

## Fully Single-Use Virus Filtration in Manufacturing – New Concepts and Strategies

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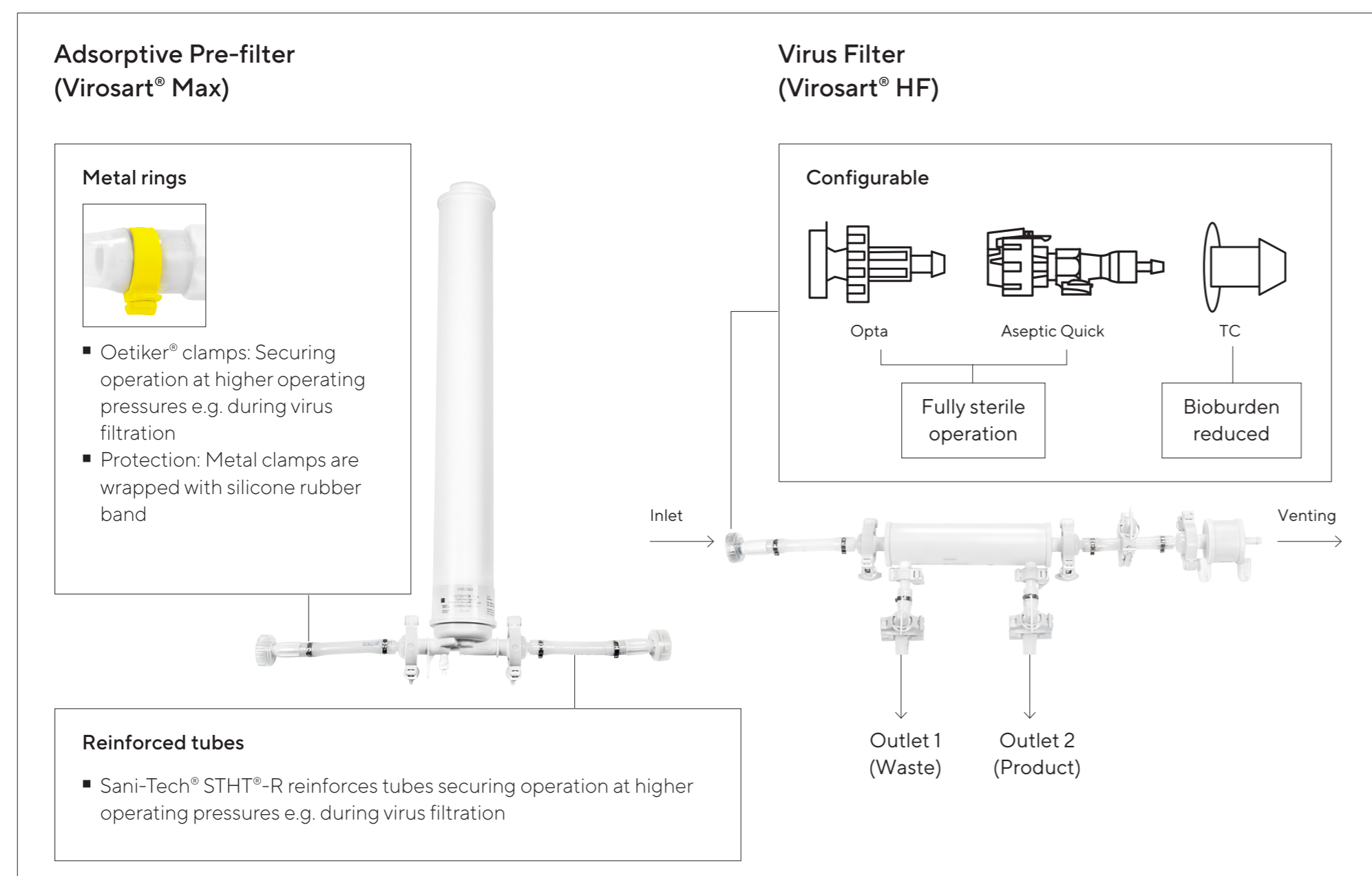
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### 1. Introduction

Current bio manufacturing processes have reached a high degree of standardization and companies are working on the basis of proven technology platforms. Single-use technology has become a viable option for clinical as well as commercial manufacturing. To reduce time to market multipurpose facilities with fully single-use technologies are used which provides highest flexibility. Investment costs are much lower and in addition preventive measures aspects are considered in a much better way. These are just some advantages of fully single-use processes. This poster will focus on concepts for creating single-use virus filtrations steps in different manufacturing ways.

### 2. Virus Filter Transfer Sets

Virus Filter Transfer Sets are pre-assembled, pre-sterilized and fully pre-qualified ready to use virus filters that allow an easy integration into a single-use set-up. Their design has been optimized to allow them to handle higher operating pressures of 2.0 up to 3.0 bar typically needed for the virus filtration steps. Therefore pressure stable reinforced tubing have been implemented and metal rings (Oetiker® clamps) have replaced cable ties to strengthen connections. Manufacturers can choose between different types of tube lengths and connectors needed for flexible process implementation.

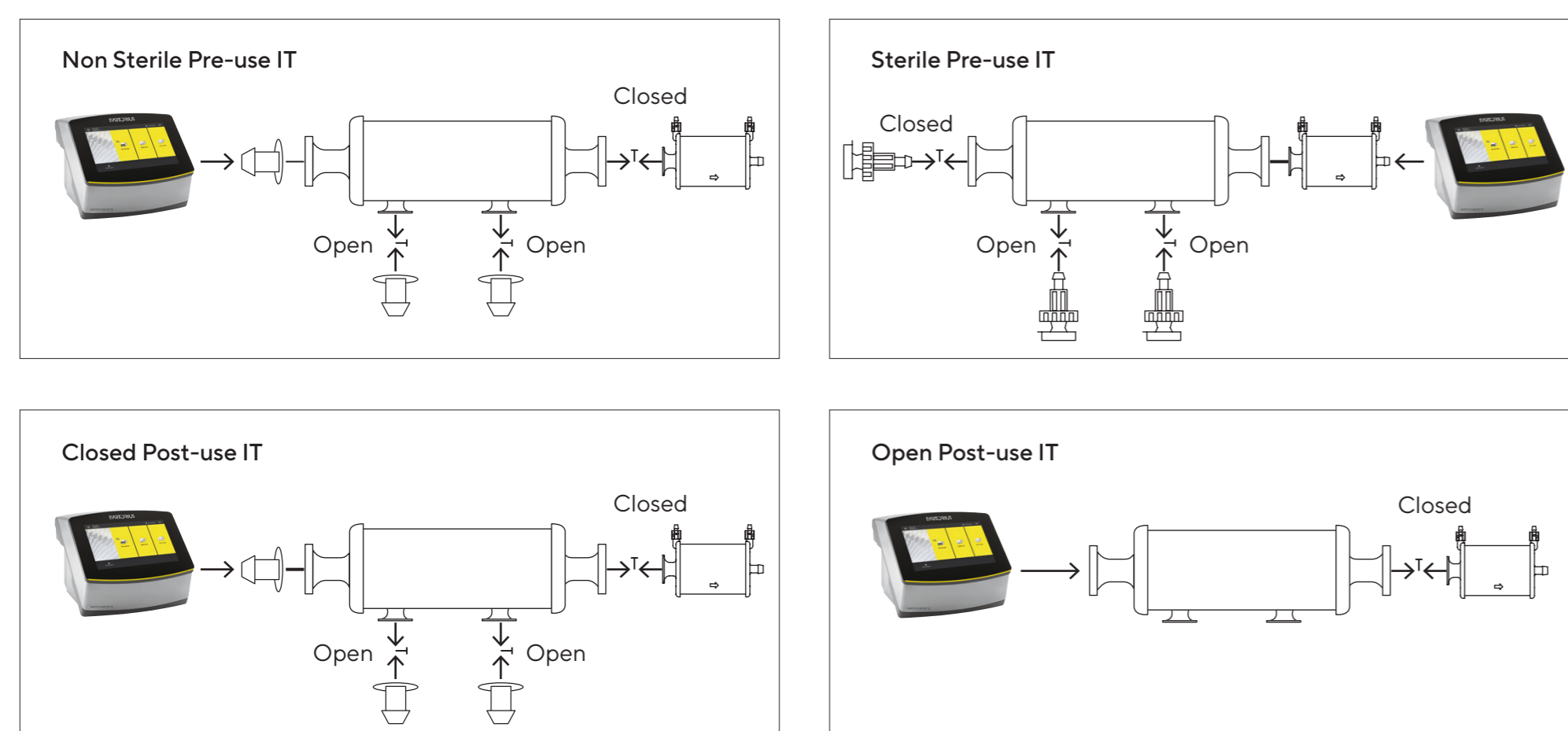


Multiple test were performed during product validation and respectively a few examples are shown:

Particle Content of the Filtrate			Water Flow Rates			Integrity Test		
Equal particle profile for Virosart® HF 2.4 m <sup>2</sup> alone and Virosart® HF 2.4 m <sup>2</sup> implemented into the filter assembly. Samples were taken after different filtration volumes. Here the particle content after 10 L filtration was compared. The test was performed according to USP 26 "Sterile water for injection" allowing a maximum of 25 particles/mL of product > 10 µm and 3 particles/mL of product > 25 µm.			No impact on water flow rates for Virosart® HF 2.4 m <sup>2</sup> alone and Virosart® HF 2.4 m <sup>2</sup> implemented into the filter assembly. Water flow rates were measured at 2.0 bar   30 psi.			Integrity (IT) test passed for Virosart® HF 2.4 m <sup>2</sup> and Virosart® HF 2.4 m <sup>2</sup> implemented into the filter assembly. The virus filter has been wetted according to the directions of use prior to the IT test. The filter assembly was first undergoing a mechanical stability test. A peristaltic pump was used for 2 hours to operate the filter assembly at an operating pressure of 3.0 bar. The tubes were dismantled prior to the IT test. The diffusion limit is 60 mL/min at a test pressure of 4.5 bar.		
Particle Size [µm]	Virosart® HF N=6	Assembly N=2	Water Flow Rate [L/min]	Virosart® HF N=30	Assembly N=2	IT Test Pressure [bar]	Virosart® HF N=30	Assembly N=2
≥10	0	0	10-17	Passed	Passed	4.5	Passed	Passed
≥25	0	0						

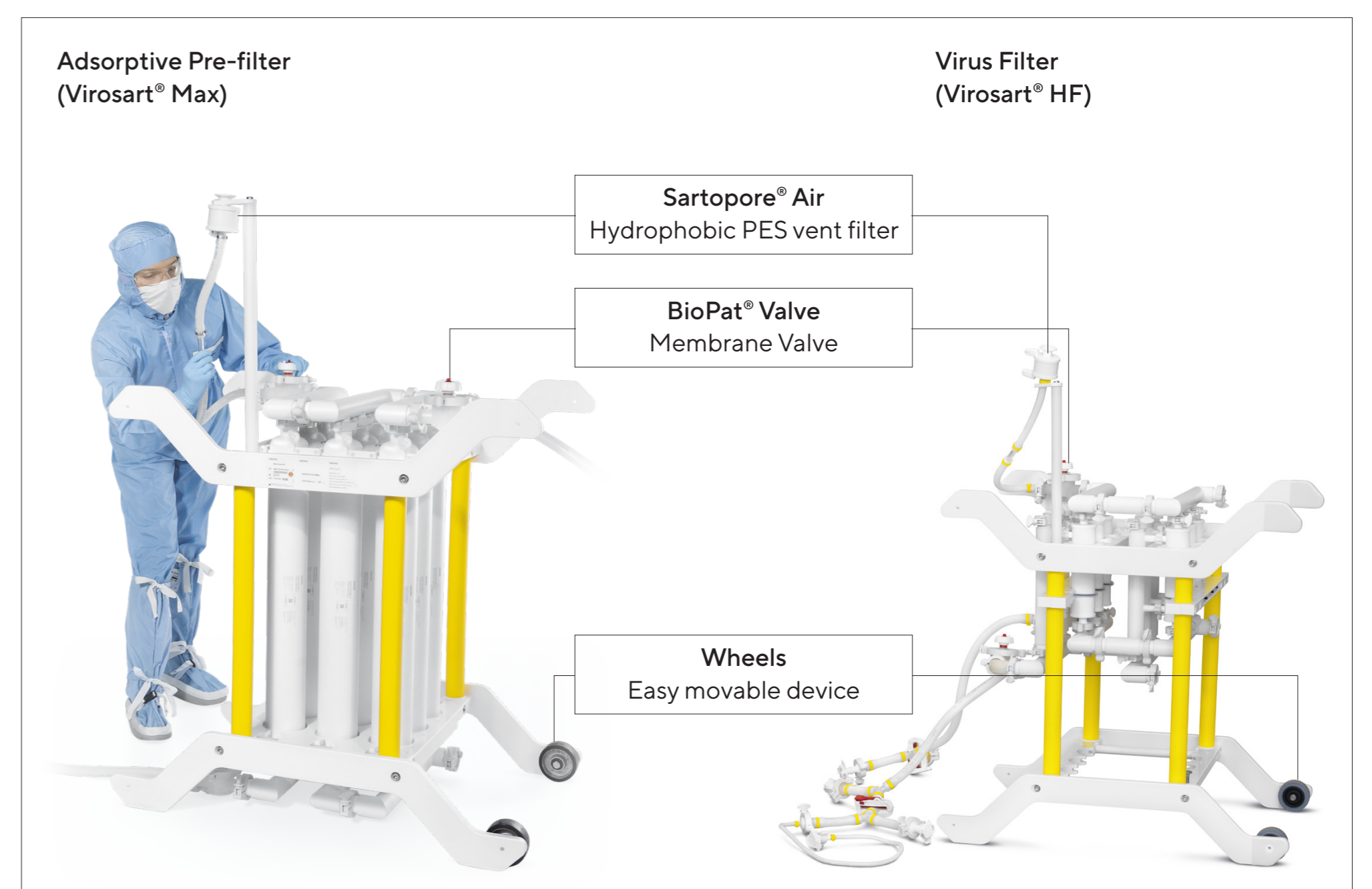
### Integrity Test

There are different options how to do an IT: Pre and | or Post use IT performed in sterile or non sterile way. Important is that the sterile IT has to be performed at a test pressure of 2.5 bar due to the pressure sensitivity of the single-use components. Non sterile IT can be also performed at 4.5 bar with tubes dismantled prior to IT.



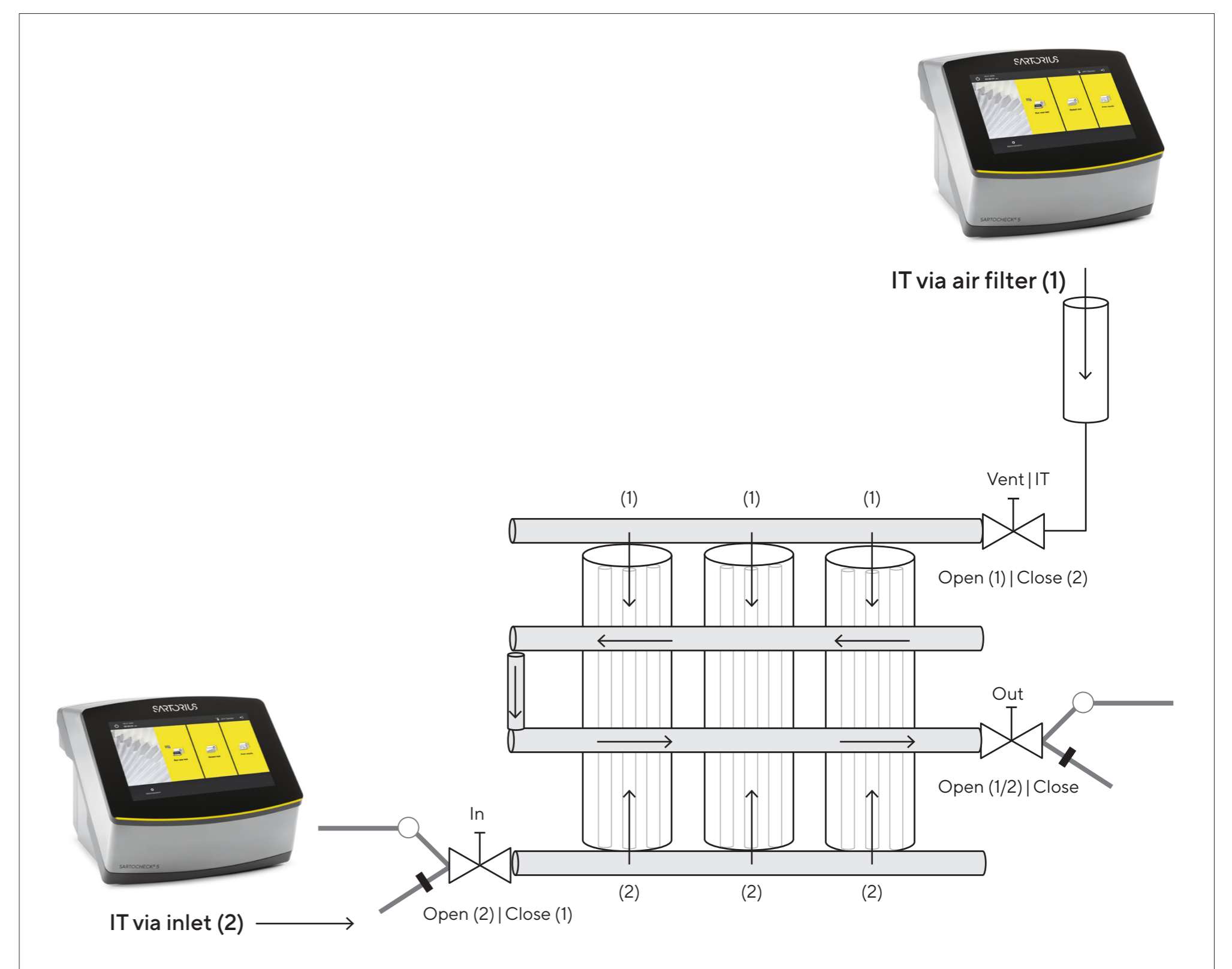
### 3. Maxicaps® MR Virosart®

Larger virus filtration areas are needed when it comes to larger bioreactor volumes (up to 20k L) or when the molecules are rather challenging to filter. Therefore a pre-filter (Virosart® Max) and the virus filter (Virosart® HF) have been implemented into the Maxicaps® MR with different areas being available. One central venting lines allows easy handling. The device comes pre-connected and ready to use with max. 4 connections at inlet and outlet have to be made on site.



### Integrity Test

There are different options how to do an IT in the Maxicaps® MR Virosart® large scale device. Prior to use the IT is recommended to be performed in a sterile manner via the air filter inside the large-scale skid. Post use there are different possibilities: Test of all filters simultaneous within the skid vs. individual filter offline, sterile way via the air filter or non-sterile way via the inlet connection.



### 4. Summary

These new developments enable a fully sterile single-use operation for the virus filtration step. Quick and easy to handle up to >14 m<sup>2</sup> pre-sterilized within one step for manufacturing scale with the option of sterile pre-use IT for excellent process reliability.