Allegro™ Connect

VIRUS FILTRATION SYSTEM

Executing any process without the right degree of monitoring, control or reporting runs the risk of process deviations. This could potentially lead to the adulteration of valuable drug substance and intermediates, whilst wasting valuable operator time.

Allegro™ Connect systems provide robust, accurate and automated platforms that integrate with your manufacturing processes on every level, keeping unit operations within critical parameters to ensure that you spend less time collating data and more time optimizing your process.

Our range of Allegro Connect systems share a compact form factor, designed with operators in mind, that are configurable to meet your process requirements without the time-consuming pain of modification.

Fig 1. The Allegro Connect virus filtration system.

The Allegro Connect virus filtration system

The Allegro Connect virus filtration system is a single-use automated filtration system designed to deliver robust process control during this critical downstream step.

This next-generation compact and elegant system is designed to minimize risk through a fully automated process with recipe-controlled steps, including pre-use manifold leak test, pre-use and post-use filter integrity tests (with the help of an integrated Palltronic® Flowstar LGR filter integrity test instrument), system priming, product filtration and buffer chase, with all data stored in a batch reporting system, significantly reducing non-conformities and manual labor.

New innovative design features enable manifolds to be configured to meet a variety of process needs; supporting a wide range of liquid filter capsules (prefilters and virus filters) and also accommodating non-Cytiva filters.

The problem

Manual and semi-automated filtration often lacks robustness, increasing the risk of critical deviations, non-conformities and sometimes even batch loss. The process data that is generated by the current systems is often insufficient and hard to access, making it very difficult to accurately evaluate any deviations or conduct routine process analysis, causing a significant impact on both cost and labor.

Current trends show an increasing number of multi-product facilities being built and/or being retrofitted together with significant investments in automated bioprocessing equipment.

Most of the existing automated virus filtration systems are designed to fit a specified process scale and are therefore less flexible.

* Eliminating human error from your list of manufacturing deviations, (podcast), Ginette Collazo, March 23, 2021

The solution

The Allegro Connect virus filtration system is a fully automated and completely flexible platform that can accommodate a product stream from 200 L to 2000 L bioreactor scale.

- Integrated Palltronic Flowstar LGR filter integrity test Instrument for *in situ* pre-use and post-use integrity testing of virus filters as well as pre-use manifold leak test.
- Configurable recipe-controlled phases to automatically perform pre-use system equilibration, product filtration and buffer chase, with maximum product recovery utilizing standard manifolds.
- Smooth transition between filtration and buffer chase phase while keeping the process parameter within the limit to eliminate impact on virus retention from back diffusion during process interruptions.
- Wide range of process options to control functions such as flow, differential pressure and inlet pressure, that covers the majority of virus filtration process strategies.
- Flexible configuration compatible with all commonly used virus filters.
- Easy-to-install single-use flow path with the shadow board concept and guided human machine interface (HMI) instructions for installation in less than 60 minutes and uninstallation in less than 15 minutes by a single operator.
- Batch reporting summary compiling data from the single-use sensors within the flow path, filter integrity testing results, and other critical process parameters.

Minimize process risk

- Fully automated process – fully integrated virus filter integrity test and pre-use manifold leak test with minimal operator intervention
- Smooth phase transition with no pressure loss
- All data in one place

Maximize configurability

- Choice of manifolds
- Choice of filters [1]
- Good fit across 200 L pilot to 2000 L production scale

Maximize productivity

- Single-use technology (SUT) for faster turnaround between batches
- Reduced deviations
- Reduced downtime

Fig 2. Key system benefits.

[1] Capsule, hollow fiber and cassette-type virus filters

Configurable for various process designs

High effective process control

Designed for easy installation and removal

- **Increased assurance**
- **Robust control**
- **Maximized productivity**

Compact footprint
1.1 m × 1.0 m × 2.0 m

Fig 3. High-performance virus filtration.

Scale the equipment to meet your process needs

Figures 4 to 8 show the scalability of the system to achieve various configuration options, tailored to meet your individual process needs. With a range of manifolds and hardware configurations available, end users are able to support all commonly used virus filters, up to 4 × 762 mm (30 in.) prefilters (PF) and up to 2 × 762 mm (30 in.) virus filters (VF) equating to throughputs typical of 200 L to 2000 L bioreactor scales.

254 mm (10 in.) configuration

Fig 4. 4 × 254 mm (10 in.) PF and 2 × 254 mm (10 in.) VF.

508 mm (20 in.) configuration

Fig 5. 2 × 508 mm (20 in.) PF and 1 × 508 mm (20 in.) VF.

Fig 6. 4 × 508 mm (20 in.) PF and 2 × 508 mm (20 in.) VF.

762 mm (30 in.) configuration

Fig 7. 2 × 762 mm (30 in.) PF and 1 × 762 mm (30 in.) VF.

Fig 8. 4 × 762 mm (30 in.) PF and 2 × 762 mm (30 in.) VF.

Increased assurance

Manual pre-use and post-use filter integrity tests of virus filters increase the risk of operator error due to mishandling, which could potentially lead to filter damage and integrity breach, impacting the batch. The integrated Palltronic Flowstar LGR filter integrity test instrument eliminates that risk by automatically performing pre-use and post-use integrity testing on virus filters. In addition, the pre-use manifold leak test provides leak-free assurance prior to starting product filtration.

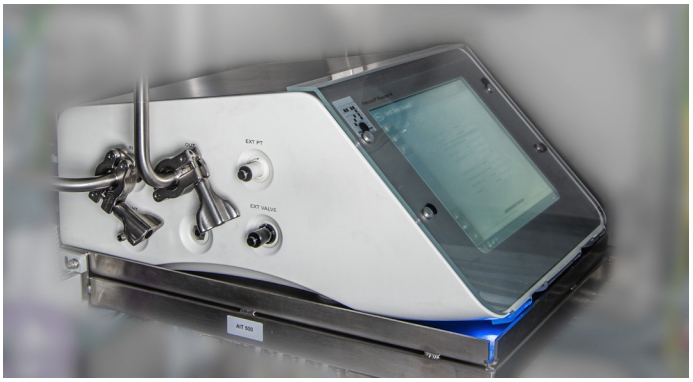

Fig 9. Integrated Palltronic Flowstar LGR filter integrity test instrument installed inside the system.

Automated pre-use manifold leak test and filter integrity test

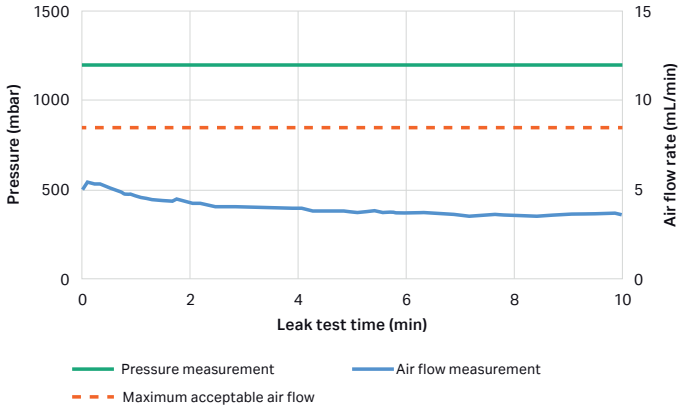

Fig 10. Automated pre-use manifold leak test.

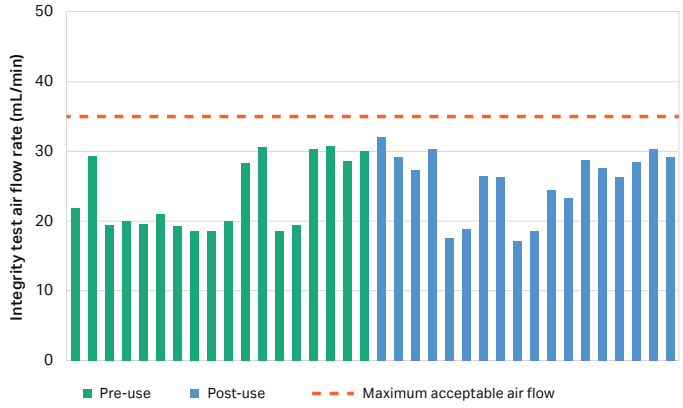

Fig 11. Automated filter integrity testing showing results of Pegasus™ Prime membrane in Kleenpak™ Nova 254 mm (10 in.) filter capsule format.

Robust filtration

Seamless phase transition from product filtration to buffer chase provides better process control by maintaining the critical process parameters within limits.

Product filtration to buffer chase phase transition

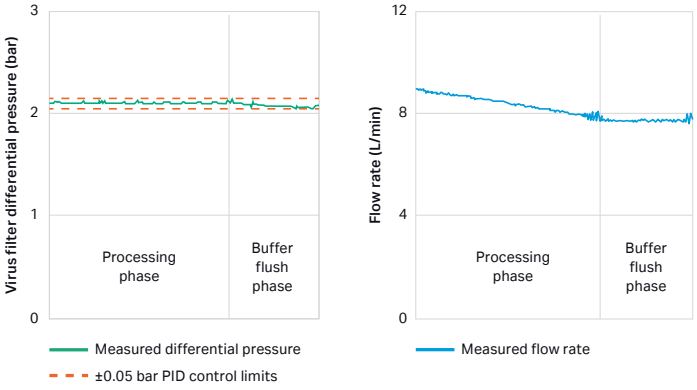

Fig 12. Differential pressure control showing flow rate in response to fouling.

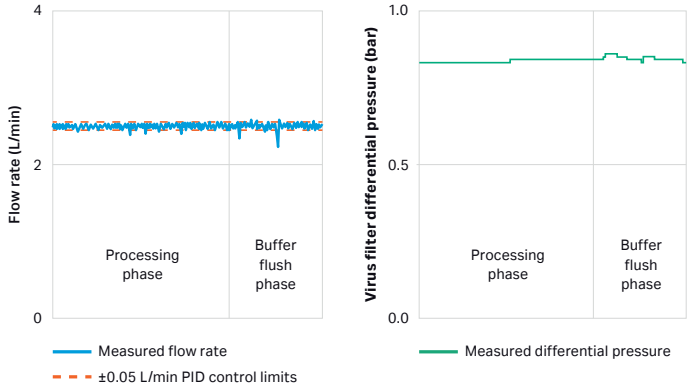

Fig 13. Fixed flow control with virus filter differential pressure shown for information.

Maximizing productivity

The Allegro Connect virus filtration system utilizes single-use technology (SUT) to ensure faster turnaround between product batches, eliminating the need for clean-in-place (CIP) and sterilization-in-place (SIP) operations and associated cleaning validation, reducing maintenance costs and system downtime, thereby ensuring increased plant productivity.

The entire flow path has been designed for easy installation and removal, with clearly marked connections and a shadow board to visibly guide the user, reducing the risk of human error.

Fig 14. Operator using the intuitive HMI screen for process monitoring.

Designed for ease of use

The Allegro Connect virus filtration system has undergone extensive usability trials to ensure the system is simple and intuitive to use. Visual instructions for installation (IFI) have been created and are accessible via the HMI screen providing operators with a step-by-step guide to installing the single-use flow paths and making the relevant fluid connections. Sample IFI screens can be seen below:

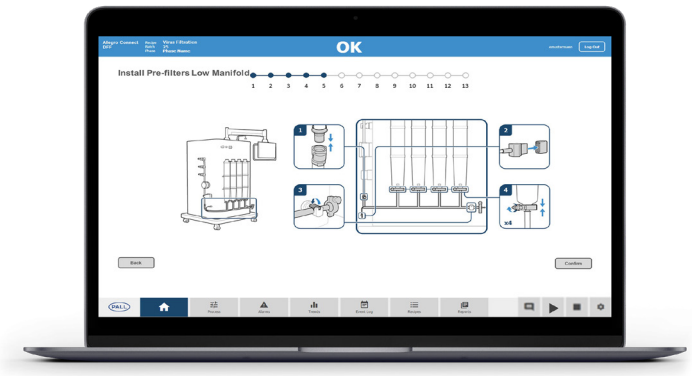

Fig 15. Guided instruction for installation (IFI), where the operator is instructed by the recipe to install prefilter inlet manifold.

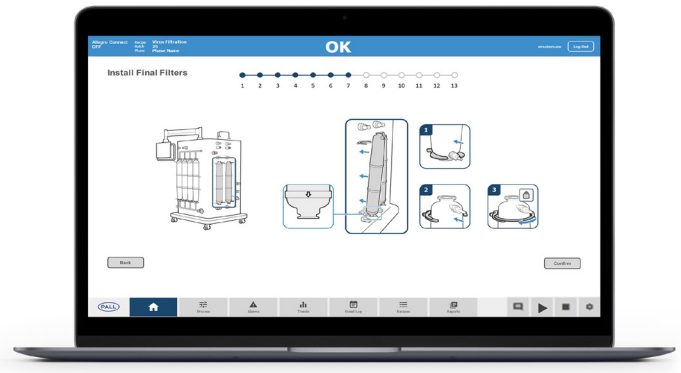

Fig 16. Guided instruction for installation (IFI), where the operator is instructed by the recipe to install virus filters.

A total virus filtration solution

The Allegro Connect virus filtration system can also be connected with some of our other single-use systems to provide a total virus filtration solution for your process, such as LevMixer™ systems for product and Allegro high-density polyethylene (HDPE) totes for buffer and water for injection (WFI).

System options

The Allegro Connect virus filtration system is available with three automation options:

- Programmable logic controller (PLC), Rockwell or Siemens, and human machine interface (HMI) for local stand-alone control
- Remote input/output (I/O) (no PLC) for integration into a DCS or supervisory control and data acquisition (SCADA) system
- Remote I/O (no PLC) controlled by centralized PLC system

The automation architecture is based on either Siemens S7 PLC or Rockwell CompactLogix PLC, an industrial PC, and a 22 in. thin client which is applied across our range of Allegro Connect bioprocessing systems enabling a truly modular 'plug-and-play' concept, with the ability to control single or multiple unit operations from one centralized cabinet.

Fig 17. The Allegro Connect virus filtration system.

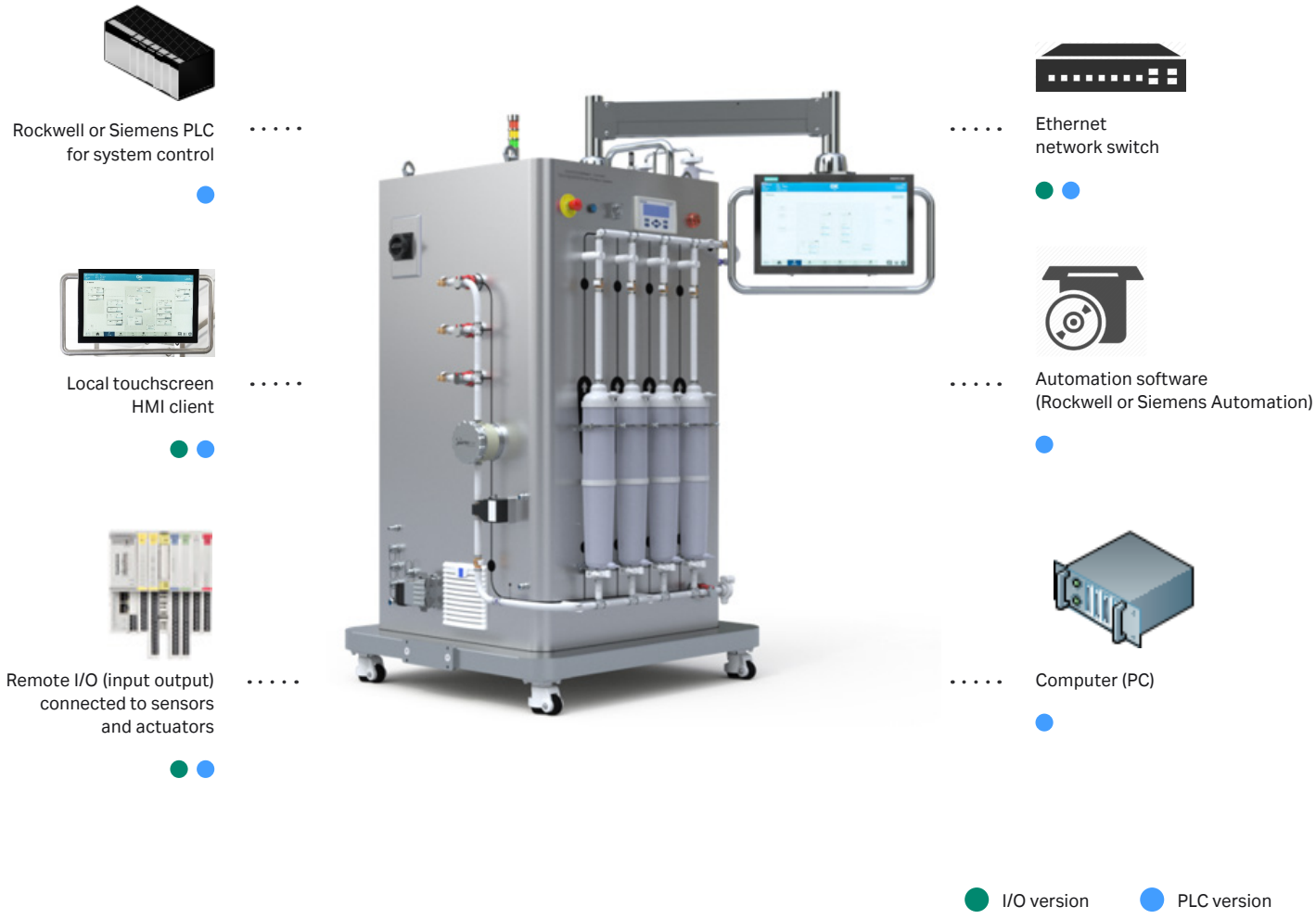

Fig 18. Automation options.

Quality standards

Detailed validation turnover package for each system according to ASTM 2500 Standards (A Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment).

Regulatory dossier, comprised of:

- Regulatory compliance ROHS I to ROHS III directives
- Raw material compliance data (USP Standards)
- Packaging and packaging waste directive 94/62/EV
- System designed in accordance with the American Society of Civil Engineers (ASCE), ASCE 7, Minimum Design Loads and Associated Criteria for Buildings and Other Structures.

Technical specifications

Process specifications

Equipment	Specification
Functionality	Filtration
Filtration configuration	Virus filters in series with prefilters
Minimum prefilter and virus filter capsule size	127 mm (5 in.)
Maximum prefilter and virus filter capsule size	762 mm (30 in.)
Feed pump	1
Pump flow rate range	20 to 1200 L/h
Number of inlets	3 (2 × water for injection [WFI]/buffer and 1 × product)
Number of outlets	3 (1 × product, 1 × drain and 1 × process waste outlet)
Tube dimension	½ in. (internal diameter [ID])
Flow path operating pressure	Non-virus filter manifolds: 0 to 4 bar (0 to 58 psi) Virus filter manifold: 0 to 3.5 bar (0 to 51 psi)
Integrity test pressure [2]	Up to 5.7 bar (83 psi) with a maximum exposure of ≤ 10 hours
Flow path operating temperature range	4 to 40°C
Pressure sensor	Up to 3 (1 after feed pump with integrated, hard-wired pressure switch; 1 before virus filter and 1 after virus filter)
External connections	6 (2 × ethernet for mixer, 2 × HC-DD24 for mixers, 2 × HAN16E for scales)

[2] Acceptable pressure rating of the air filters

System specifications

System	Specification
System dimensions (W × D × H)	112 × 102 × 197 cm (44 × 40 × 78 in.)
System mass (empty)	500 kg (1102 lbs)
System floor clearance	115 mm (4.5 in.)
Environmental conditions	5 to 30°C, relative humidity 10 to 70% (non-condensing)
Materials of construction	Stainless steel 304
Surface finish	Cold-rolled steel (typically Ra < 1 µm)
Ingress protection rating	IP54 (main, outer panel or chassis)

Utility specifications

Utilities	Specification
Electrical supply	230 VAC, 50 Hz (European), 208 VAC, 60 Hz (North American)
Operating voltage control	24 VDC, 20 A
Ingress protection for internal electrical cabinets	IP 56 (European), NEMA 4X (North American)
Recommended FI switch	RCD 30 mA, Type B
Power consumption	≤ 2.4 kVA
Amperage	10 A
Motor power	0.75 kW (pump)
Process air	6 bar (87 psi) minimum 10 bar (145 psi) maximum 40 m^3/h minimum flow rate Pressure reducer. ON/OFF valve. Pressure safety valve
Instrument air	10 bar (145 psi) maximum. Instrument air, clean, dry and oil free. Manual pressure regulator and integrated Palltronic Flowstar LGR filter integrity test instrument

Component specifications

Component specifications, sensor range and accuracies are as per OEM datasheets and correct at the time of compiling this proposal. Cytiva does not accept any responsibility in the case of deviation to the specifications outlined below.

Process equipment	Type	Specification
Primary pump	QF1200 single-use diaphragm pump	Flow: 20 to 1200 L/h
Process valves	Gemü Q30	Pneumatically operated pinch valve
Pressure	PendoTECH – single-use sensor with pressure sensitivity chip	Range: -0.48 to 5.20 bar Accuracy: ± 2% from 0 to 0.41 bar, ± 3% from 0.41 to 2.07 bar, ± 5% from 2.07 to 4.10 bar
Level detector	Rechner – capacitive sensor	Operating distance: 0.5 mm (min.) to 15 mm (max.)
Conductivity sensor	Optek ACF60 single-use sensor	Range: 0 to 10 µS/cm to 850 mS/cm Accuracy: ± 1% of MV ± 0.25 µS/cm, from 0 to 250 mS/cm, ± 2% of MV ± 0.25 µS/cm, from 250 to 500 mS/cm, ± 5% of MV ± 0.25 µS/cm, from 500 to 850 mS/cm
Integrity test instrument	Palltronic Flowstar LGR integrity test instrument	Forward flow test: 0.1 to 1000 mL/ min., ± 3% of value or ± 0.05 mL/min, whichever is the greater

Recommended process equipment and fittings

Process equipment	Recommendation
Product input and output mixer	LevMixer stainless steel cubical tank (ASME available upon request)
Product input and output mixer drive	LevMixer drive unit LMG403
Buffer tote	Allegro 200 L HDPE tote

The Allegro Connect virus filtration system is compatible with all Cytiva single-use mixing technology and can also be integrated with most mixing equipment from other suppliers.

Cleaning

The system can be cleaned with the following typical cleaning solutions:

- 70% ethanol
- 70% IPA
- 0.5% sodium hypochlorite
- 0.02% w/w benzalkonium chloride
- 2% sodium hydroxide
- Spor-Klenz Ready-to-Use (RTU)

Automation specification

The system is equipped with Wonderware Batch Management and Wonderware System Platform, which enables end users to create recipes based on their process needs. Recipes are created using operations that are comprised of predefined phases. Each phase is parameterized to allow the end user to tailor the recipes as per their requirements.

The system also provides flexible phases, that allow for a fully manual creation of recipes.

Automation architecture is based on either Siemens S7 PLC or Rockwell CompactLogix PLC, an industrial PC, and a 22 in. touch screen HMI.

The automation platform allows the end user to create an unlimited number of recipes.

An OPC UA client is installed if a communication link is desired with the unit operation. The Cytiva automation platform enables compliance with 21 CFR Part 11 and follows the GAMP V life cycle for software development.

Automation hardware specification [3]

Utilities	Specification
PLC vendor (option 1)	Siemens
PLC model (option 1)	SIMATIC S7-1500, CPU 1516-3 PN/DP
PLC software (option 1)	Siemens TIA V16
PLC vendor (option 2)	Rockwell
PLC model (option 2)	5069-L380ERM
PLC software (option 2)	Rockwell Studio 5000 V32
Database	SQL
Operating system	Windows Server 2016
Batch engine	Wonderware Batch Management
Historian	Wonderware Historian
Reporting	AVEVA Reports for Operations / Wonderware System Platform
HMI	SIMATIC ITC2200 V3 PRO, Industrial Thin Client, 22
Panel PC	INDUSTRY PC Stratus ztC Edge 110i
UPS	QUINT-UPS/ 24DC
Remote I/O	Turck BL20 series
Ethernet switches	Phoenix Contact 8 port (managed switch)
OPC server	Archestra Client

[3] Technical equivalent replacements are possible depending on market availability, refer to Cytiva's Turnover Package (TOP) documentation.

Process sequence

The generalized configurable virus filtration phases are shown in the following figure:

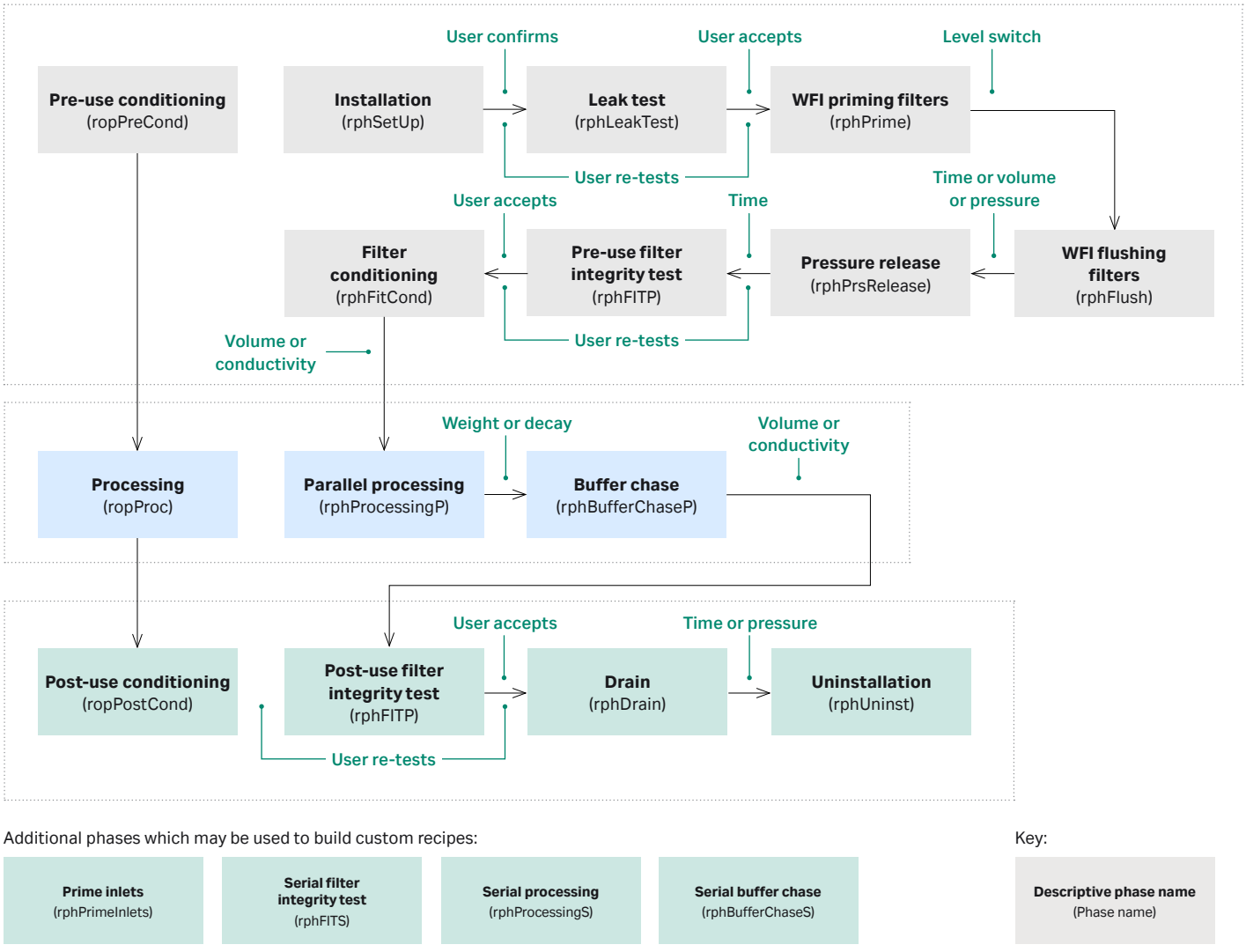

Fig 19. Example virus filtration process model for buffer-wetted, parallel filters.

Process screens

Process screens have been created to summarize and expand on critical process information throughout the operation. The integrated Palltronic Flowstar LGR filter integrity test instrument will also be controlled via the system HMI when performing filter integrity testing and/or leak testing – sample screens are also shown below.

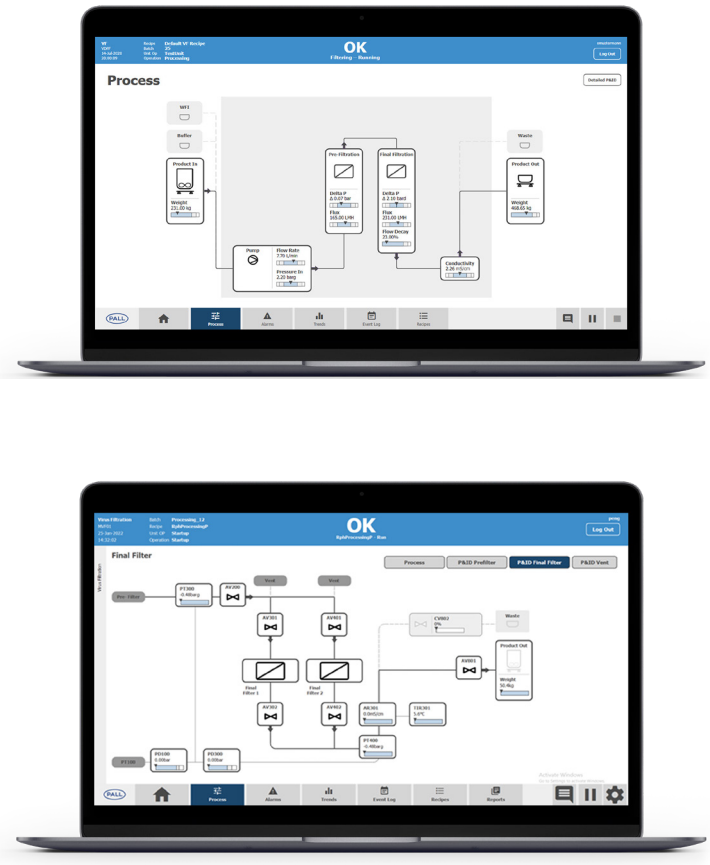

Fig 20. Process screens highlighting critical processes.

Batch report

Upon operator selection, batch reports will be generated automatically at the end of a batch for each single step. Both a summary and detailed batch report is generated, and the content of these batch reports is predefined. Batch reports can be configured to specific needs by the end user via AVEVA Reports (Dream Reports). Sample batch reports can be provided upon request.

Predefined batch records contain the following major information:

- General batch information, phase information and transition conditions
- Global and recipe parameters
- Audit trails excerpt
- Alarms summary
- Trends for differential pressure across filters
- Trends for input product weight
- Trends for filtered product weight

Ordering information

System hardware and accessories

Product	Product code
Main system	
Allegro Connect virus filtration system: PLC 230 VAC, software automation	ACVFSEUPLC
Allegro Connect virus filtration system: PLC 208 VAC, software automation	ACVFSWHPLC
Allegro Connect virus filtration system: I/O 230 VAC, DCS ready no automation	ACVFSEUIO
Allegro Connect virus filtration system: I/O 208 VAC, DCS ready no automation	ACVFSWHIO
FAT	
Allegro Connect virus filtration system: FAT 2.5 days with flow kit	ACVFSFAT
Seismic feet	
Allegro Connect system seismic leveling feet	ACSEISMIC
Other accessories	
Allegro Connect system GEN3 mixer communication cable	ACGEN3COMSCBL
Allegro Connect system GEN4 mixer communication cable	ACGEN4COMSCBL
Allegro Connect system LGR mixer communication cable	ACLGRCOMSCBL

Contact our sales team for UL61010 certification (1) requirement.

Single-use assemblies

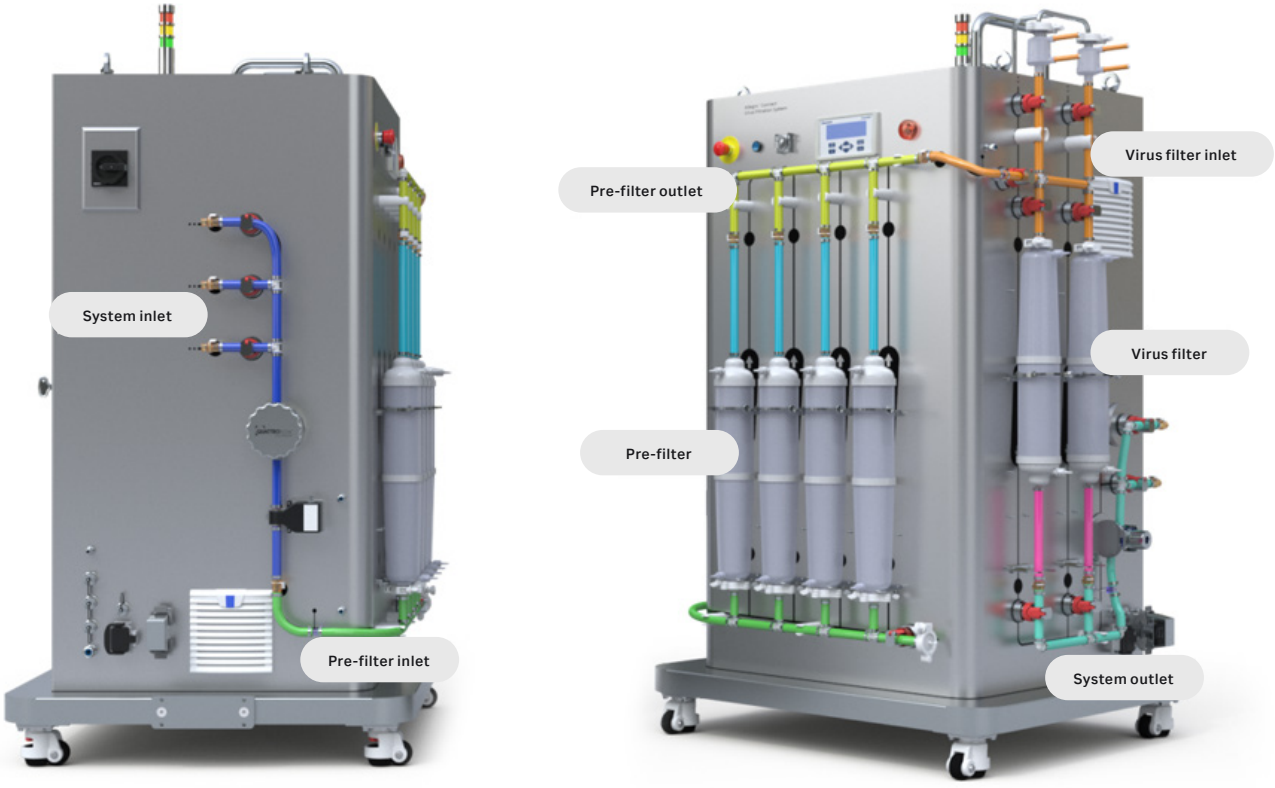

Fig 21. Schematics showing location of the single-use assemblies.

The flow path selection table on the next page lists the standard product codes of the Cytiva products designed and approved to support the Allegro Connect virus filtration system. Due to the configurability of the system enabling multiple different combinations of filter capsules (membrane and size), we are only able to list a limited number of the possible filtration assemblies in the table below. Filtration combination sets which do not appear in this table but are within the scope of the system are available from Cytiva, on request. Figure 21 shows images of the single-use flow paths sections with ½ in. internal diameter (ID).

Single-use assemblies for virus filtration (for capsule type filters)

Flow path selection	Product	Product code
Step 1: Pick inlet manifold		
Inlet and pump	System inlet manifold with MPX connector	7465-1485T
Step 2: Choose prefilter inlet manifold depending on the number of prefilters required		
Prefilter inlet	1 × prefilter inlet manifold with MPX connector	7465-1841C
	2 × prefilter inlet manifold with MPX connector	7465-1485S
	4 × prefilter inlet manifold with MPX connector	7465-1488D
Step 3: Choose your prefilters [4] (Skip Step 3 and proceed to Step 8 if off-the-shelf filters with 1½ in. tri clamp at the downstream connection is used)		
Prefilter	Pegasus Protect 254 mm (10 in.) filter module with MPX connector	7465-1557U
	Pegasus Protect 508 mm (20 in.) filter module with MPX connector	7465-1526N
Step 4: Choose prefilter outlet manifold depending on the number of prefilters required		
Prefilter outlet	1 × prefilter outlet manifold with MPX connector	7465-1778Y
	2 × prefilter outlet manifold with MPX connector	7465-1485R
	4 × prefilter outlet manifold with MPX connector	7465-1487Y
	1 × prefilter outlet manifold with 1½ in. tri clamp connector	7465-1778Z [4]
	2 × prefilter outlet manifold with 1½ in. tri clamp connector	7465-1779A [4]
	4 × prefilter outlet manifold with 1½ in. tri clamp connector	7465-1526T4 [4]
Step 5: Choose virus filter inlet manifold depending on the number of virus filters required		
Virus filter inlet	1 × virus filter inlet manifold with MPX connector	7465-1485U
	2 × virus filter inlet manifold with MPX connector	7465-1488K
Step 6: Choose your virus filters [4] (Skip Step 6 and proceed to Step 8 if off-the-shelf filters with 1½ in. tri clamp at the downstream connection is used)		
Virus filter outlet	Pegasus Prime 127 mm (5 in.) filter module with MPX connector	7465-1488X
	Pegasus Prime 254 mm (10 in.) filter module with MPX connector	7465-1488C
	Pegasus Prime 508 mm (20 in.) filter module with MPX connector	7465-1863U
Step 7: Choose virus filter outlet manifold depending on the number of virus filters required and if a conductivity sensor is required for the process		
Virus filter outlet	1 × virus filter system outlet manifold with MPX connector	7465-1484Q
	2 × virus filter outlet manifold with MPX connector	7465-1527H
	1 × virus filter system outlet manifold with MPX connector and conductivity sensor	7465-1535J
	2 × virus filter system outlet manifold with MPX connector and conductivity sensor	7465-1488W
	1 × virus filter system outlet manifold with 1½ in. tri clamp connector	7465-1607N [5]
	2 × virus filter system outlet manifold with 1½ in. tri clamp connector	7465-1607M [5]
	1 × virus filter system outlet manifold with 1½ in. tri clamp connector and conductivity sensor	7465-1841K [5]
	2 × virus filter system outlet manifold with 1½ in. tri clamp connector and conductivity sensor	7465-1841L [5]
Step 8 (optional): **Choose adaptor kit to connect to the downstream side of the prefilters and virus filters if off-the-shelf filters with 1½ in. tri clamp at the downstream connection is used**		
Filter adaptor kit	NP5 filter module adaptor kit with MPX outlet connector	7465-1727K
	NP6 filter module adaptor kit with MPX outlet connector	7465-1527J
	NP7 filter module adaptor kit with MPX outlet connector	7465-1484P

[4] Contact our sales team if a different filter configuration is required.

[5] Only applicable for 762 mm [30 in.] filter capsules.

Single-use assemblies for in-process/intermediate filtration

Flow path selection	Product	Product code
Step 1: Pick inlet manifold		
Inlet and pump	System inlet manifold with Kleenpak Presto sterile connector	9465-1763D
Step 2: Choose prefilter inlet manifold depending on the number of prefilters required		
Prefilter inlet	2 × prefilter outlet and 2 × prefilter inlet manifold with Kleenpak Presto sterile connector	9465-1763E
	2 × prefilter outlet and 4 × prefilter inlet manifold with Kleenpak Presto sterile connector	9465-1841D
Step 3: Choose your prefilters (Skip Step 3 and proceed to Step 8 if off-the-shelf filters with 1½ in. tri clamp at the downstream connection is used)		
Prefilter	Refer to our website for a range of pre-filters to suit your process needs	
Step 4: Choose final filter inlet manifold depending on the number of filters required		
Final filter inlet	2 × prefilter outlet and 1 × final filter inlet manifold with Kleenpak Presto sterile connector	9465-1774Q
	2 × prefilter outlet and 2 × final filter inlet manifold with Kleenpak Presto sterile connector	9465-1526R
Step 5: Choose final filter (bioburden/sterilizing grade filter) depending on the number of filters required		
Final filter	Refer to our website for a range of sterilizing grade and/or bioburden reducing filters to suit your process needs	
Step 6: Choose final filter outlet manifold depending on the number of filters required		
Final filter outlet	2 × final filter outlet manifold with Kleenpak Presto sterile connector	9465-1526S
Step 7 (optional): Choose adaptor kit to connect to the upstream and downstream side of the prefilters and final filters if off-the-shelf filters with 1½ in. tri clamp at the downstream connection is used		
Inlet filter and outlet adaptor kit	NP5 filter inlet or outlet adaptor kit with Kleenpak Presto sterile connector	9465-1840M
	NP6 filter inlet or outlet adaptor kit with Kleenpak Presto sterile connector	9465-1840L
	NP7 filter inlet or outlet adaptor kit with Kleenpak Presto sterile connector	9465-1840K

In order to reduce our carbon footprint, we strive to provide single-use systems manufactured regionally. However, to ensure security of supply, you may receive products from multiple global sites.

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For local office contact information, visit cytiva.com/contact
CY40873-04Dec23-DF