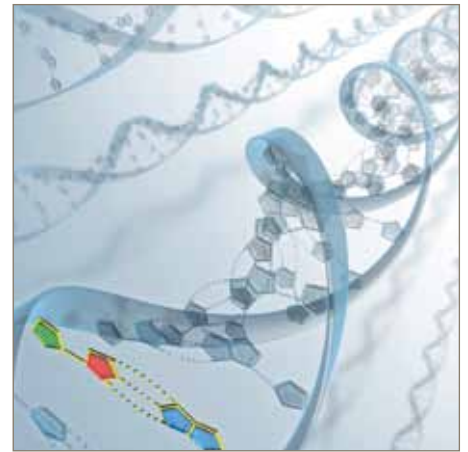


Application Note

Technical Application Publication

Media filtration

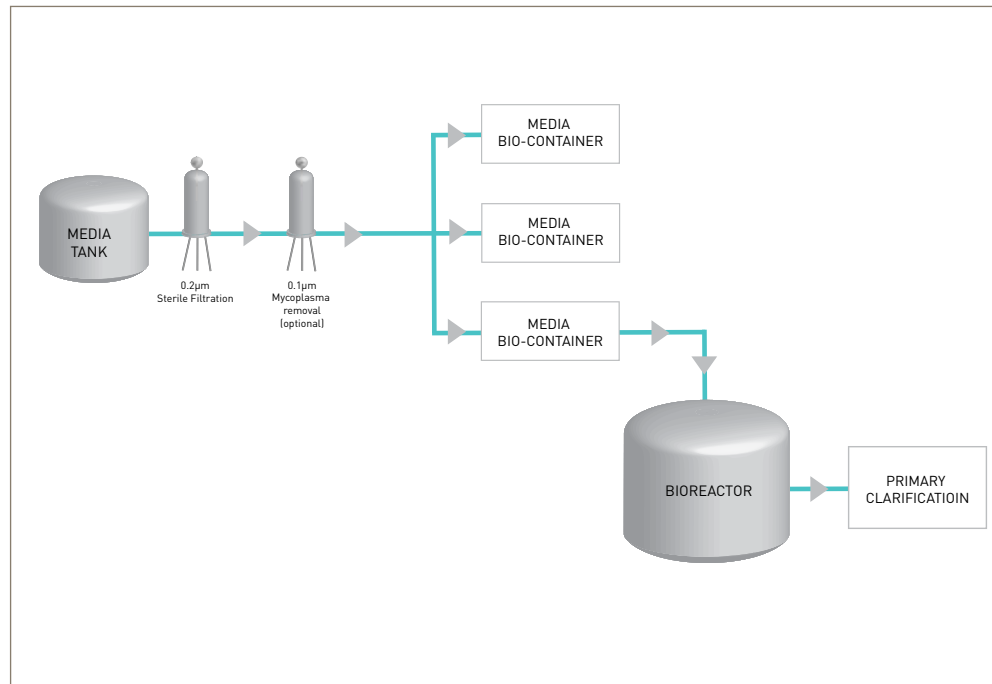


Introduction

Bacteria including Mycoplasma can be present in cell culture growth media used in biopharmaceutical production processes. If not removed these bacteria can result in contamination and loss of valuable final product. To remove this risk, cell culture media is typically sterile filtered prior to transfer to the bioreactor. This is often followed by 0.1 micron filtration where greater defence against mycoplasma is required.

Batch to batch variability and the complex nature of today's serum-free and chemically defined media can present challenges in the design of a sterile filtration system. If not correctly specified, this system can be the source of process bottlenecks and significant additional costs from resulting downtime.

Parker domnick hunter can work with you to reduce your processing costs by careful optimization of your cell culture media filtration system. We can offer products that minimize the size of your system while allowing full batch processing within a time-frame that prevents potential contamination.



Contact Information:

Parker Hannifin Ltd
domnick hunter
Process Filtration - Europe
Durham Road
Birtley, Co. Durham
DH3 2SF, England

phone +44 (0)191 4105121
fax +44 (0)191 4105312
dhprocess@parker.com

www.parker.com/processfiltration

The key specification requirements for media filtration are

High Permeability:

Due to the susceptibility of cell culture to potential contamination, the time allowable to sterilize the batch is often limited to a maximum of three hours. High flow rates are therefore necessary to process the batch economically in the required time.

High Capacity:

High flow rates must be maintained throughout the batch. This is achieved by using a dual layer filter with a high capacity integral prefilter.

Low Non-specific Binding

Any change to the composition of the cell culture due to the binding of media components to the filter can have a serious affect on the efficacy of the cell culture.

In addition the filter must:

- Incorporate a sterilizing grade membrane validated to ASTM F838-05 and where necessary provide protection against Mycoplasma species.
- Have low extractables when used with cell culture media
- Be physically robust to withstand physical, thermal and/or chemical stress on the membrane and other components.

The most efficient filtration system is achieved through the optimal combination of these requirements.



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Media filtration optimization

Choice of filter configuration

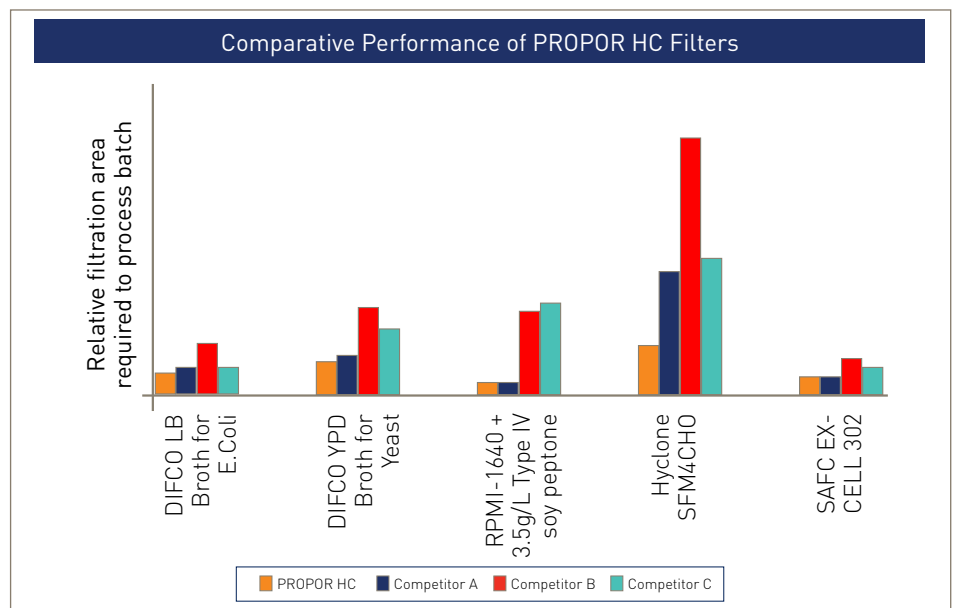
Parker domnick hunter's PROPOR HC dual layer sterilizing grade filters are ideal for cell culture media filtration. The filters use a polyethersulphone membrane which is well known for its high flow rates and low binding properties. Incorporating a highly asymmetric prefilter layer, the PROPOR HC has been specifically designed with an optimal membrane configuration to maximize capacity. Used alone or as protection to a final 0.1 micron filter, the PROPOR HC can ensure flow rates are maintained throughout processing of the full cell culture media batch. Incorporating a highly asymmetric prefilter layer, the PROPOR HC has been specifically designed with an optimal membrane configuration to maximize capacity and ensure flow rates are maintained throughout processing of the full media batch. The filters are fully validated and integrity testable as well possessing low extractables and excellent physical, chemical and thermal robustness.

Reducing filtration system size

Using the PROPOR HC, Parker domnick hunter has had experience of successfully optimizing cell culture media filtration systems for several pharmaceutical manufacturers. This includes a 30 per cent reduction in filtration system size for a 3000 litre per batch soy peptone-based media used in a perfusion reactor.

To help in the sizing and specification of sterile filters, Parker domnick hunter has conducted filterability studies on a broad range of commonly used media including both chemically defined and serum-free media:

- DIFCO LB Broth for E. Coli
- DIFCO YPD Broth for Yeast
- RPMI-1640 + 3.5 g/L Type IV soy peptone
- Hyclone SFM4CHO
- SAFEX-CELL 302



*For further details please contact Parker domnick hunter.

Comparative testing has been completed on a number of competitor dual layer sterilizing grade polyethersulphone discs and scaled up to estimate the number of 10 inch filters that would be required to sterilize a 12,000 litre batch. In many cases, the PROPOR HC was shown to significantly reduce the required system size and could not be beaten by any of the competitive products for any media tested.

Conclusion

When using Parker domnick hunter's PROPOR HC high capacity filters for cell culture media filtration, high flow rates are maintained to ensure fast batch processing. It has been shown that this can be achieved while simultaneously reducing filtration system size by up to 5 times. This in turn can decrease processing costs and afford a smaller system footprint.