Simplifying Progress

Adsorptive Pre-Filtration to Increase Virus Filter Performance and Overall Process Robustness in Blood Derived Processes

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Adsorptive pre-filters

The evaluation of virus filters is not confined only to their capacity to retain viruses. Indeed, selection of a virus filter is influenced by numerous factors. One factor gaining increase importance is process economics. Different adsorptive pre-filters have been introduced to the marked for capacity increase of virus-retentive filters. Todays established adsorptive pre-filters are compared in the table below.

Depth Filter	CEX Membrane	Virosart® Max[1]
⊕ Nearly independent of conductivity	⊖ Affected by process conditions (pH, conductivity)	⊕ Performance independent from process conditions (conductivity)
⊖ High extractable | particle load	⊕ Low extractable | particle load	⊕ Low extractable | particle load
⊖ Integrity test not available	⊖ Integrity test not available	⊕ Integrity test by air diffusion

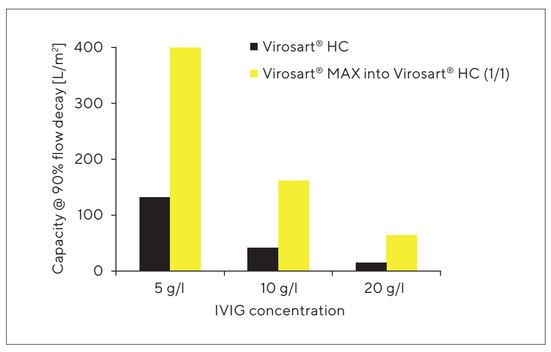
[1] Sartorius patent DE102011105525-B4; US, EP and WO patents pending, 'Method for removing biopolymer aggregates and viruses from a fluid'

Characteristics of Virosart® Max

Working principle
- Combination of adsorptive capacity and size exclusion leads to removal of virus filter foulants
- Aggregates and | or small hydrophobic molecules are typical virus filter foulants

Filter Configuration
- Material: Optimized polyamide
- Pore size: 0.1 µm (nominal)
- Format: Triple-layer pleated elements
- Size: Available from 5 cm² to 30" elements

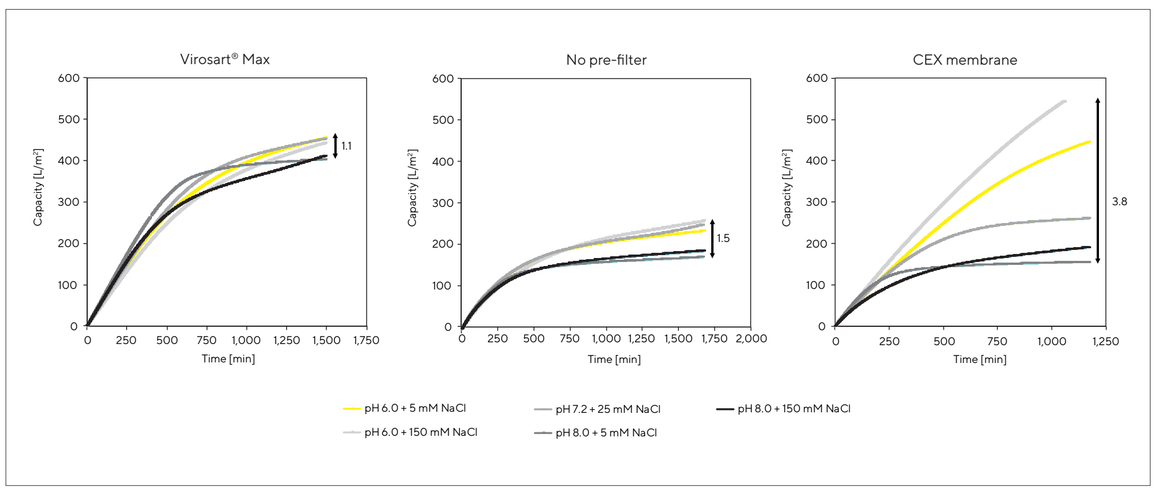
Higher capacity through aggregate reduction
The impact of Virosart® Max on the filtration of different IVIG concentrations (5, 10 and 20 g/L) through Virosart® HC 20 nm virus filter (5 cm² Minisart® devices) was analyzed. Filtrations have been performed with and without the use of Virosart® Max at 2.0 bar | 30 psi filtration pressure. Results were compared at 90% flow decay.



As a result, filtration capacity scales with solution concentration because the concentration of membrane fouling impurities scales accordingly.

Robust against process conditions
The effect of different pre-filtration strategies was evaluated for IVIG (5 g/L) in different buffer conditions at varying pH and ionic strength using Virosart® HC 20 nm virus filter (5 cm² Minisart® devices) at 2.0 bar | 30 psi.

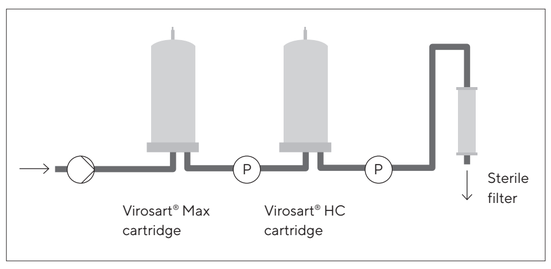
As a result, the use of Virosart® Max results in lowest performance spread by varying process conditions.



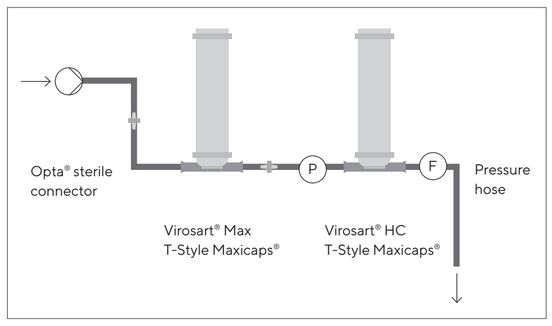
Implementation

Cartridges and capule format of the filter allows flexible process implementation:

Stainless steel housing setup
- Robust setup
- Steam sterilization and pre-use integrity testing possible



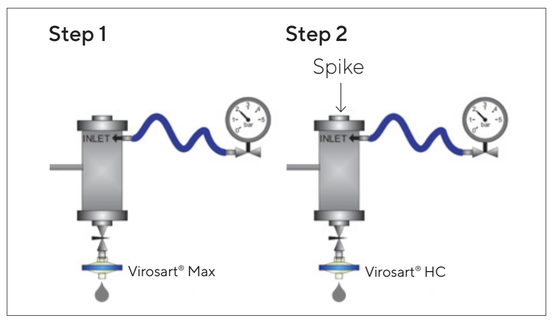
Single-use setup
- Ease of use
- Flexible
- Pre-use integrity testing limited under fully-contained sterile conditions



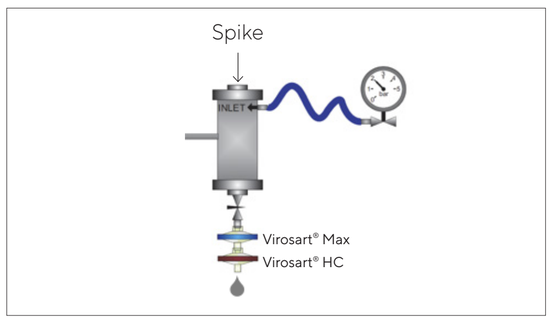
Automated setup
- Customized set-up
- High level of automation

Spiking studies

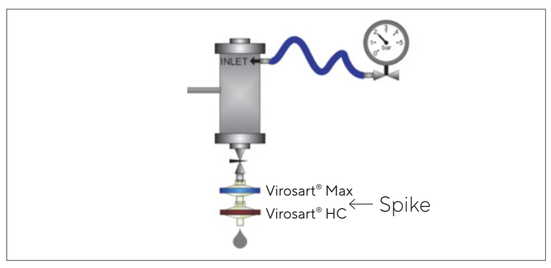
Preferred Option:
Off-line pre-filtration (decoupled)
Product is pre-filtered off-line and afterwards virus spike is added to the product feed
⊖ Pressure | flow adaption over pre-filter
⊖ Low capacity of virus filter by highly fouling feed streams
⊕ Common approach in the industry
⊕ Pre-filtration before validation to restore sample



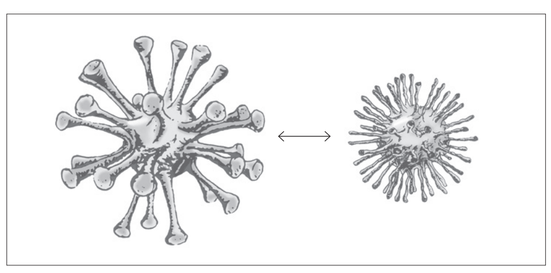
Alternative 1:
In-line pre-filtration (coupled)
Pre-filter and virus filter are run in-inline and virus spike is added in-line.
⊖ Virus retention by pre-filter not rated as robust
⊕ Possible if pre-filter is tested independently for virus retention



Alternative 2:
In-line pre-filtration with in-line spiking
Pre-filter and virus filter are run in-inline, but the virus spike is added in-line after the pre-filter.
⊖ Complex setup
⊖ Difficult control of feed titer



Alternative 3:
Spiking virus selection
Validate virus-retentive filter for parvoviruses (PPV, MVM) and imply sufficient LRV for larger viruses (MuLV, PRV)
⊖ Accepted by regulatory authorities?



References

'Artifacts of Virus Filter Validation', P. Genest, H. Ruppach, C. Geyer, M. Asper, J. Parrella, B. Evans, A. Slocum, BioProcess International 2013.