

Contamination Risk Mitigation in Cell Culture Media Preparation

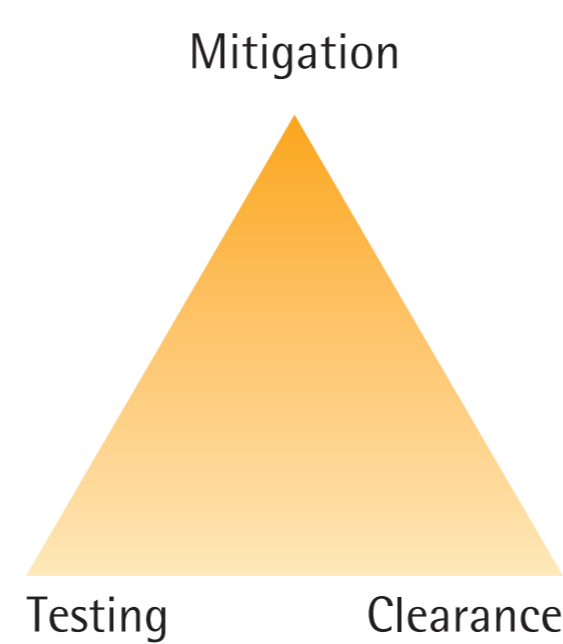
New developed virus retentive membrane as upstream barrier

B. Hansmann, V. Thom, A. Manzke; Sartorius Stedim Biotech GmbH; August-Spindler-Str. 11; Goettingen, Germany

Background

The contamination of bioreactors with various infective entities like bacteria, mycoplasma and virus is a great risk for the biopharmaceutical industry. Multiple contaminations have been reported in the past years including virus contaminations even within chemical defined media. Whereas contamination with bacteria and mycoplasma are effectively prevented with various methods, the contamination risk with small non-enveloped viruses (e.g. MVM) poses a greater challenge due to the properties of these contaminants. Virus filtration of cell culture media and HTST are two methods to mitigate this risk upstream of the bioreactor. Both technologies have pro's and con's as shown in table one.

The triangle for safety

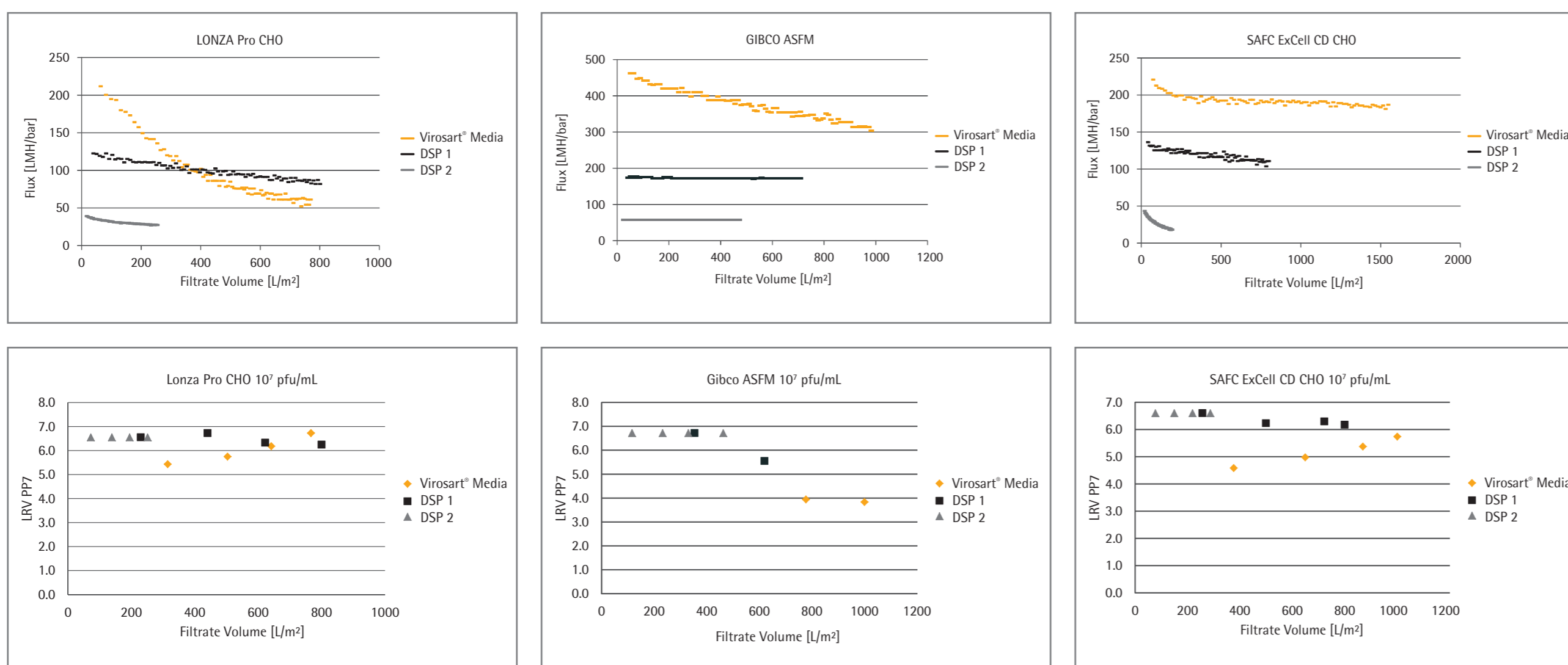


Technology	Robustness of Virus Retention	Scalability	Media Integrity	Flow Rates Large Volumes
HTST (High temperature short time)	+	-	±	+
Virus filtration	+	++	+	±

Table 1: Advantages and Bottlenecks of different technologies within upstream risk mitigation

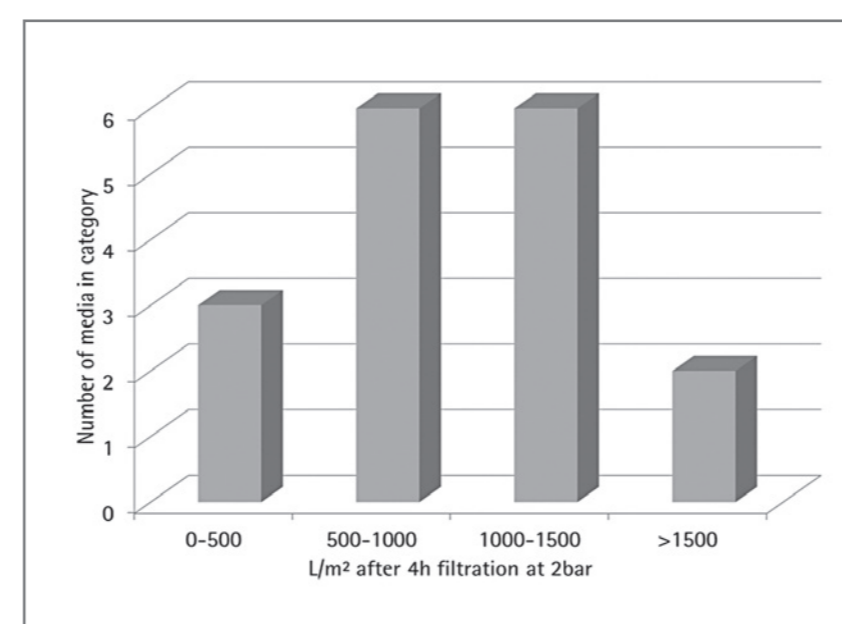
Performance data of a newly developed upstream virus filter membrane

The performance of a newly developed virus retentive filter for risk mitigation within cell culture media was evaluated for different commercially available media. Product flow rates, filtration capacities as well as retentive capabilities are shown for three representative cell culture media below. Classical downstream virus filter are used as reference.



In all cases, the newly developed upstream virus filter shows significant higher flux and capacity compared to the reference DSP virus filters. The observed retention for the commonly used parvovirus model PP7 shows a robust level above 4 LRV, typically between 4.5 and 6 LRV, also depending on the respective media type.

In total >25 different commercially available cell culture media were tested with the new filter. For most media, a cost effective filtration step can be implemented when using Virosart® Media (filter cost < approx. 1 €/liter).



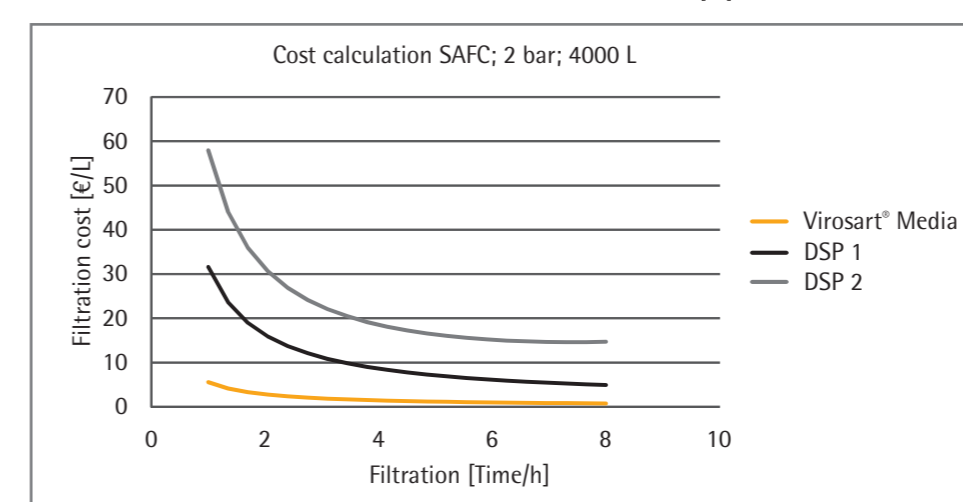
Process implementation of the newly developed Virosart® Media into media preparation



New developed virus retentive membrane for upstream risk mitigation – Virosart® Media

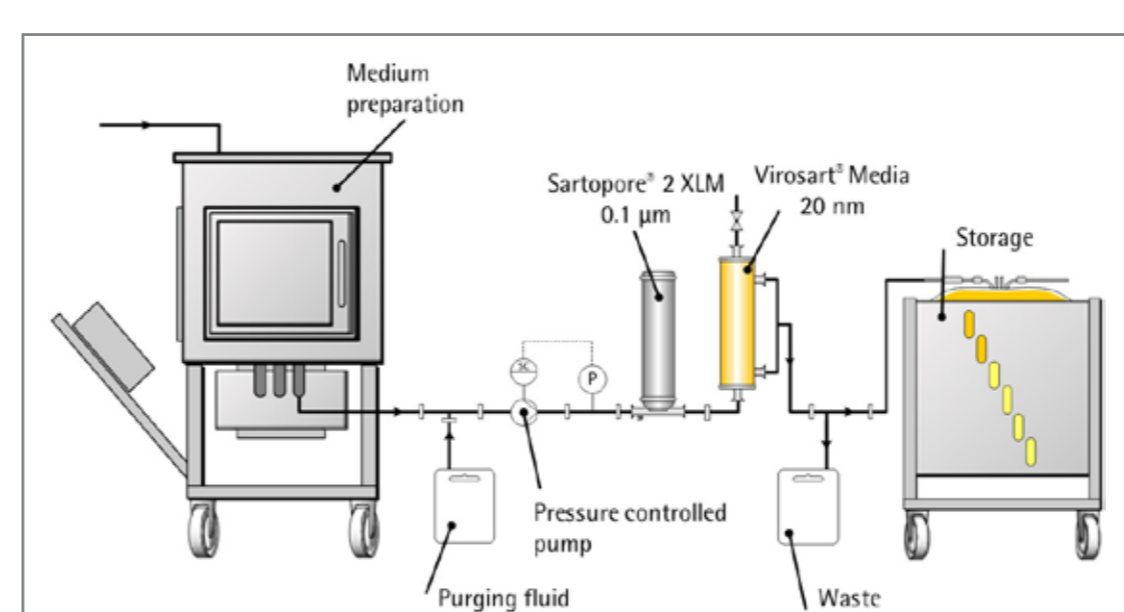
- ≥ 4 LRV for small non-enveloped viruses
- ≥ 6 LRV for large enveloped viruses
- No impact on cell growth or product expression

Economical feasible within USP applications:



Virosart® Media

- PES asymmetric membrane
- high capacity of 1000 L/m² @ 2 bar in 4 h filtration time
- hollow fiber format
- high packing density
 - up to 3 m²/capsule
 - low foot print
 - low hold up volumes
- operate at up to 5 bar



Developed for:

- fully single use applications
- gamma sterilization
- self contained
- ease of use
- chemical defined media
- serum & hydrolysate free media
- batch sizes 100 – 5000 L