Allegro™ Connect

BUFFER MANAGEMENT SYSTEM

Allegro™ Connect buffer management systems (Fig 1) provide robust, accurate and automated platforms that integrate with your manufacturing processes, 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.

Fig 1. The Allegro Connect buffer management system.

Providing in-line dilution of buffer at point of use

The Allegro Connect buffer management system is designed to simplify and improve 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% [1].

[1] Buffer cost overview model (please contact your representative for further details).

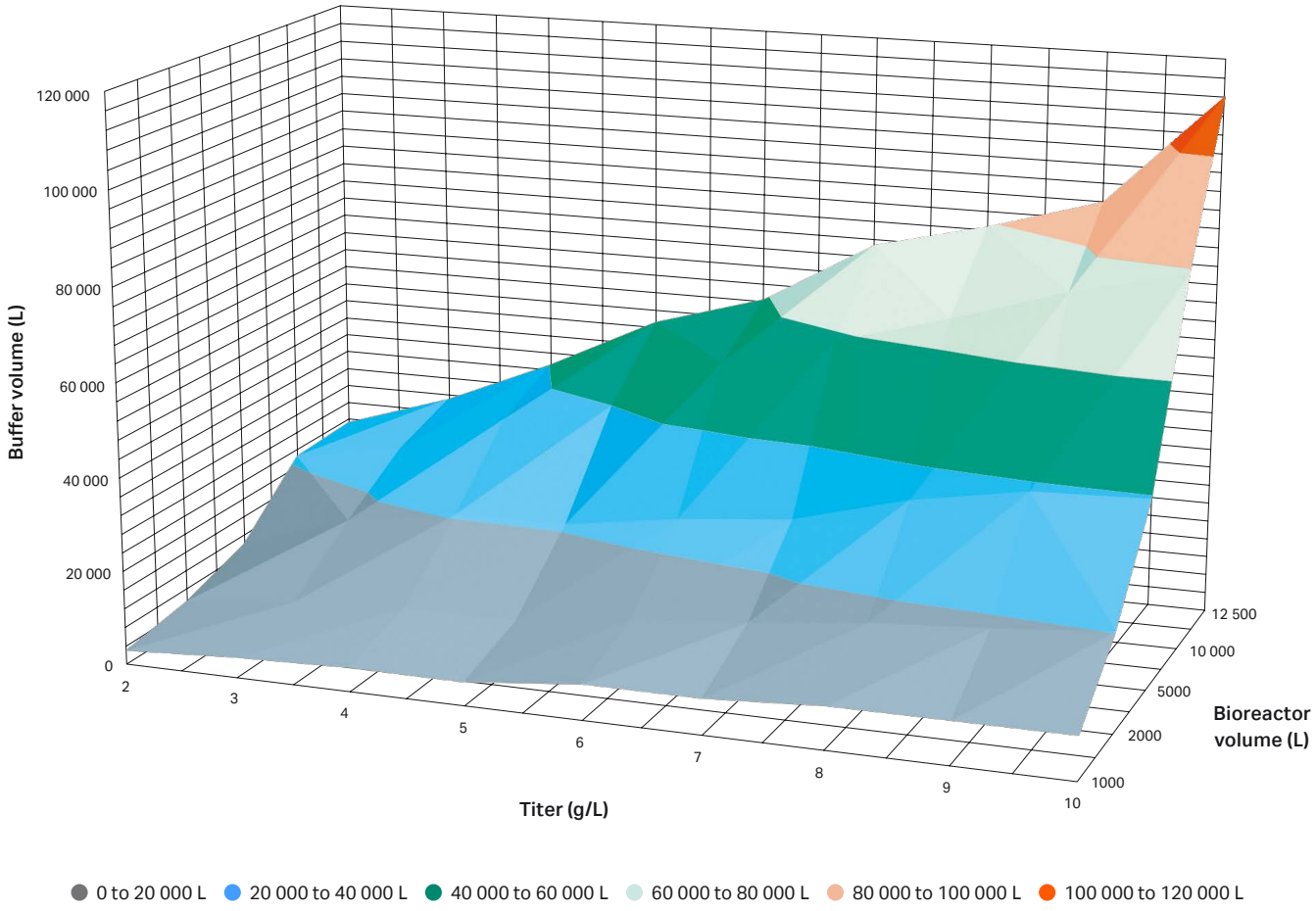
The problem

With increasing product titers, greater volumes of process buffer are required to meet processing demand (Figure 2). 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.

Fig 2. Buffer demand across various scales of production.

The solution

The standard Allegro Connect buffer management system comprises a control unit and two buffer workstations (Fig 3). 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.

Fig 3. Touchscreen, maneuverable human machine interface (HMI) for efficient operator interaction.

Flexible design for multiple applications

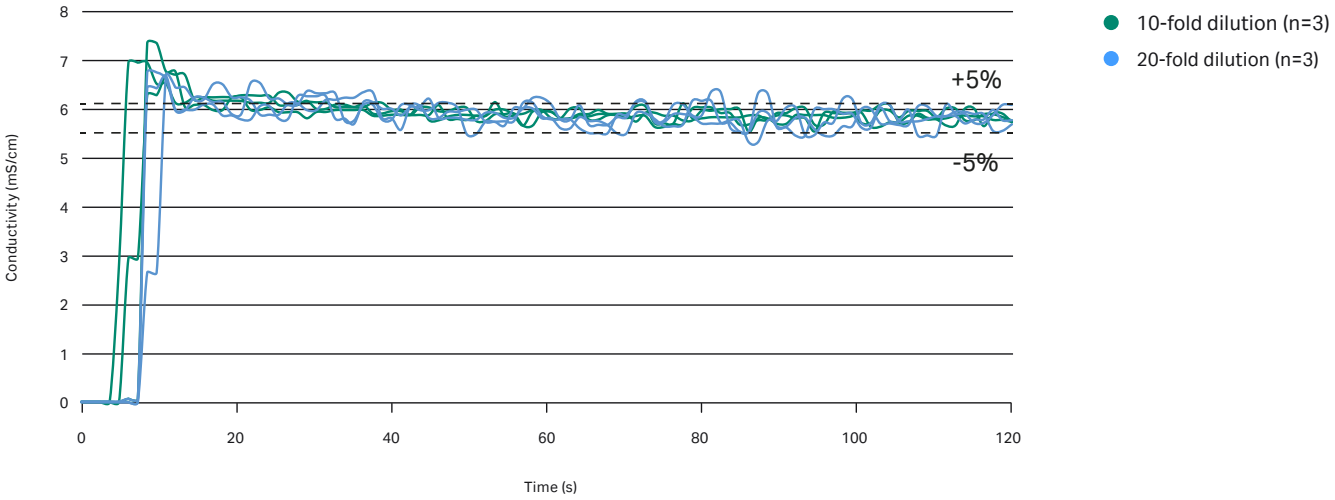
The Allegro Connect buffer management system is a flexible system designed for pilot scale, clinical batches, and commercial production.

The modular system design enables up to six high-volume process buffers to be supplied as required [2], 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 (Fig 4). 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 to 20-fold resulting in much smaller initial volumes of buffer required, reduced capex spend on large mixing/hold vessels, and reduced labor costs (Fig 5).

Fig 4. Allegro Connect buffer management system in six buffer configuration.

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



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

Fig 5. In-line dilution buffer stability conductivity control at 10-fold and 20-fold dilution to 0.01 M Tris-HCl, 0.05 M NaCl, pH 8.

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 (Fig 6 and 7). This allows buffer prep/ buffer hold areas to be re-purposed for value added activities, therefore, increasing plant productivity kg/m^2 and increasing facility utilization, which is especially important when multiple therapeutics are manufactured at one site.

Fig 6. Mobile workstations.

Fig 7. Installed single-use manifold.

Utilizing single-use technology for maximum productivity

The Allegro Connect buffer management system utilizes single-use (SU) technology to minimize 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 helping to improve plant productivity (Fig 8).

Special SU 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. Minimal hold-up volume and an optimized flow path design help ensure rapid flushing between different process buffers.

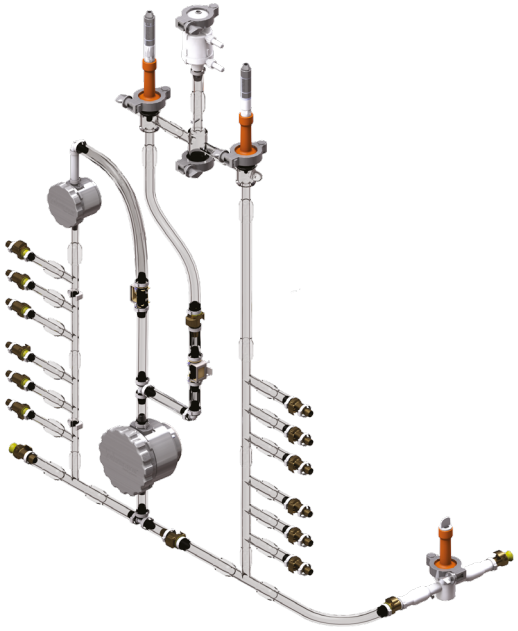


Fig 8. Allegro Connect buffer system single-use inline dilution manifold.

An in-line buffer dilution level control in a process biocontainer at a draw rate of 1200 L/h and 10-fold dilution factor is shown in Figure 9. The 10-fold dilution to 0.01 M Tris-HCl, 0.05 M NaCl, pH 8 remained stable for > 60 minutes of production.

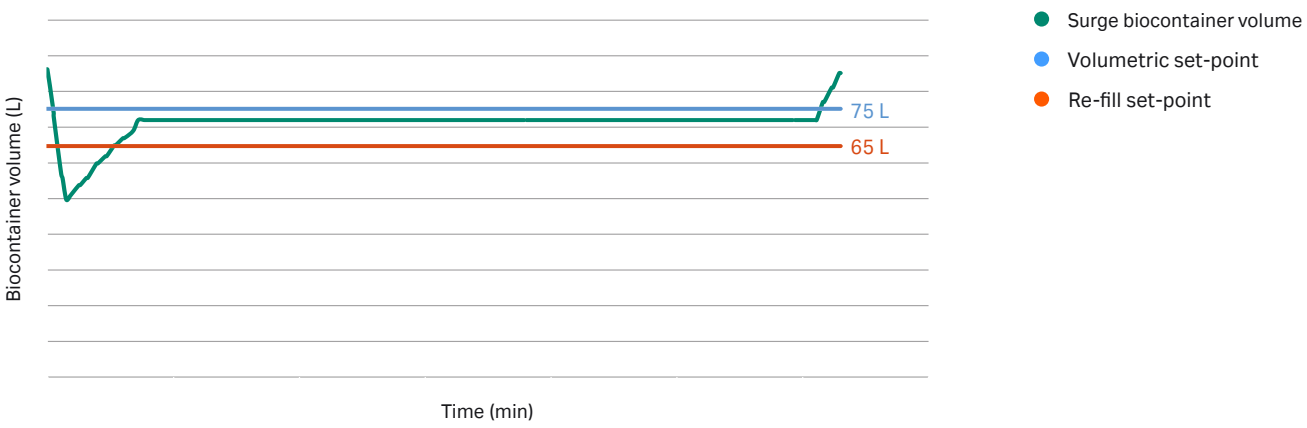


Fig 9. In-line buffer dilution level control in process biocontainer at a draw rate of 1200 L/h and 10-fold dilution factor.

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 Connect buffer management system has a bioburden protection option to provide increased assurance against microbial contamination (Fig 10). 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.

Fig 10. 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 minimizes the risk of user error.

The system features on-screen visual instructions (Fig 11) 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.

Fig 11. Touchscreen HMI with on-screen visual instructions.

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 (Fig 12). Please contact Cytiva for details.

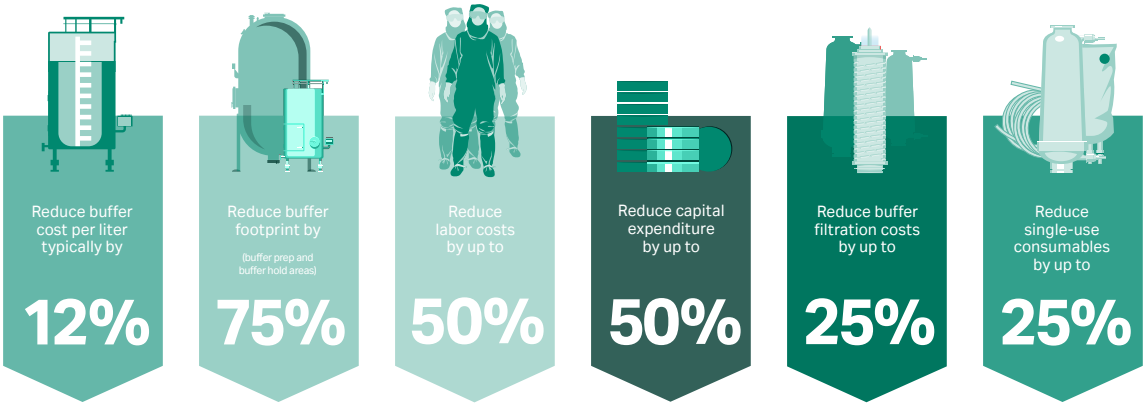


Fig 12. Comparative savings.

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 our range of Allegro Connect bioprocessing systems, enabling a truly modular 'plug-and-play' capability, with the ability to control single or multiple unit operations 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 Cytiva 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

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

Fig 13. Automation options.

Technical specifications

System dimensions and weight

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

Allegro Connect buffer management system specifications

Equipment	Quantity	Specification
WFI pump (single-use diaphragm)	1	20 to 1200 L/h
Buffer concentrate pump (single-use diaphragm)	1	1 to 180 L/h
Tubing internal diameter (ID)	N/A	½ in. (1.27 cm)
Pressure sensor range	1	0 to 4 barg (2 barg max)
Temperature rating		4°C to 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 to 10 pH ± 0.15 pH unit
Conductivity probe range and accuracy	2	1 µS/cm to 300 mS, ± 3% at 1 to 100000 µS/cm, ± 5% at 100 to 300 mS/cm
Workstation liquid level sensor range and accuracy	4 per workstation	20 to 100 L ± 10%
Manifold installation test port	1	N/A
Flowmeter-electromagnetic (option)	2	0 to 20 L/min, (± 1%) of measured value
Pneumatic air supply	1	6 barg
Power supply	1	280 V AC, 50 to 60 Hz (UL version), 230 V AC, 50 to 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; Ethylene Propylene Elastomer (EPDM), 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, Polyetheretherketone (PEEK), EPDM
Allegro storage biocontainer bag chamber, 100 L	High-density polyethylene (HDPE), ultra-low density polyethylene (ULDPE)
Gaskets 1½ 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

Product	Product code
Allegro Connect buffer management system: PLC 230 V AC, software automation, buffer workstations (maximum 4 buffers)	ACBMSEUPLC
Allegro Connect buffer management system: PLC 208 V AC, software automation, 2 buffer workstations (maximum 4 buffers)	ACBMSWHPLC
Allegro Connect buffer management system: I/O 230 V AC, DCS ready no automation, 2 buffer workstations (maximum 4 buffers)	ACBMSEUIO
Allegro Connect buffer management system: I/O 208 V AC DCS ready no automation, 2 buffer workstations (maximum 4 buffers)	ACBMSWHIO
Allegro Connect buffer management workstation (concentrate or process), provides capability for additional 2 buffers	ACBMSWS
Allegro Connect buffer management system flow sensor kit	ACBMSFSK
Allegro Connect buffer management system bioburden filter trolley (230 V AC)	ACBMSFT
Allegro Connect buffer management system bioburden filter trolley (208 V AC)	ACBMSFTWH

Single-use manifolds

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

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
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