Application Note

Technical Application Publication

The role of prefiltration in the optimization of bioprocess filtration systems

Summary

Filtration is commonly used in biopharmaceutical manufacturing in order to control bioburden within the production process. Filtration costs within manufacturing facilities can be optimized by the appropriate use of prefilters.
A correctly selected and sized prefilter positioned upstream of a sterilizing grade or bioburden control filter can significantly reduce the required area of these membrane filters. The cost of operating a prefilter and sterile filter with a low membrane area is generally less than the cost of operating high membrane area sterile filters without an upstream filter.

Through a structured application led application, Parker domnick hunter can work with you to develop optimized filtration solutions for your process.

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Key filtration requirements:

- High throughput
- High capacity
- Minimum system size
- Minimum Cost

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Prefiltration medias and their applications

Prefilters suitable for use in biopharmaceutical applications can contain different types of filtration media. The appropriate media to use will depend on the application. Typical prefiltration media are described in Table 1 along with their properties and when they should be used.

Filter media	Polypropylene	Glass fibre	Dual layer glass fibre / polypropylene
Media properties	High physical robustness	High capacity	Greatest retention of solid particles
	Compatible with a broad range of chemicals	Less chemically resistant and physically robust than polypropylene	High capacity
	Typically inert	Interactions with products sometimes observed	Chemically resistant and physically robust
When to use ?	Use for aggressive solutions such as solvents, buffers and pH adjustment solutions when capacity is not an issue	Use when high capacity is a priority such as cell and precipitant removal steps	Use in situations when a high level of protection of downstream membranes is required

Table 1

Optimization of two stage filtration systems

Use of a prefilter to optimize the sterile filtration of a serum containing solution

The following case study illustrates the importance of prefiltration in designing a cost-effective sterilizing filtration system for a viscous, serum-containing biologic solution. The lower line in Figure 1 shows filter sizing data at constant flow for the high capacity, sterilizing-grade PROPOR HC membrane filter. A single 10" capsule would only be able to process half the batch. Doubling the filtration capacity would enable the entire batch to be processed, however, this would be an expensive solution.

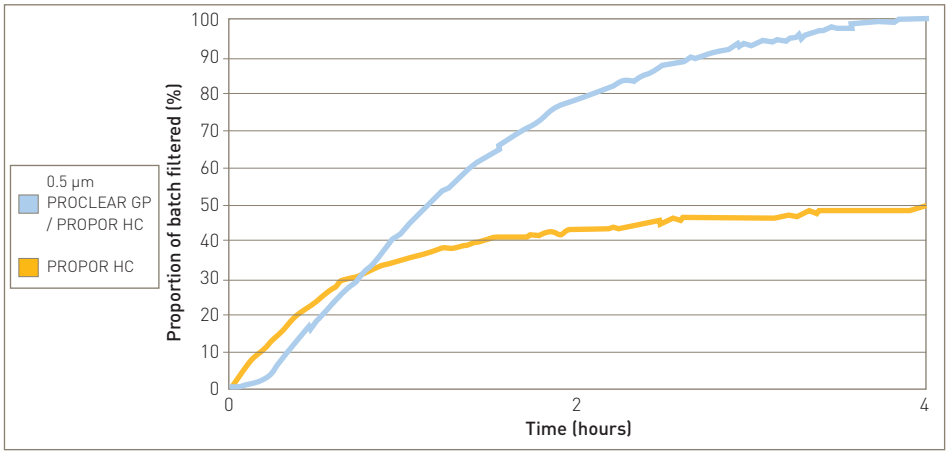

Figure 1 - Filter sizing data showing the proportion of a batch of a serum containing biologic solution that can be sterilized using a 10" sterilizing-grade PROPOR HC capsule filter with and without a PROCLEAR prefilter.

The upper line in Figure 1 is filter sizing data for the same PROPOR HC membrane but with the PROCLEAR GP prefilter operated upstream of the sterilizing-grade filter. The PROCLEAR GP combines glass microfibres with polypropylene to achieve both high capacity and physical robustness. The results show that a single 10" PROPOR HC capsule can be used to filter the entire batch if a 10" PROCLEAR GP capsule is used as a prefilter. This solution is approximately 25% more cost effective than doubling the sterile-filtration membrane area as shown in Figure 2. In many cases prefiltration will protect the membrane filter to a greater extent than in this example, thereby magnifying the cost savings available to manufacturers.

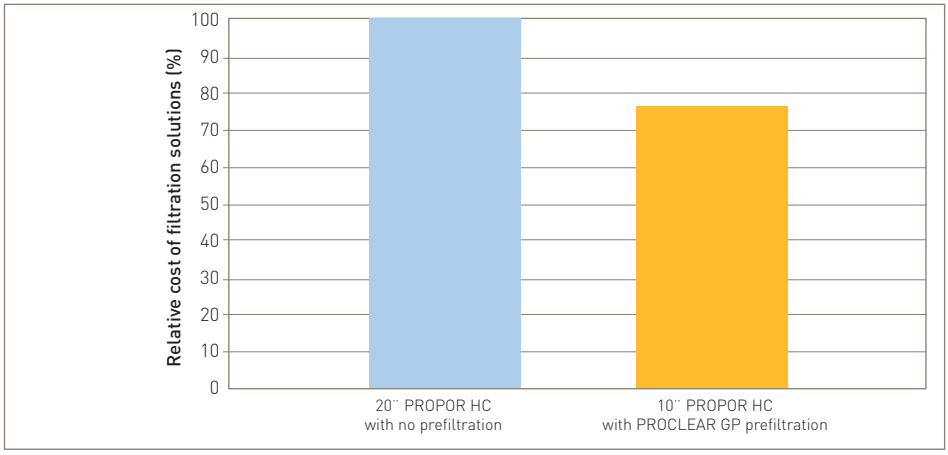

Figure 2 - Relative cost of filter sterilizing and entire batch of a serum containing biologic solution using either a 20" PROPOR HC capsule or a 10" PROPOR HC with an upstream PROCLEAR GP prefilter.

This case study illustrates the savings in filtration costs that can be achieved by using prefiltration to optimize sterilizing and bioburden controlling filtrations in the biopharmaceutical industry. Where filter cartridges are being used instead of single-use capsules the cost of installing additional filter housings needs to be considered. Manifolding together an extra single-use capsule can require additional labour in the facility, however, suppliers are able to manifold complete filtration systems together prior to delivery allowing biomanufacturers to eliminate these non-value adding activities.

Sizing prefilters

Recommended approach for sizing prefilters in biopharmaceutical process

Sizing prefilters can be a difficult and time consuming activity due to the large number of variables and parameters to be optimized. Filtration suppliers are often happy to provide technical support scientists to conduct experiments on behalf of customers.

The following points provide some recommendations for the sizing of filtration systems that incorporate prefilters.

1. Establish the requirement for prefiltration by first sizing the downstream membrane filter.

2. Where possible gather information about the properties of the process stream by collating all existing relevant data and by performing experiments to determine the concentration and particle size of particulates and the viscosity of the process solution.

3. Select likely prefilter media based on the properties of the process stream and whether retention, compatibility or capacity is likely to an issue.

4. Based on previous knowledge and process stream analysis select the prefilter grades you expect to be most effective at protecting the membrane filter. A 0.2 micron filter is likely to require a prefilter with a micron rating of 0.5-0.6 microns, a high-capacity membrane filter with integral prefiltration layer is likely to benefit from a prefilter with a more open pore structure.

5. Use the constant flow sizing method to compare the capacities of the grades selected and retain the filtrate to allow re-sizing of the downstream membrane filter. (Constant pressure filtration can be used for prefiltration screening but use low pressures in the range of 5-10 psig to mimic likely operating conditions).

6. Additional prefiltration stages should be considered for process fluid with a high solids content. In these cases an initial coarse prefilter that provides high solids-holding capacity followed by a finer secondary stage to protect membrane filtration can provide a cost effective solution.

7. Confirm the results at larger-scale using a pleated format to give greater confidence in the performance at the final scale.

8. Once the results are confirmed then scale-up to the production scale.

Conclusion

The use of prefilters to reduce total filtration costs in the manufacture of biopharmaceuticals can be easily demonstrated. Prefilter medias should be selected based on the properties of the process stream to be filtered. Guidance on the sizing of prefilters can be provided, however, it is technically difficult and can be performed for on behalf of customers by the technical support groups of filtration suppliers.

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