



Allegro™ Single-Use Tangential Flow Filtration System



A compact easy-to-use and fully automated TFF system, providing flexibility in manufacturing

The Allegro single-use TFF system is designed specifically for the incorporation of single-use components. It is not a disposable version of a traditional TFF system design because new concepts for ease-of-use in single-use processing have been used to achieve this unique design.

This includes careful consideration of the layout and installation, allowing full access to components from one side of the system.

Key Attributes:

- ▶ Good engineering design provides reliability, control and ease-of-use
- ▶ Full automation provides control and monitoring of key process parameters
- ▶ Gamma-irradiated manifolds with pre-calibrated sensors ensure quick installation

System Concept

Single use technology is widely accepted in bioprocessing, with key benefits being the elimination of cross contamination and cleaning, and greater system flexibility.

Tangential Flow Filtration (TFF) is more complex than many other unit operations for which single-use approaches have been adopted. In TFF, cleaning of the TFF cassettes and system is essential to maintain flux and minimize the risk of cross contamination in a multi-product facility.

The Allegro system provides a platform onto which five single-use manifolds are attached. The five manifolds – feed, retentate, permeate, retentate biocontainer and recovery – are provided gamma irradiated and ready to install on the system.

The single-use flowpaths have incorporated single-use sensors where possible. These sensors are manufactured to defined tolerances and minimize downtime in system set up.

Integration of sensors in this system:

- ▶ Allows tracking of key process parameters
- ▶ Provides notification when processing is not within specification
- ▶ Enables automated control of processing to optimum conditions
- ▶ Facilitates fully automated process sequences

Components in the single-use flowpaths have been selected to achieve the performance requirements of the system. Use of components and materials which:

- ▶ Meet the flow and pressure requirements of typical TFF processes
- ▶ Achieve scalability of performance
- ▶ Have full specification and certification
- ▶ Have easy attachment and connectivity



System Description

The Allegro single-use TFF system has been designed for ultrafiltration and diafiltration (UF/DF) processes.

Typical applications are concentration and diafiltration of proteins, recombinant molecules, potent biological and cytotoxic drugs, and vaccines.

It is fully automated, with a disposable flow path comprising high quality components in five easy to install manifold sets. The ½ in. ID (internal diameter) system has a recirculation pump capacity of 1000 L/hour, and can typically run 0.5 - 2.5 m² cassettes (running at a crossflow of 5 L/min/m²). It can be fitted with a 20 L or 100 L retentate biocontainer, and operated in fed batch mode. Cassettes are placed between single-use distribution plates, which are components of the feed and retentate flow paths. The cassette assembly is torqued between two stainless steel plates (non wetted parts), to ensure correct sealing.

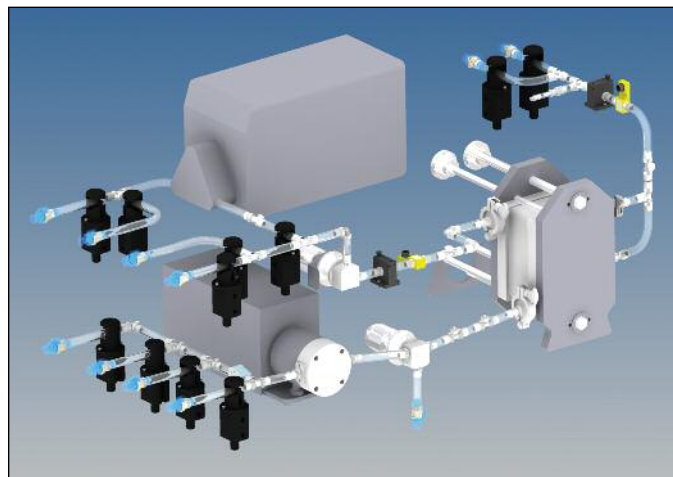
Connections can easily be made to Allegro 2D and 3D biocontainers for supply of WFI, diafiltration buffer and process fluid in fed batch operations. Product temperature control, either cooling or heating, is available using a heat exchange plate under the retentate biocontainer.

Key features:

- ▶ Pressure independent flow provided by a positive displacement diaphragm pump ensures that critical parameters do not vary during the concentration step
- ▶ Fully automated system for control and monitoring of key process parameters
- ▶ Good accessibility for installing flowpaths and daily operation
- ▶ Pre-irradiated manifold sets for feed/retentate/permeate/fed batch/recovery
- ▶ Installation of manifold sets is intuitive, and typically takes 15 minutes

Figure 1

CAD image showing manifolds, valves and pumps



Designed for Ease-of-Use

Single-use technology brings many benefits in bioprocessing and can make unit operations simpler to carry out. The fully automated single-use TFF system makes UF/DF a straightforward process with full control over the key parameters.

- ▶ Actuated valves
- ▶ Fully automated TMP and retentate flow control
- ▶ Pressure and flow sensors for monitoring
- ▶ ½ in. ID high pressure silicone tubing
- ▶ Optional conductivity sensors on retentate and permeate
- ▶ Positive displacement diaphragm pump
- ▶ Fed batch and diafiltration buffer feed control
- ▶ User-configurable phases and recipes
- ▶ Can be run in automatic or manual mode
- ▶ All process signals and component status are shown on the main screen
- ▶ Pall analytical tool supplied for trending and calculation
- ▶ Data logging and batch reporting

Performance

Performance of Allegro single-use TFF system using Omega™ T-series cassettes with 10 kD membrane (0.5 m² for 20 L, 1.5 m² for 100 L).

Figure 2

Concentration of 20 L batch 10 g/L IgG and 100 L of 10 g/L BSA in 1m NaCl

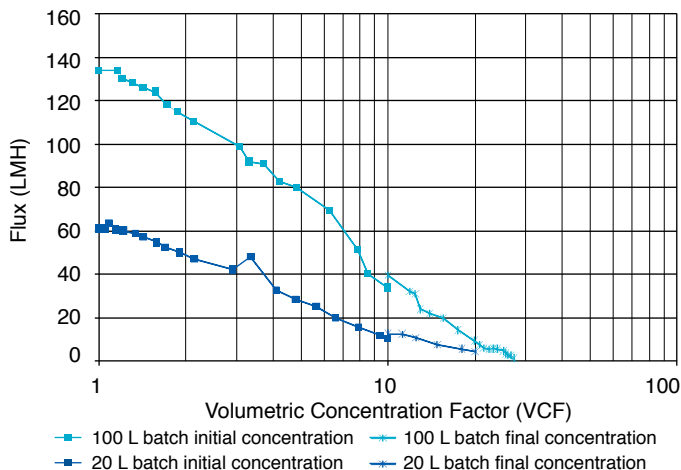
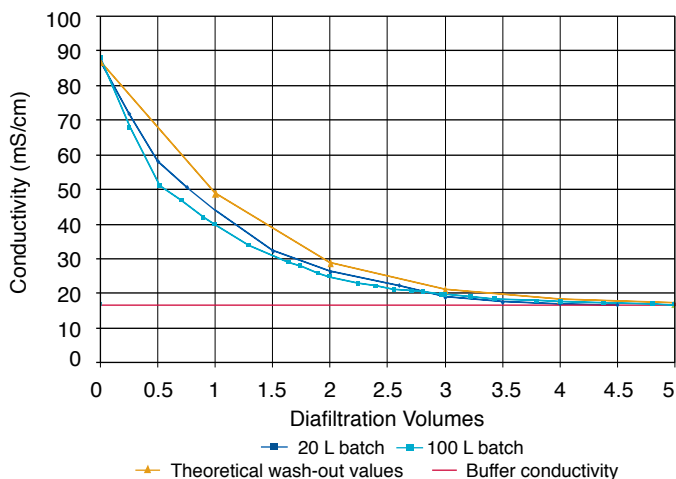


Figure 3

Conductivity



Results

- ▶ Both batches achieved target concentration factors while maintaining a linear decrease in flux on a semi-log curve. This linear relationship is expected and is comparable to what would be achieved on a conventional TFF system
- ▶ The system design allows sufficient mixing: the conductivity wash out profiles for each batch was comparable to the theoretical wash out curve

Quality Standards

Pall maintains a very stringent approach to quality of purchased and manufactured components. The system is designed and built to well recognized industry standards, including but not limited to:

- ▶ EMC 89/336/EEC
- ▶ Good Automated Manufacturing Practice (GAMP) current version
- ▶ Software meets CFR 21 Part 11 for electronic records, signatures and audit trail
- ▶ The rules governing medicinal products in the European Community, Volume IV, Good Manufacturing practice for medicinal products, Annex 11, computerized systems

The single-use flowpaths:

- ▶ Are assembled in a dedicated Class 10000 Clean Room, to ISO standards 9001:2008 and 14001:2004 using validated assembly methods
- ▶ Have components which have been tested for biocompatibility and certified to USP <88> Biological Reactivity Tests, *in vivo*, for Class VI plastics
- ▶ Components are certified TSE/BSE free
- ▶ Are supplied double bagged and irradiated at 30 - 50 KGy

Technical Specifications

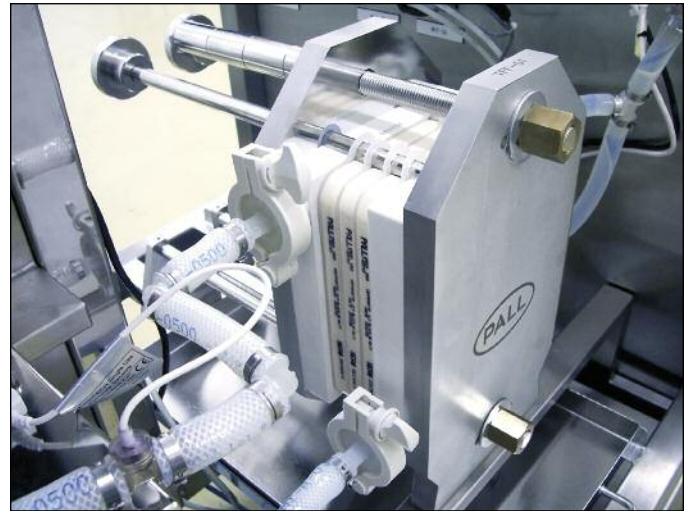
Operating Conditions

Pressure Range	0 – 4 bar (on feed and retentate)
Flow Range	6 – 1000 L/hour
Temperature Range	4 – 40 °C
Surface Area of Membrane	0.5 – 2.5 m ² (typically)
Minimum Working Volume	1 L

Component Specifications

Utilities

Power Supply	230 V 1-phase 50 Hz 120 V 1-phase 60 Hz
Compressed Air	Air source at 6 bar for operation of valves



Base System	Type	Materials	Capacity/Other
System Frame	1800 x 800 x 1600 mm (L x W x H) - EU 74 x 36 x 69 in. - USA	304 stainless steel	–
Cassette Holder	Centrasette™ single-use holder	316 stainless steel	5.0 m ²
Recirculation Pump	4 piston diaphragm pump with single-use pump head	EPDM elastomers	1000 L/hour
Pinch Valves	Pneumatic actuated		OD range 0.75 in. to 1.0 in.
Flow Meter	Single-use turbine with reusable sensor	PVDF	30 – 1200 L/hour
Diafiltration Pump	Peristaltic		600 L/hour
Control System	Fully automated with Pall phase step concept	Siemens (230 V), Allen Bradley (120 V)	–
Temperature Control	Heat exchange plate		5 – 50 °C

Product Contact Materials	Type	Materials	Capacity/Other
Flowpath Tubing	½ in. internal diameter	Platinum cured silicone	–
Recirculation Pump	Single-use pump head	EPDM elastomers	–
Pressure Monitoring	Single-use pressure sensor	Polysulfone	-0.48 to 5.2 bar
Pressure Control	Pneumatic actuated single-use diaphragm valve	Polypropylene	–
Cassette Distribution Plate	Plastic manifold plates around cassettes	Polypropylene	–
Flow Meter	Single-use turbine with reusable sensor	PVDF	–
Tubing Connectors	Quick connectors	Polysulfone, Silicone	–
Connectors for Distribution Plate	Triclamp-hosebarb Triclamp gasket	Polypropylene Silicone	– –
Biocontainers	Allegro 2D and 3D biocontainers	LDPE	5 L, 10 L, 20 L, 100 L
Conductivity	Single-use flow cell	Polypropylene	1 µS/cm to 200 mS/cm

Part Numbers

Feed Manifold

Part Number	PT01	TT01	Connectors
	Pressure	Temperature	
709-10W	X	X	MPX
709-13W	X	–	MPX

Retentate Manifold

Part Number	PT02	PT04	FT01	AT01	Connectors
	Pressure	Flow	Flow	Conductivity	
709-10X	X	X	X	X	MPX
709-13X	X	X	X	–	MPX
709-13Y	X	X	–	X	MPX
709-13Z	X	X	–	–	MPX

Permeate Manifold

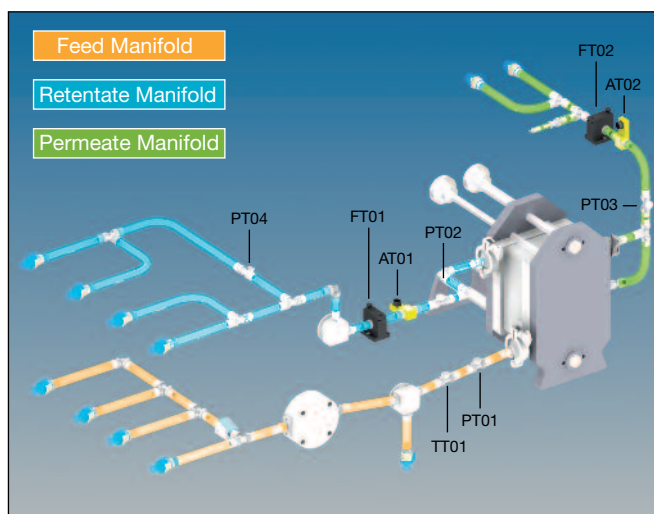
Part Number	PT03	FT02	AT02	Connectors
	Pressure	Flow	Conductivity	
709-10Y	X	X	X	MPX
709-14C	X	X	–	MPX
709-14E	X	–	X	MPX
709-14G	X	–	–	MPX

Hardware

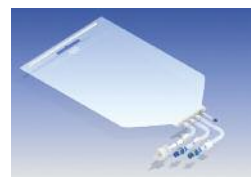
Part Number	Description
LGRTFFCS120AEU	½ in. single-use TFF system with Q1200 feed pump, 230 V 50 Hz 1-Phase
LGRTFFCS120AUS	½ in. single-use TFF system with Q1200 feed pump, 120 V, 60 Hz 1-Phase

Figure 4

CAD image showing feed, retentate and permeate manifolds



Retentate Biocontainer



Part Number	Biocontainer Size
709-12A	5 L
709-12B	10 L
709-10Z	20 L
709-11D	100 L

Product Recovery Biocontainer



Part Number	Biocontainer Size
709-11E	5 L
709-14H	10 L
709-14J	20 L
709-14K	100 L



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