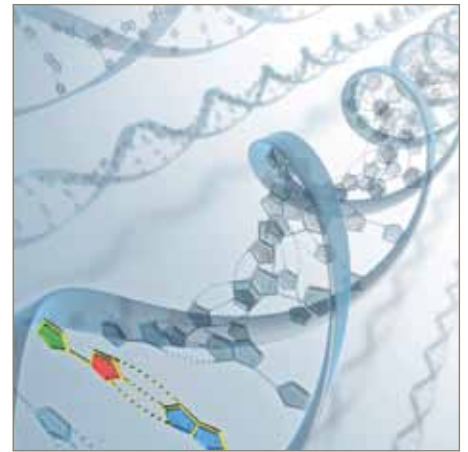


# Application Note

## Technical Application Publication

### Effective filtration of common buffers



## Introduction

Buffers are used throughout the production of pharmaceuticals from cell culture and fermentation to downstream processes and final drug formulation. Buffer filtration is essential in protecting downstream chromatography and ultrafiltration equipment, controlling bioburden throughout the process and producing an endotoxin free final product. The growing pressure to maximize throughputs and minimize production time means the optimization buffer filtration stages has never been more important.

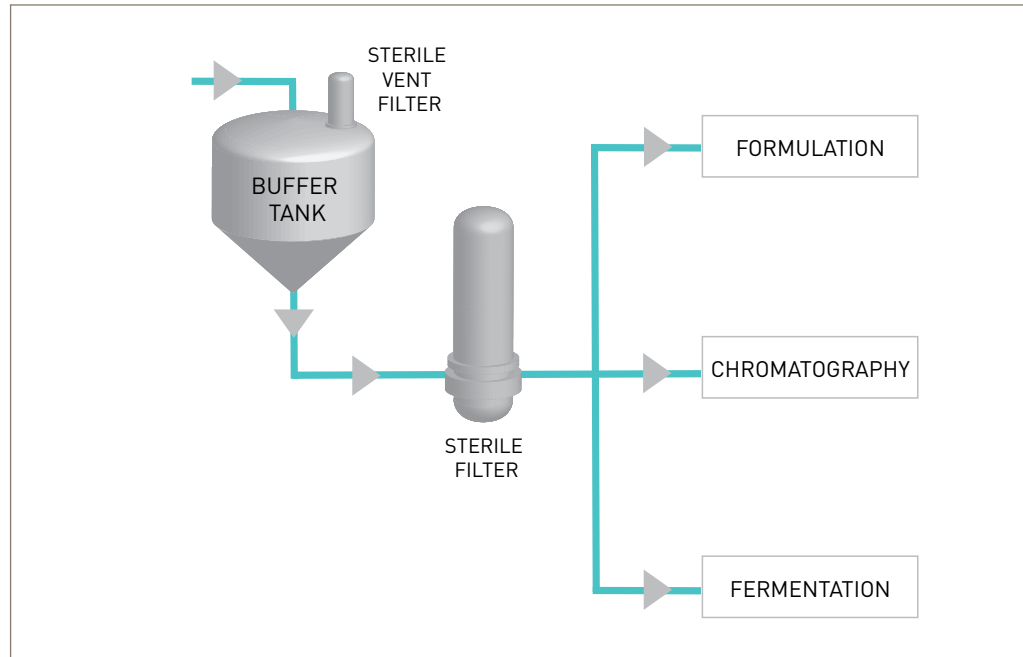
**Parker domnick hunter's PROPOR range of pharmaceutical filters have been designed to bring significant cost benefits and process improvements to your production process by maximizing throughputs and reducing system size. Bottlenecks in the buffer preparation area can be eliminated, giving faster turnaround time, greater production capacity and lower processing costs.**

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## The key specification requirements for filtering buffers are

- **Validated bacterial retention:**  
Buffers are used widely throughout biopharmaceutical production and, in line with FDA Guidelines on Sterile Drug Products, it is incumbent on the user to reduce and control bioburden within the process. Whether bioburden reduction or sterile filtration is required, the filter must be validated for the retention of bacteria and this must be correlated to a non-destructive integrity test.
  - **High flux rates:**  
Minimizing transfer times of buffers is key to quick turnaround of buffer batches leading to increased daily production capacity on the existing plant. The use of a high flux filter can also significantly reduce system size decreasing filtration consumable costs.
  - **Excellent chemical compatibility:**  
Buffers used in biopharmaceutical processes span a broad pH range (1-14) and a buffer filter must be compatible across this entire range.
- Filtration not only ensures this happens but brings many other benefits such as:
- **Process control:**
    - Guard against coagulation or precipitation from unforeseen upsets in upstream processing
    - Removal of any remaining cells so reducing the risk of endotoxins
  - **Cost avoidance**
    - Reduce irreversible resin pore plugging by contaminating proteins and cells that may decrease resin life
    - Decrease stress on resin by reducing the use of cleaning chemicals

# Buffer filtration optimization

## Choice of filter configuration

PES membrane is widely recognised as having exceptional flux rates compared to alternative membrane such as PVDF, as well as being more chemical resistant to solutions such as caustic. Parker domnick hunter supplies a choice of PES based filters for bioburden reduction or assurance of sterility, which can be used for a wide range of buffers, including difficult to filter buffers such as 6M urea.

## Product selection

### PROPOR SG

- Accelerated filtration rates to reduce batch processing time for standard buffers requiring sterility when used as additions to fermentations or in final product formulations
- Single layer PES 0.2 configured for maximum flow rates and assured sterility

### PROPOR BR

- For buffers used in chromatography / diafiltration that only requires bioburden reduction
- Single layer PES 0.2 membrane with integral depth pre filter layer to extend filter life under high precipitate loading and deliver bioburden reductions >log5

### PROPOR HC

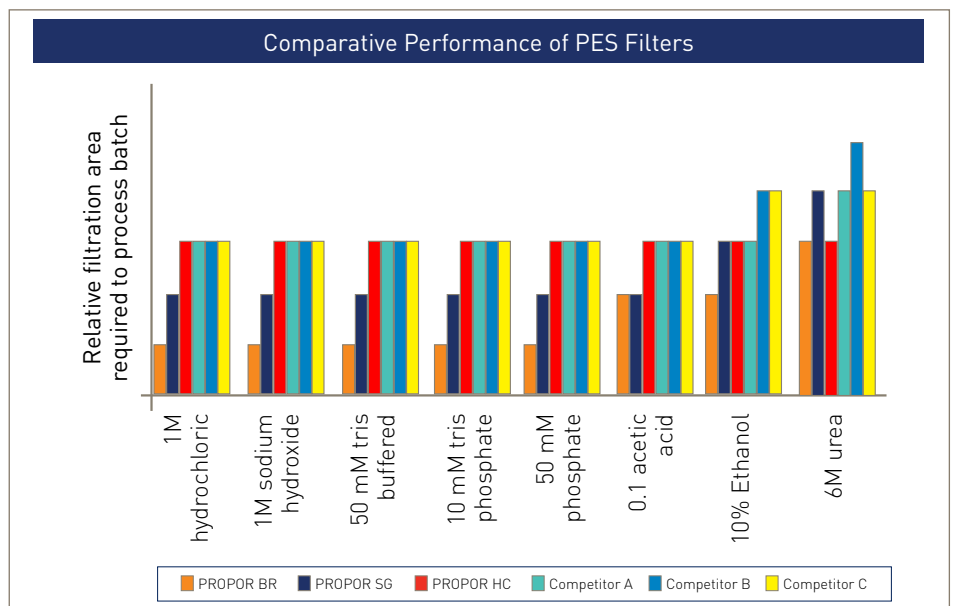
- Maximizing throughputs on more difficult to filter buffers and reducing system size
- Dual layer PES 0.2 membrane incorporating highly asymmetric PES prefilter layer to provide capacity improvement up to 10 times that of a single layer membrane

## Reducing filtration system size

Comparative testing has been completed on a number of competitive sterile grade PES membrane products using a standard range of buffers that show significant benefits can be achieved using the PROPOR range. Buffers chosen for test were:

- 1M hydrochloric acid (pH=1)
- 1M sodium hydroxide (pH=13)
- 50mM tris- buffered saline (pH=8)
- 10mM phosphate -buffered saline (pH=7)
- 50mM phosphate-citrate buffer (pH=5)
- 0.1M acetic acid
- 10% ethanol
- 6M Urea

Test were conducted on membrane disc and then scaled up to give the equivalent system size to filter a typical 12000 litre batch in 1 hour.



\*For further details please contact Parker domnick hunter.

## Conclusion

Parker domnick hunter's PROPOR range of filters have been shown to outperform competitive products for the filtration of a wide range of common buffers including 6M urea, which is often more difficult to filter.

Implementing the use of the appropriate filter from the PROPOR range can bring significant benefits by:

- Providing a smaller system size and thereby reducing the cost per batch for consumables
- Reducing the filtration time for the batch, (by up to 40% in some cases) creating the opportunity to process more batches per day and relieving the bottleneck that often occurs in the buffer preparation area