



Allegro™ Connect Buffer Management System

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Introduction

Executing any process is a significant logistical challenge requiring all process components to be available when needed and, without the right degree of process control or reporting, risks process deviations, the potential adulteration of valuable drug products or intermediates, and wastes valuable manufacturing time from unscheduled process interruptions. 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.

The range of modular systems share a compact form factor, designed with operators in mind and are configurable to meet your process requirements without the time consuming pain of modification.

Providing in-line dilution of buffer at point of use

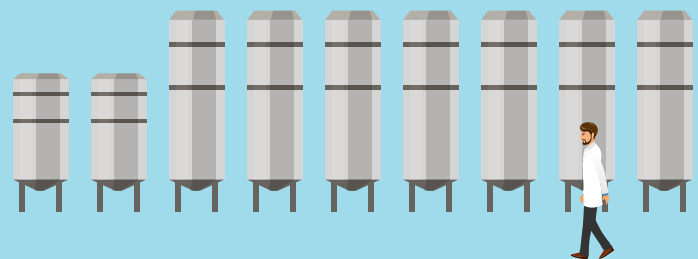
The Allegro Connect Buffer Management System

Designed to simplify and improve process buffer workflow by providing 'just-in-time' process buffer directly to the unit operation. Valuable floor space is saved by using in-line dilution of buffer concentrates and water for injection (WFI) at point of use, to meet the target buffer specifications. Buffer workflow is simplified by eliminating the need to prepare and store large volumes of process buffer in advance. Operator workspace is improved with a more compact footprint around unit operations requiring high buffer volumes. In addition, total buffer cost/L is also reduced by typically 12%.

* Buffer cost overview model (please contact your Pall representative for further details).

The problem

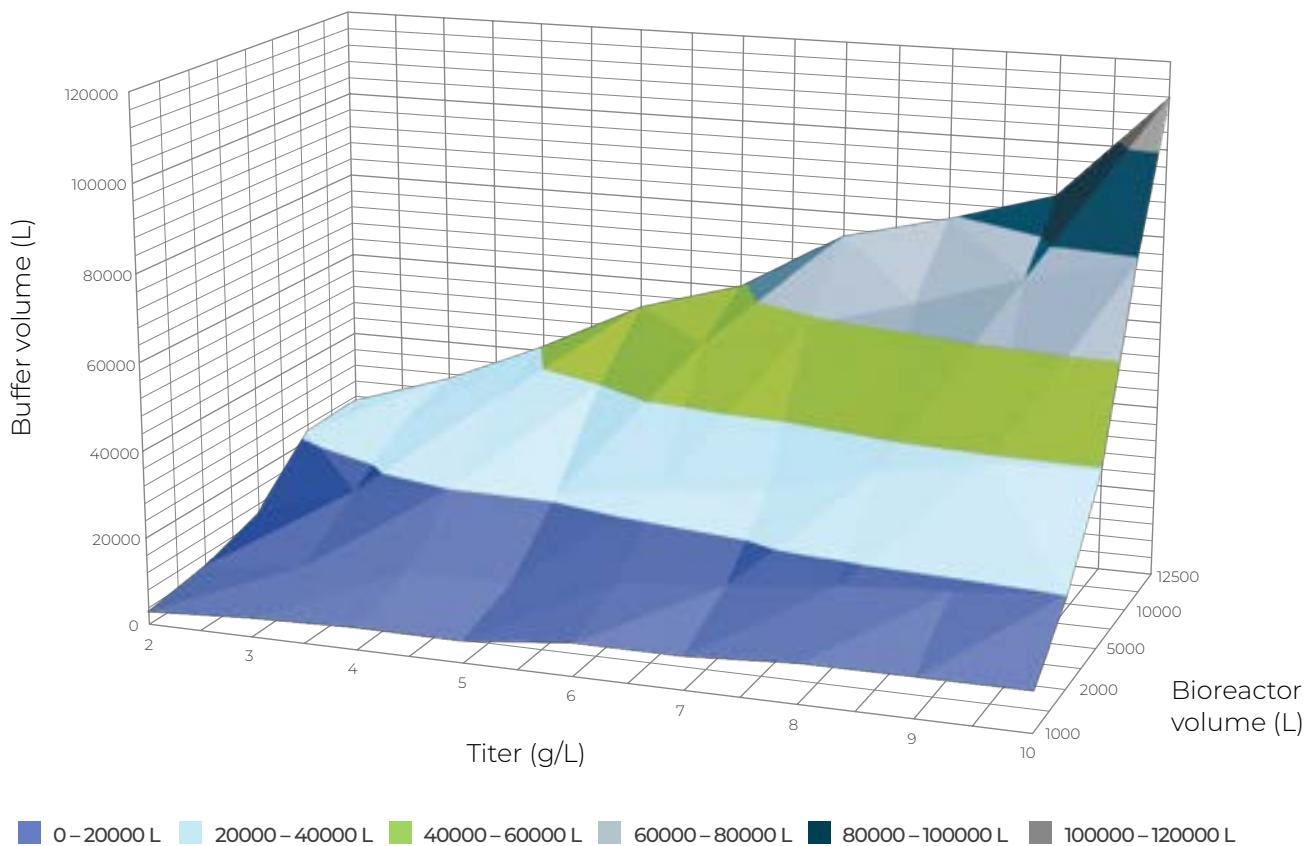
With increasing product titers, greater volumes of process buffer are required to meet processing demand. Increased buffer volumes place additional pressure on buffer hold and storage area constraints, with some companies resorting to using corridor walkways when storage capacity is exceeded.



Buffer solution requirements per batch versus product titer and bioreactor volume

The inefficient use of floor space is exacerbated as buffer is usually made a week or more in advance, QC tested, and then held until required. The buffer then needs to be moved in heavy large vessels from buffer hold areas to the relevant processing areas, which increases labor costs and the potential risk for injury.

In addition, complex scheduling of staff and equipment is required to ensure there is an adequate quantity of QC released process buffers prepared and ready for an entire batch, with companies often preferring to prepare their buffers at least a week in advance. And in plants producing multiple products, the logistical challenges are increased by the need for different buffer solutions for different process applications.



Source: Kevin Gibson *et al.*, An economic evaluation of buffer preparation philosophies for the biopharmaceutical industry, BioPhorum Operations Group Ltd, December 2019.



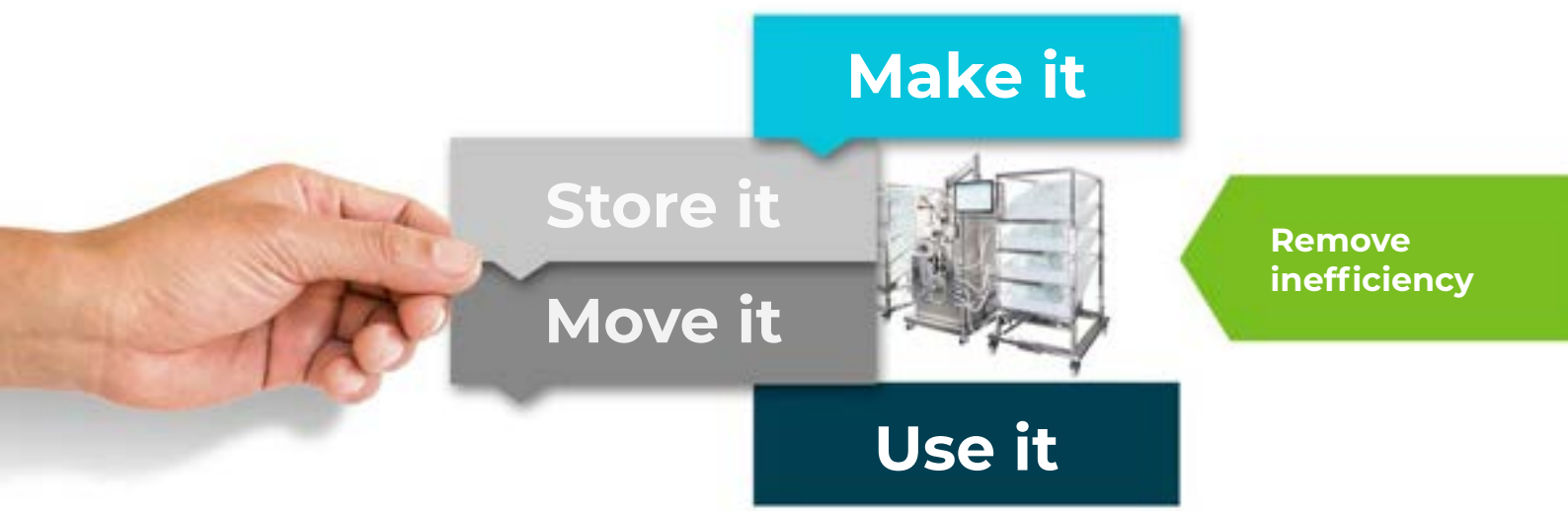
The solution

The standard Allegro Connect Buffer Management System comprises of a control unit and two buffer workstations. The system uses buffer concentrates and dilutes in-line at point of use, thereby reducing the space requirement dedicated to buffer storage hold areas and reducing the labor required to move heavy vessels from the buffer storage area to unit operations.



Streamlined, efficient workflow

The holistic solution streamlining the entire buffer management workflow.



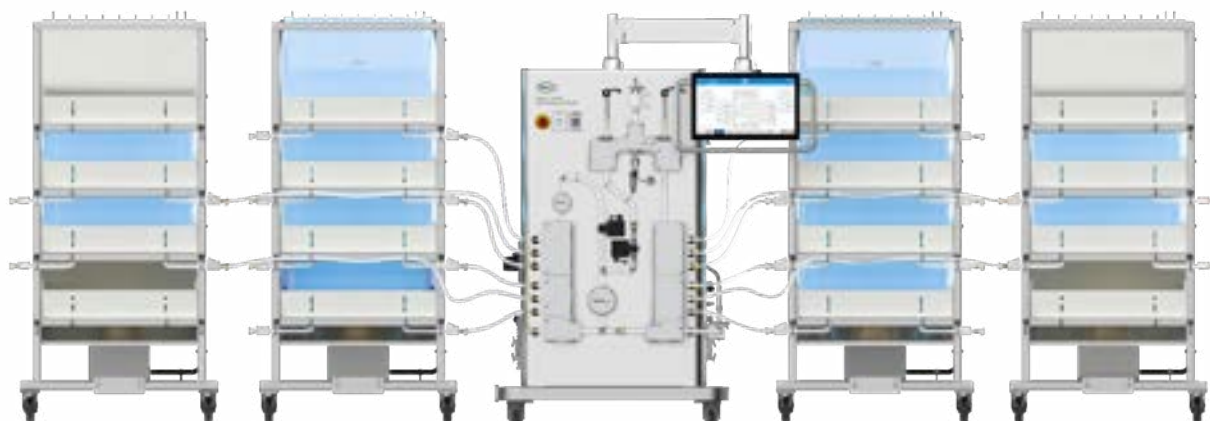
Flexible design for multiple applications

The Allegro Connect Buffer Management System is a flexible system designed for pilot scale, clinical batches, and commercial production.

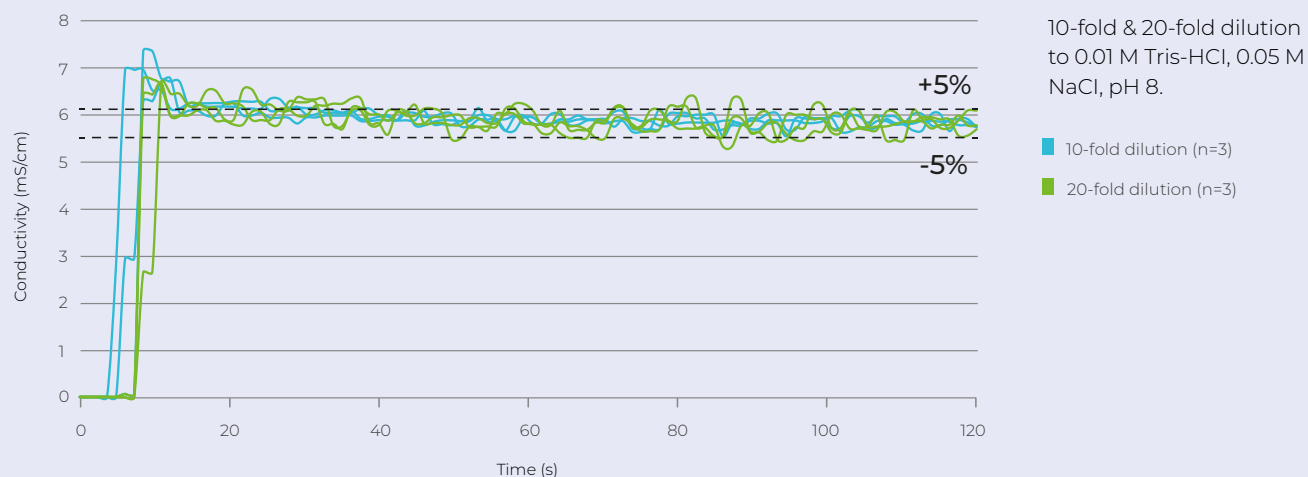
The modular system design enables up to six high volume process buffers to be supplied as required*, one at a time, directly to the batch unit operation such as chromatography or tangential flow filtration (TFF) based on buffer inline-dilution and utilizing a single-use flow path. Multi-column chromatography (MCC) application buffer requirements can also be met by the Allegro Connect Buffer Management System, delivering a maximum of four process buffers at the same time to the MCC chromatography system.

Buffer concentrates are diluted in-line with WFI; dilution factors are typically 5 – 20-fold resulting in much smaller initial volumes of buffer required, reduced capex spend on large mixing/hold vessels, and reduced labor costs.

* Six buffers can be supplied when using two workstations on each side (concentrate and process).



In-line dilution buffer stability conductivity control (10-fold and 20-fold)



Conductivity set-point = 5.83 mS/cm \pm 5%, pH set-point = 8 \pm 0.15

Up to 75% footprint reduction

The Allegro Connect Buffer Management System has been designed to simplify and compact the buffer workflow.

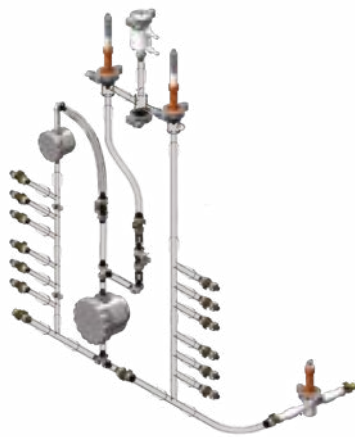
The reduction in the overall footprint of buffer preparation/hold and storage vessels enables up to 75% valuable facility floor space savings. This allows buffer prep/buffer hold areas to be re-purposed for value added activities, therefore, increasing plant productivity kg/m² and increasing facility utilization, which is especially important when multiple therapeutics are manufactured at one site.



Utilizing single-use technology for maximum productivity

The Allegro Connect Buffer Management System utilizes single-use technology (SUT) to ensure faster turnaround times between product batches, eliminating the need for clean-in-place (CIP) and steam-in-place (SIP) operations and associated cleaning validation, and reducing maintenance costs and system downtime, thereby ensuring that plant productivity is higher.

Unique SUT components ensure that process control and monitoring are robust and with an option for single-use flowmeters for additional process assurance if required. The entire flow path has been designed for easy installation and removal, with clearly-marked connections and a shadow board to clearly guide the user. With minimal hold up volume and optimized flow path design to ensure rapid flushing between different process buffers.

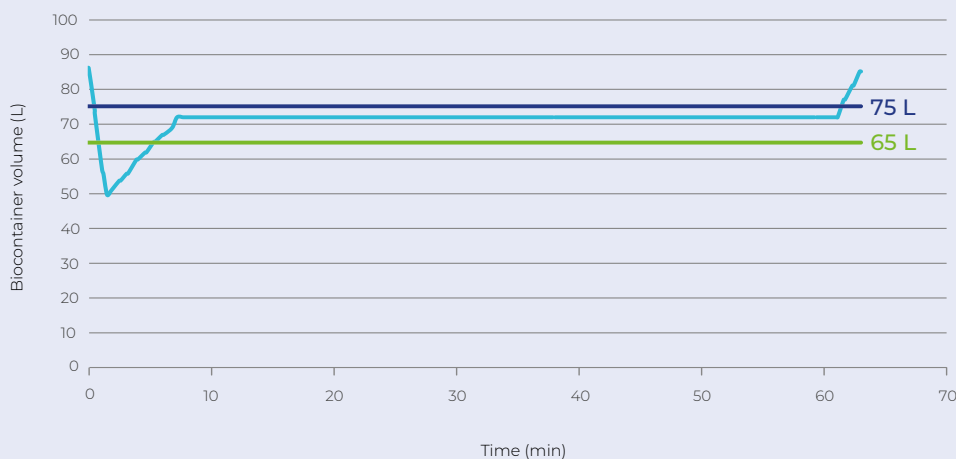


Allegro Connect Buffer System single-use inline dilution manifold



Installed single-use manifold

Process biocontainer volume during 1200 L/h draw



In-line buffer dilution level control in process biocontainer at a draw rate of 1200 L/h and 10-fold dilution factor.

- Surge biocontainer volume
- Volumetric set-point
- Re-fill set-point

10-fold dilution to 0.01 M Tris-HCl, 0.05 M NaCl, pH 8 remained stable for > 60 minutes of production

Process flexibility

The growth in the type and number of different therapeutic drugs results in increasing buffer volumes and number of buffers required for unit operations such as chromatography.

The Allegro Connect Buffer Management System can deliver up to **6 process buffers with 100 L concentrates** or **4 buffers with 200 L** concentrates to meet high-volume demands.



Increased assurance

The Allegro Buffer Management System has a bioburden protection option to provide increased assurance against microbial contamination. Each in-specification buffer can be filtered prior to filling the process biocontainer, with up to six single-use capsule filters with automated capsule venting to ensure ease-of-use. Additional bioburden protection can be achieved by using SU manifolds with sterile connectors to maintain a low bioburden.



Allegro Connect Buffer System with optional filtration step for increased assurance

Designed for ease of use

The Allegro Connect Buffer Management System has undergone extensive user testing, to ensure the system is simple and intuitive to use, fits with operators' existing workflows, and eliminates the risk of user error.

The system features on-screen visual instructions and shadow-boarding to guide users to ensure correct manifold installations of the single-use systems. In-line monitoring of buffer concentrates acts as an additional safety check that manual installation activities have been successfully completed.



Cost of ownership model

A total cost of ownership model will enable comparison between existing in-house buffer costs/L and the impact of investing in the Allegro Connect Buffer Management solution. Please contact Pall for details.



System options

- PLC and HMI for local stand-alone control
- Remote I/O (no PLC) for integration into a DCS or SCADA system
- Remote I/O (no PLC) controlled by centralized PLC system

The Industry 4.0 ready automation platform will be applied across Pall's range of bioprocessing systems enabling a truly modular 'plug-and-play' capability, with the ability to control single or multiple unit operation from one centralized cabinet. All PLC options are available in both Siemens* and Rockwell* platforms.

The Allegro Connect Buffer Management System is compatible with chromatography/TFF systems from other vendors. The Allegro Connect System monitors the liquid level in the process solution biocontainers and automatically produces buffer when it detects that buffer is being drawn by the unit operation. This eliminates the need for communication between systems and simplifies compatibility for use with non-Pall systems.



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-compiled of:

- Regulatory compliance ROHS I to ROHS III directives
- Raw material compliance data (USP Standards)
- Packaging and packaging waste directive 94/62/EV

Pall automation platform enables compliance with 21 CFR Part 11 and follows the GAMP life cycle for software development.

Technical specifications

System dimensions and weight

Capacity	System	Workstation	Bioburden filter trolley
Weight	751 kg	171 kg	90 kg
Dimensions (W × D × H)	1120 mm × 1120 mm × 1990 mm	1000 mm × 1300 mm × 2000 mm	400 mm × 1200 mm × 1300 mm

Allegro Buffer Management System specifications

Equipment	Quantity	Specification
WFI pump (single-use diaphragm)	1	20 – 1200 L/h
Buffer concentrate pump (single-use diaphragm)	1	1 – 180 L/h
Tubing internal diameter (ID)	N/A	½ in. (1.27 cm)
Pressure sensor range	1	0 – 4 barg (2 barg max)
Temperature rating		4 – 40 °C
Inlets	Maximum 6 inlets per system, 4 inlets per workstation	
Outlets	Maximum 6 outlets per system, 4 outlets per workstation	
pH probe range and accuracy	1	3 – 10 pH ± 0.15 pH unit
Conductivity probe range and accuracy	2	1 µS/cm – 300 mS, ± 3% at 1 – 100000 µS/cm, ± 5% at 100 – 300 mS/cm
Workstation liquid level sensor range and accuracy	4 per workstation	20 – 100 L ± 10%
Manifold installation test port	1	N/A
Flowmeter-electromagnetic (option)	2	0 – 20 L/min, (± 1%) of measured value
Pneumatic air supply	1	6 barg
Power supply	1	280 V AC, 50 – 60 Hz (UL version), 230 V AC, 50 – 60 Hz (CE version)

Materials of construction

Single-use manifold

Components	Materials
Tubing	Platinum cured silicone
Diaphragm pump head (1200 L/h and 150 L/h versions)	Polypropylene; EPDM (ethylene propylene elastomer), Santoprene*
Manifold connectors	Polysulfone, silicone
Fittings	Polypropylene
Pressure sensor	Polysulfone
Flow sensor	Polysulfone, Hastelloy* C22
pH sensor	Silicone (platinum-cured), glass
Conductivity sensor	Stainless steel 1.4435, PEEK (polyetheretherketone), EPDM (ethylene propylene elastomer)
Allegro storage biocontainer bag chamber, 100 L	High-density polyethylene (HDPE), ultra-low density polyethylene (ULDPE)
Gaskets ½ in. sanitary connection	Silicone (platinum-cured)
MPX connector (male) to ½ in. hose barb	Polysulfone

Workstation

Components	Materials
Workstation tray	Polypropylene (non-wetted)
Workstation frame	Stainless steel 1.4301 (304)

Control system

Components	Materials
System cabinet	Stainless steel 1.4301 (304)

Ordering information

Automated system, workstations and bioburden filter trolley

Part number	Description
ACBMSEUPLC	Allegro Connect Buffer Management System: PLC 230 V AC, software automation, buffer workstations (maximum 4 buffers)
ACBMSWHPLC	Allegro Connect Buffer Management System: PLC 208 V AC, software automation, 2 buffer workstations (maximum 4 buffers)
ACBMSEUIO	Allegro Connect Buffer Management System: I/O 230 V AC, DCS ready no automation, 2 buffer workstations (maximum 4 buffers)
ACBMSWHIO	Allegro Connect Buffer Management System: I/O 208 V AC DCS ready no automation, 2 buffer workstations (maximum 4 buffers)
ACBMSSWS	Allegro Connect Buffer Management workstation (concentrate or process), provides capability for additional 2 buffers
ACBMSSFSK	Allegro Connect Buffer Management System flow sensor kit
ACBMSSFT	Allegro Connect Buffer Management System bioburden filter trolley (230 V AC)
ACBMSSFTWH	Allegro Connect Buffer Management System bioburden filter trolley (208 V AC)

Single-use manifolds

Part number	Description
6431-1417W	½ in. tubing with 100 L biocontainer
6431-1457D	½ in. tubing with 100 L biocontainer and Kleenpak® Presto Sterile Connectors
6431-1417Z	½ in. EKV filter capsule set
6431-1418A	½ in. EKV filter capsule set with Kleenpak Presto Sterile Connectors, 1 m tubing
6431-1418B	½ in. EKV filter set with Kleenpak Presto Sterile Connectors, 1.5 m tubing
6431-1418C	½ in. EKV filter set with Kleenpak Presto Sterile Connectors, 2 m tubing
6431-1418E	½ in. buffer transfer line, 0.7 m tubing
6431-1418F	½ in. buffer transfer line, 1.6 m tubing
6431-1418G	½ in. buffer inlet tube kit 1 m
6431-1418H	½ in. buffer inlet tube kit 1.5 m
6431-1418J	½ in. buffer inlet tube kit 2 m
6431-1418K	½ in. buffer outlet tube kit 1 m
6431-1418L	½ in. buffer outlet tube kit 1.5 m
6431-1418M	½ in. buffer outlet tube kit 2 m
6431-1418N	¼ in. capsule filter bleed line
6431-1420S	½ in. inlet buffer manifold including flow sensor
6431-1420T	½ in. inlet buffer manifold excluding flow sensor
6431-1420U	½ in. outlet buffer manifold
6431-1420V	½ in. drain control manifold
6431-1568K	½ in. waste transfer line 2 m
6431-1567F	½ in. WFI transfer line 2 m

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 product from multiple global sites.

Process development services

Prior knowledge is a rare and valuable commodity, especially when preparing to take a new direction or when under pressure to deliver to a tight deadline. Take advantage of Pall's experience, process knowledge and technical know-how to help you achieve your goals.

From the optimization of an end-to-end continuous process to establishing the right parameters for a single unit operation, our teams of scientists are ready to work with you and to generate the data you need to make the critical decisions necessary for success.

Scientific and laboratory services

The scientific and regulatory knowledge that supports the selection, adoption and ongoing use of critical process technology, coupled with analytical, imaging and measurement capabilities, creates a versatile and practical resource ready to respond to an ever changing industry. Pall duplicates these laboratories across the globe and leverages their cumulative knowledge to deliver practical scientific and regulatory support to all process technologies to keep you moving forward.

Technical support

The accessibility of local technical support networks minimizes delays in your journey at all points. From the early stage of process development to on-site support for mature processes, Pall's technical support groups are there to help remove barriers to progress and to make your journey as rapid and stress free as possible. Our knowledge of the technology and the process can be applied to everything from training to trouble-shooting and consultancy. Our global team of technology experts are on hand to respond to your changing needs.

Advanced separation systems

Operating within the defined design space demands the monitoring and control of critical process parameters to assure product quality. Systems that control critical unit operations and that communicate with your existing process components can control process risks and maximize productivity by reducing operator involvement for many processes, Pall applies strong engineering and regulatory understanding to deliver compliant and qualified systems that safeguard and simplify your journey.

Integrated solutions

Coupling critical technologies removes process risk and simplifies manufacture with automated, turn-key processes. Our teams of dedicated engineers and scientists apply the best engineering practices to define, design and deliver the systems you need to ensure you arrive at a solution that advances your manufacturing operations. Once delivered we continue to support you to ensure trouble-free operation throughout the life-cycle of your process.

Validation services

Arriving at your destination counts for nothing without the necessary paperwork to proceed to the next stage. Pall's Validation Services are committed to delivering the supporting data packages and analysis required to quantify process risk and to support regulatory submission.

Our strengths include critical filtration technologies such as the performance validation of sterilizing-grade filtration, and we are at the forefront of the evolving needs in the area of extractables and leachables for all product contact components. We combine the generation of data with interpretation and consultancy to deliver data packages that are ready for regulatory scrutiny and to ensure there are no barriers to progress.

Service plans

Having access to agile and proprietary service and support is pivotal to every facility. Pall Corporation has over 70 years of experience in providing repair, calibration, maintenance, and other services. Whether you work in research, process development, clinical or commercial manufacturing, we have a service plan tailored to you. We understand and are cognizant of the criticality surrounding planning to service biotechnology capital equipment, which is why we provide a tiered level of support in our Pall service plans to provide the assistance you need to protect your investment and optimize your workflow productivity, ensuring cost savings when compared to purchasing services individually.



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