-down procedure markedly improves product recovery, which translates to substantial economic benefits for production processes.

Introduction

Final sterile filtration of formulated parenteral products is performed late in production in a highly controlled aseptic environment; the safety of these products for administering to patients relies on successful sterile filtration.

While filter membrane selection is based on compatibility with the process fluid as well as the unique needs of the manufacturer, the filter format will have a direct impact on product recovery and process yield. After processing, liquid is retained between membrane layers and in filter connections; this is referred to as hold-up volume and is effectively non-recoverable product.

Millipak® Final Fill filters were designed to minimize hold-up volume and contain membrane discs stacked in a capsule housing, rather than the pleated membrane format of more traditional filters. In this application note, we compare hold-up volume of both pleated and stacked disc filters and highlight the benefits of filter blow-down for maximizing product recovery. Hold-up volumes of pleated filters containing sterilizing-grade polyethersulfone (PES) and polyvinylidene fluoride (PVDF) membranes were compared with those of Millipak® Final Fill stacked disc filters containing Durapore® 0.22 µm PVDF membrane.

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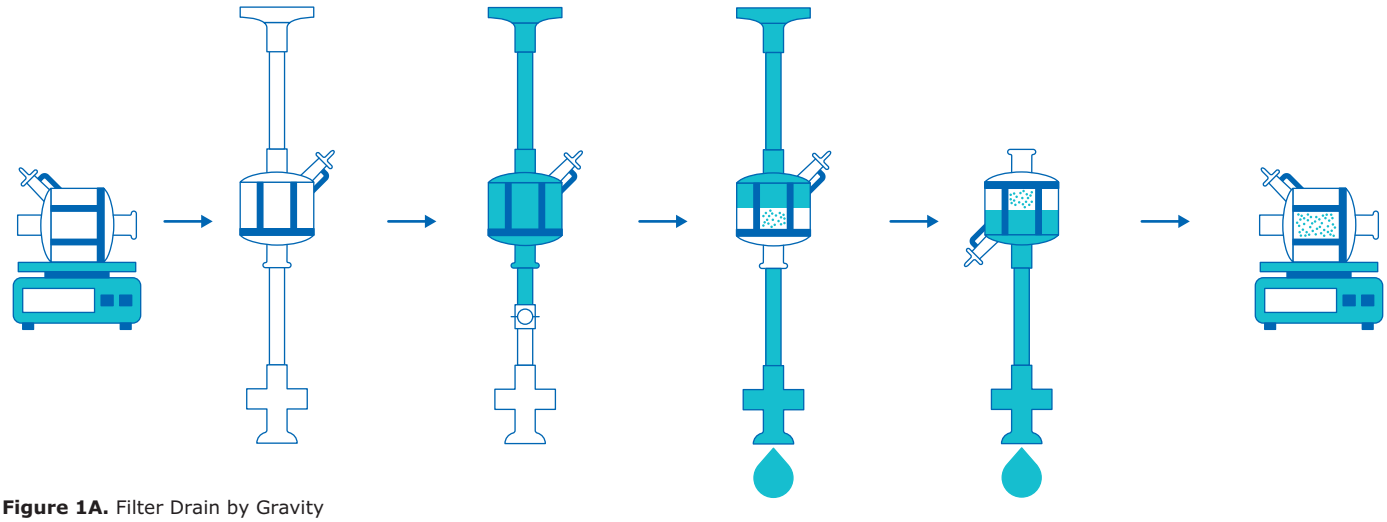

Figure 1A. Filter Drain by Gravity

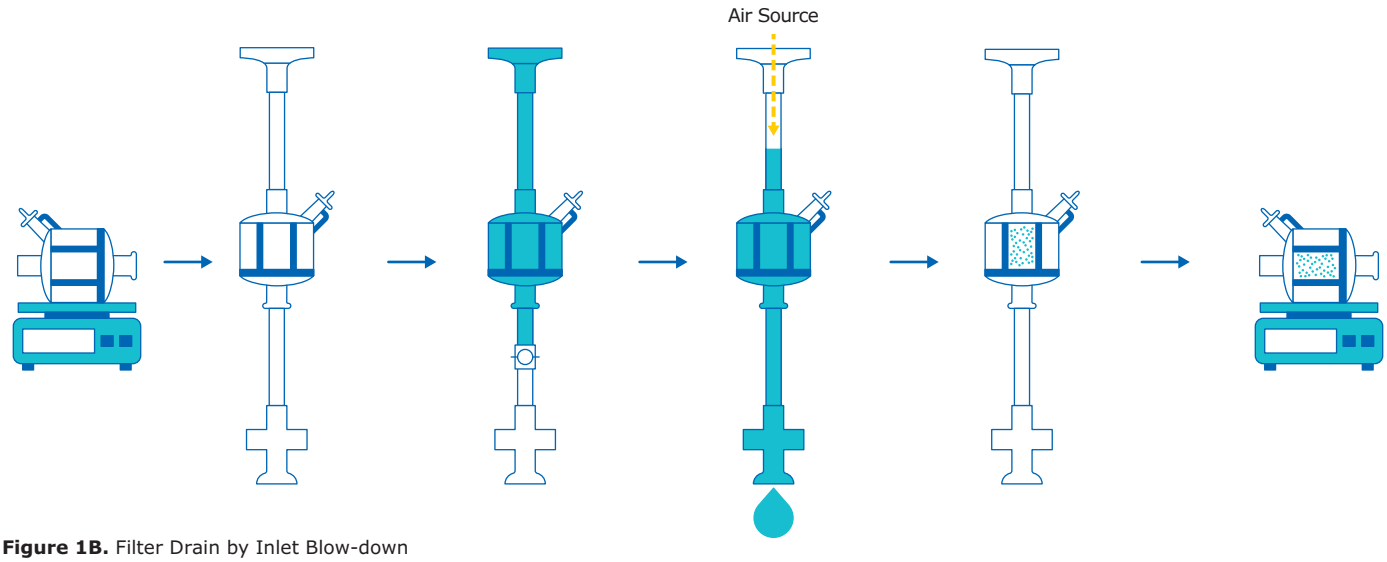

Figure 1B. Filter Drain by Inlet Blow-down

Experimental Methods

The hold-up volumes of a range of market-leading commercially available capsule filters containing pleated PES and PVDF 0.2 µm or 0.22 µm sterilizing-grade membranes were compared after filter draining or blow-down. The hold-up volumes of pleated capsule filters were compared to Millipak® Final Fill filters following blow-down. A minimum of three replicate filters were tested for each condition and in all tests, the hold-up volume was the difference in weight between the drained filter and the dry weight of the filter.

Filter drain hold-up volume was determined by weighing each dry unit then filling the filters with water. Fittings were removed so the liquid downstream of the filters could drain by gravity. Filters were then inverted to allow upstream liquid to clear, and the drained filters were weighed, Figure 1A.

The hold-up volume following blow-down was determined after connecting an air source to the inlet of pre-wet filters and applying pressure to exceed the bubble point specification of each filter by 20 psi for one minute, Figure 1B. After blow-down, the filters were disconnected and weighed.

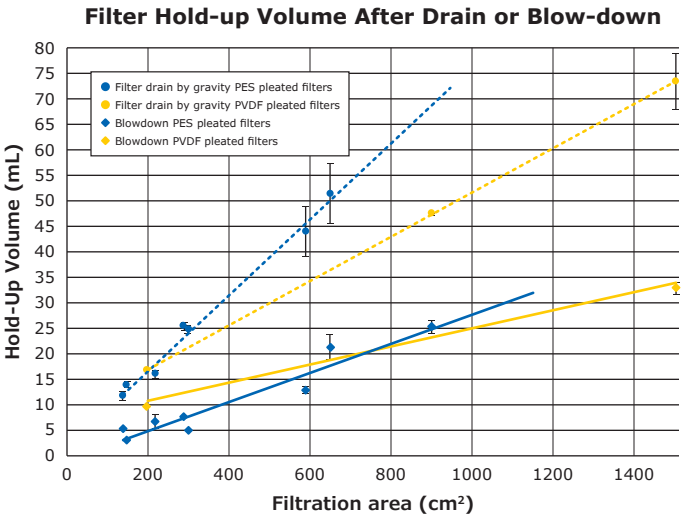

Figure 2. Mean hold-up volume of pleated PES (shown in blue) and PVDF (shown in yellow) filters following a filter drain (dashed lines) or a 1-minute blow-down with air at 20 psi above the filter bubble point specification (solid lines). Each value represents the mean and SD from three replicate filters.

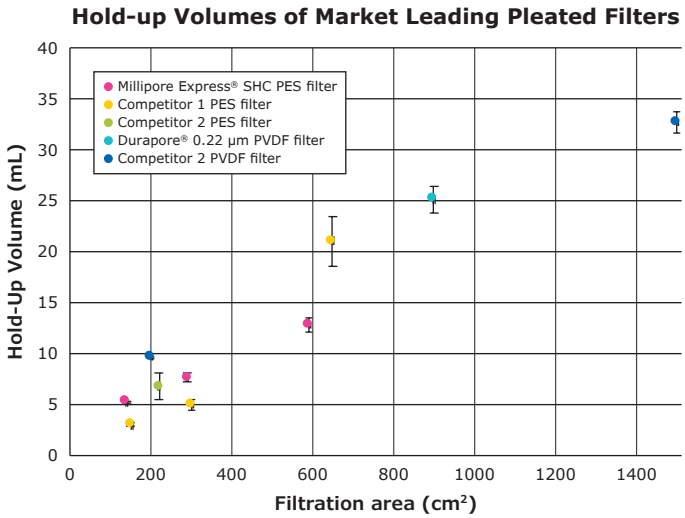

Figure 3. Mean hold-up volume of pleated PES and PVDF filters following a 1-minute blow-down with air at 20 psi above the filter bubble point specification. Each value represents the mean and SD from three replicate filters.

Results & Discussion

Benefits of blow-down

It is not surprising that filter hold-up volume is dependent on the method of draining: more liquid will be removed if the filter is blown-down with air than simply allowed to drain by gravity. Figure 2 shows the hold-up volumes of pleated filters following a gravity drain and following blow-down at 20 psi above the filter's bubble point specification for 1 minute.

For both PES and PVDF pleated filters, across all filtration areas, blowing the filter down with air at pressures above the bubble point of the membrane reduced the hold-up volume in the filters, and resulted in markedly improved liquid recovery as compared to filter drain.

Figure 3 compares the hold-up volume from pleated capsule filters containing Millipore Express® SHC PES membrane with market-leading PES filters, and pleated capsule filters containing Durapore® 0.22 µm PVDF membrane with market-leading PVDF filters. In all cases, hold-up volume was determined after a 1-minute blow-down with air at 20 psi above the filter's bubble point specification.

Filter hold-up volume of the filters after blow-down was most closely related to filtration area and no meaningful difference related to membrane composition or filter manufacturer was identified. Figure 4 shows the hold-up volumes of the stacked disc Millipak® Final Fill filters following blow-down above the filter's bubble point specification, overlaid on the hold-up volumes of the pleated filters presented in Figure 3. For simplicity, pleated filters are grouped by filtration area, irrespective of filter manufacturer or membrane composition.

After blow-down, Millipak® Final Fill filters have substantially lower hold-up volumes than pleated filters for a given filtration area. Although this differential is particularly noticeable with larger filtration areas, the hold-up volumes of smaller area filters is 1.5-5 times higher for pleated filters than for Millipak® Final Fill filters.

These results illustrate the benefits of a higher-pressure blow-down but it is also possible to reduce filter hold-up volume in constant flow operations. If the pump could run dry following processing, the volume upstream of the filter would be minimized, reducing hold-up and improving recovery.

In summary, blowing down a filter with air reduces hold-up volume for both pleated and stacked disc filters. When this practice is implemented, the hold-up volume of Millipak® Final Fill stacked disc filters is substantially lower than that of pleated filters across all filtration areas.

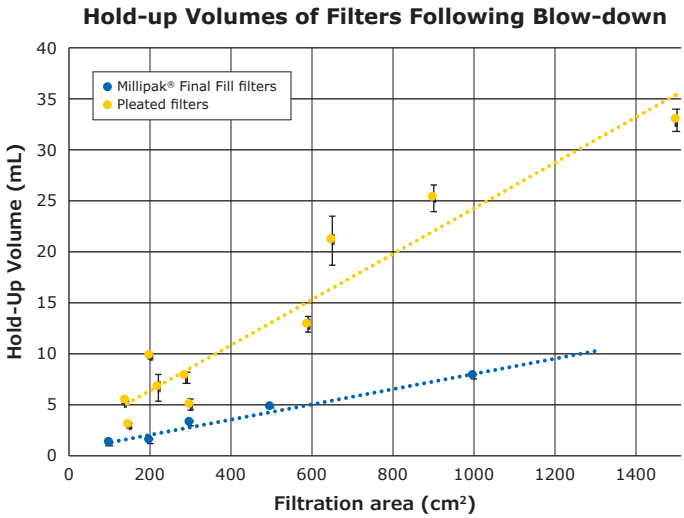

Figure 4. Mean hold-up volume of pleated filters compared to Millipak® Final Fill filters following a 1-minute blow-down with air at 20 psi above the filter's bubble point specification. Each value represents the mean and SD from three replicate filters.

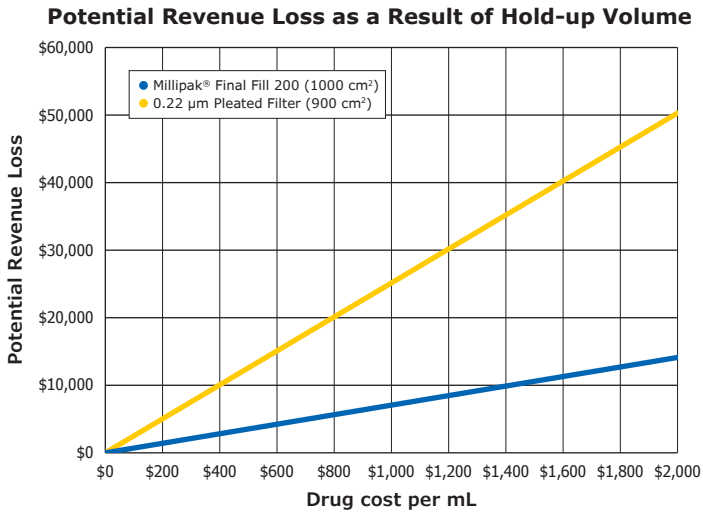

Figure 5. Comparison of revenue impact to manufacturer for parenteral products at different price points due to hold-up volume (after blowdown) in PVDF pleated filters (~900 cm²) and Millipak® Final Fill 200 filters (~1000 cm²).

Less Hold-up Means Improved Economics

Although blow-down procedures improve product recovery for both pleated and stacked disc filters, this added step has profound benefits with Millipak® Final Fill stacked disc filters, especially when comparing larger area filters or higher value products. Figure 5 illustrates the potential revenue impact for parenteral products at different price points. All costs are based on product recovery following blow-down for 1 minute at 20 psi above the filter's bubble point specification.

The economic benefits of reduced hold-up volume and improved product recovery scales with the dollar value of the parenteral products being processed. As the cost of the product increases, the benefit differential between filter formats also increases, with maximum benefit of Millipak® Final Fill stacked disc filters aligning with high value products.

Conclusions

The specialized format of Millipak® Final Fill filters is designed to minimize hold-up volume as compared to standard pleated filters, resulting in improved product recovery. Implementation of a filter blow-down minimizes hold-up volume for both pleated and stacked disc filters. For any given filter membrane area, the stacked disc format of Millipak® Final Fill filters results in the lowest hold-up volume and highest product recovery. The combination of stacked disc filter and filter blow-down markedly improves product recovery, which for high value medicinal products, translates to substantial economic benefits for production processes.

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