



Biotech

USD 3304¹



The freedom to choose
your biotech journey

Buffer and Media Preparation Technology Guide

Preparation, Storage and Transfer
of Buffers, Media and Process Additives



Continuously Improving Bioprocesses

Upstream

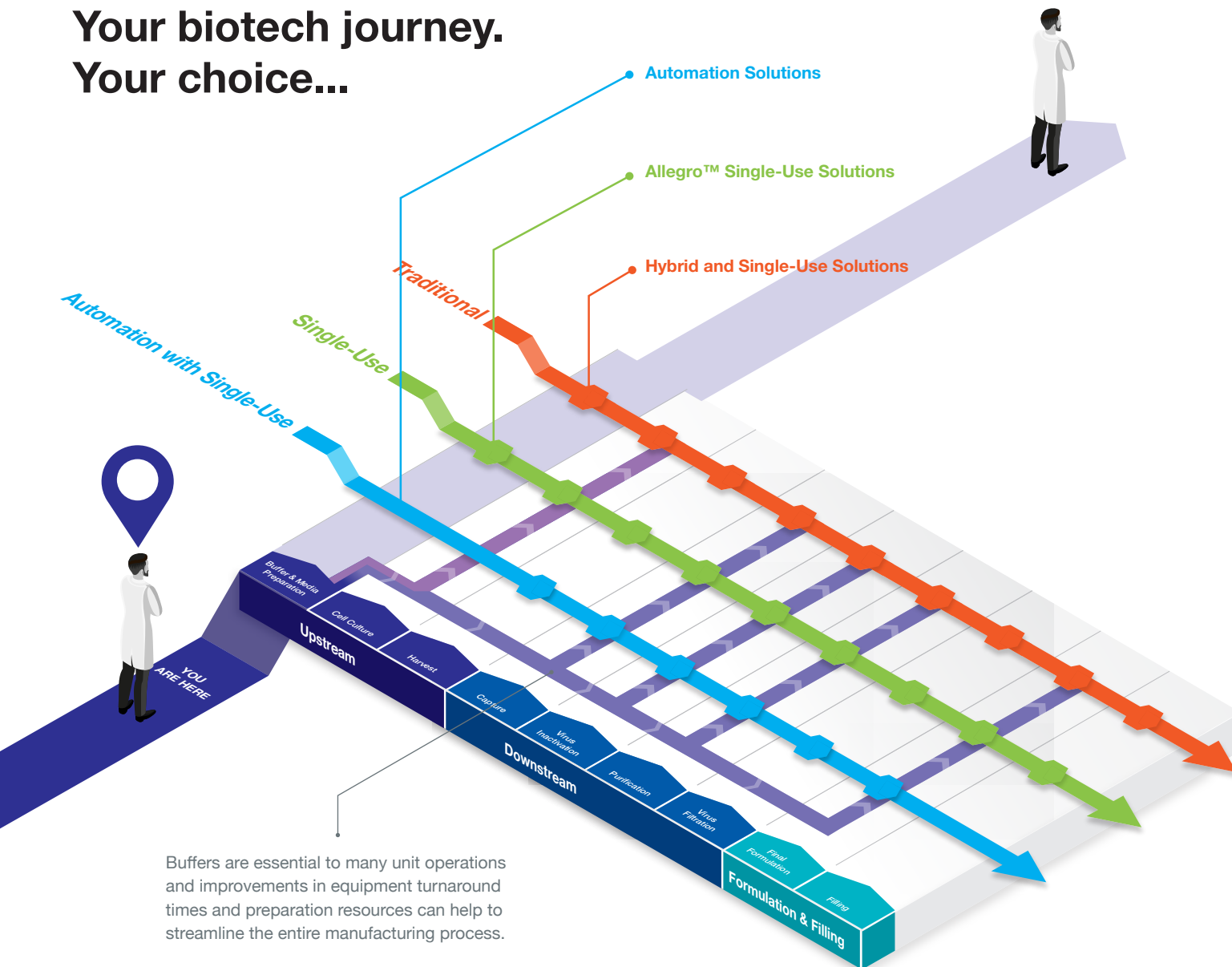
Buffer and Media Preparation

The ongoing evolution of biotech manufacturing technology multiplies the choices relating to the best approach to processing.

Historically process choices may have been limited to the selection of the critical consumables and level of system automation and restricted by the availability of solutions at the desired volume. The maturation and acceptance of single-use technology to meet the changing manufacturing drivers and the realization of long-awaited continuous processing options has multiplied the opportunities for change and with it, the complexity of the decisions.

At Pall Biotech we not only have the technology but we have the know-how to help you make the best choice depending on your unique process requirements.

**Your biotech journey.
Your choice...**



Buffers are essential to many unit operations and improvements in equipment turnaround times and preparation resources can help to streamline the entire manufacturing process.

On your own unique journey, you have reached buffer and media preparation – the next step is critical because it involves choices – choices that relate to the best route towards your process optimization, whether it be **hybrid**, **single-use** or **automated**.

With real-world facility and regulatory constraints, not all choices are accessible to every process. Pall's unique portfolio offers end-to-end solutions that support all manufacturing choices. From reusable systems or single-use alternatives to the cutting-edge of continuous processing, Pall Biotech delivers consumables, systems and know how to support you at every stage of every possible journey.

Buffer - The Forgotten Process

The preparation, filtration and storage of process buffers, prior to use in numerous unit operations throughout a typical process, can often be a serious bottleneck. The careful scheduling to assure the delivery of preparative fluids, including the provision of cleaned vessels, fluid preparation, storage, transport, use and then cleaning of any re-usable fluid contacting parts combines to create a logistical challenge that can quickly erode available resources.

The adoption of single-use and automated equipment may minimize the resources required to deliver these fluids where they are needed. These same choices may be applied differently depending on the process scale and can integrate with existing infrastructure to create a hybrid solution tailored to the individual facility and process needs.

Journey Choices

Your guide to buffer and media preparation using Pall technology.

Whether your preference is to leverage the benefits of a manual single-use processing philosophy or to incorporate a degree of automation to improve productivity, this guide provides a technology overview to rapidly identify the best-fit technology, enable quick selection, and fast-track process expansion.

**The freedom to choose
your biotech journey**

Supporting Every Step

Every process is unique however, there are common challenges that are met throughout the process with a versatile set of technologies that support the total process.

Fluid Transfer

Kleenpak® Presto Sterile Connectors

Simple and secure connectivity to support flexible fluid preparation and transfer.

Kleenpak Sterile Disconnectors

Secure, tool-free flowpath disconnections for robust and flexible processing.

Buffer and Media Preparation

Allegro™ Powder Handling Bags

Supporting the containment and controlled addition of formulation powders and solids.

Powder Bag Lifts and Accessories to support, and control, the filling and movement of powder handling bags.

Contamination Control

Bioburden Reduction Filtration

High flow, high capacity, single-use filters and capsules for the control of microbial contamination.

Supor® EAV 0.2 µm bioburden reduction filters are perfect for the filtration of large volumes of non-critical fluids.

Supor EKV 0.2 µm sterilizing grade filters are the universal choice and offer the highest bioburden controls for cell culture media, culture additions, process buffers and drug intermediates.

Supor EX ECV 0.2 µm sterilizing grade filters for high flow and excellent throughput for the efficient filtration of large volumes of buffers and high viscosity fluids.

Fluorodyne® EX EDT 0.1 µm mycoplasma control filters are optimized for the control of non-chemically defined media including serum and soy containing cell culture media.

Palltronic® Flowstar IV Integrity Test Instruments

For critical buffers, process additives and intermediates requiring the assurance of filter integrity.



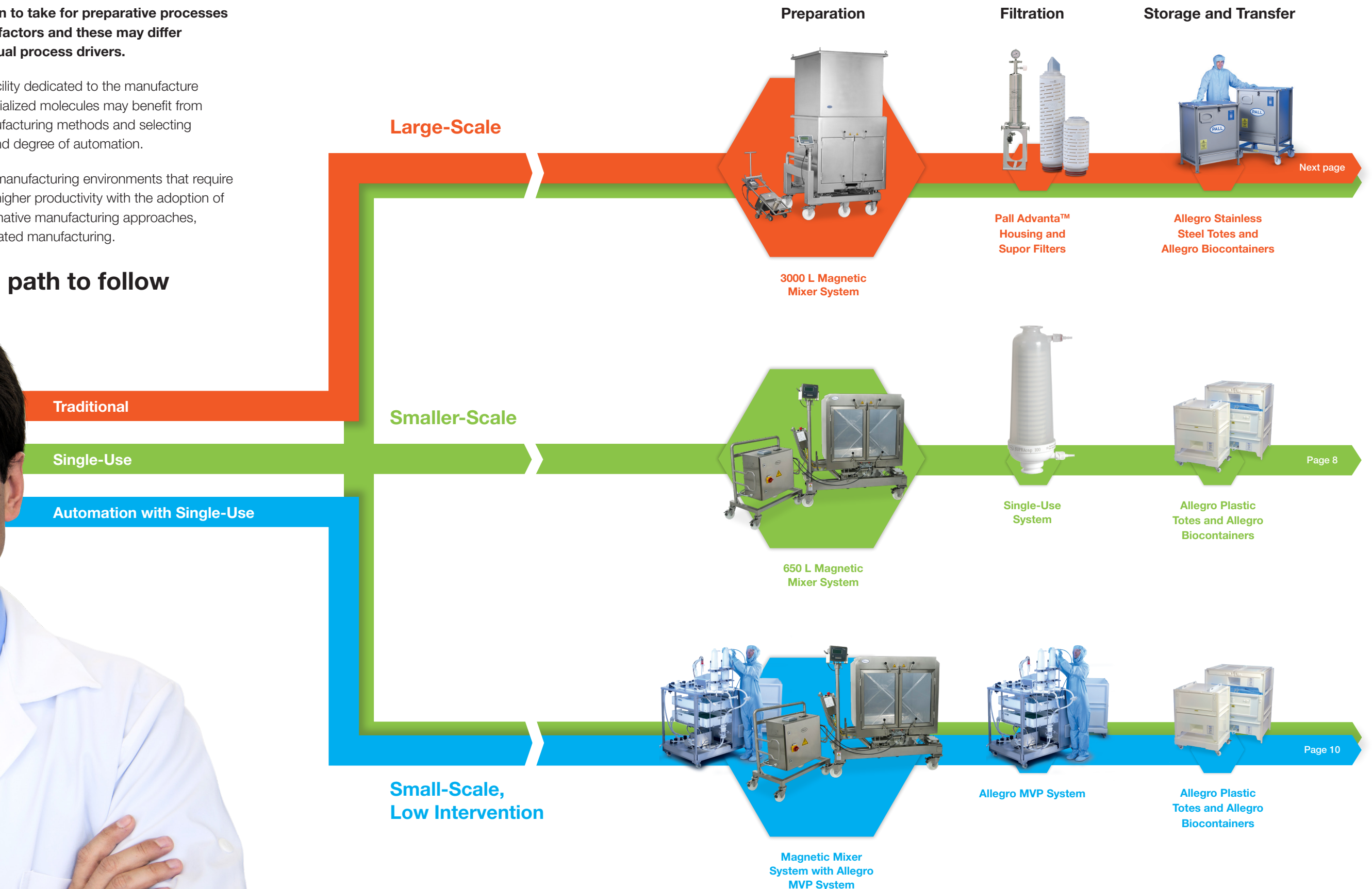
Buffer and Media Preparation Guide

Identifying the best direction to take for preparative processes is dependent on numerous factors and these may differ depending upon the individual process drivers.

Process expansion within a facility dedicated to the manufacture of a small number of commercialized molecules may benefit from maintaining the historical manufacturing methods and selecting hardware based upon scale and degree of automation.

Processes that look to fit into manufacturing environments that require greater flexibility may achieve higher productivity with the adoption of technology that supports alternative manufacturing approaches, such as single-use and automated manufacturing.

Deciding which path to follow



Taking the Traditional Route

Buffer and Media Preparation

The use of large scale, stainless steel vessels and mixers for the preparation, transport and storage of buffers and cell culture media is the historical norm. Unlike product contact surfaces, the validation burdens associated with the adoption of single-use alternatives for cell culture media and non-critical process buffers are significantly lower, aligned with appropriate risk assessments. This reduces the barriers to change and many start their journey towards greater adoption of single-use technology by creating hybrid processes including elements of single-use for the preparation, and storage of these fluids.

Pall's extensive range of mixers, filtration and storage solutions extends to support the large volumes common in mature, large-scale manufacturing processes.

Autoclaved components and other reusable hardware integrate easily with single-use components through the use of sterile connectors, disconnectors and well designed manifolds. Each design draws upon Pall's long history in helping to access the benefits of single-use without compromise to the existing process.

- Rapid process changeover
- Ergonomic, easy to operate and control hardware
- One portable universal drive for all biocontainer sizes
- Accommodates scaling from 6 L to 3000 L
- Robust mixing for challenging powder applications
- Simple and quick single-use system installation

Fluorodyne EX EDT 0.1 µm Filtration
High mycoplasma control for the filtration of non-chemically defined media formulations

Supor ECV or EKV 0.2 µm Filtration
High flow, scalable filtration for the highest bioburden controls in buffer and chemically defined media



Cleansteam™ Autoclave Bags
Sterilizable packaging to support the autoclaving and movement of process components



Kleenpak II Sterile Connectors
Large bore sterile connections to support the rapid transfer of high volumes of buffer and media



Kleenpak Sterile Disconnectors
Secure disconnections made simple, separating process elements to keep production areas free from used equipment

Pall Advanta Filter Housings
Quality housings with aseptic design for process security and cleanliness

Traditional



Allegro Stainless Steel Totes
100 - 3000 L totes and biocontainers for the storage of liquid buffer components and concentrates



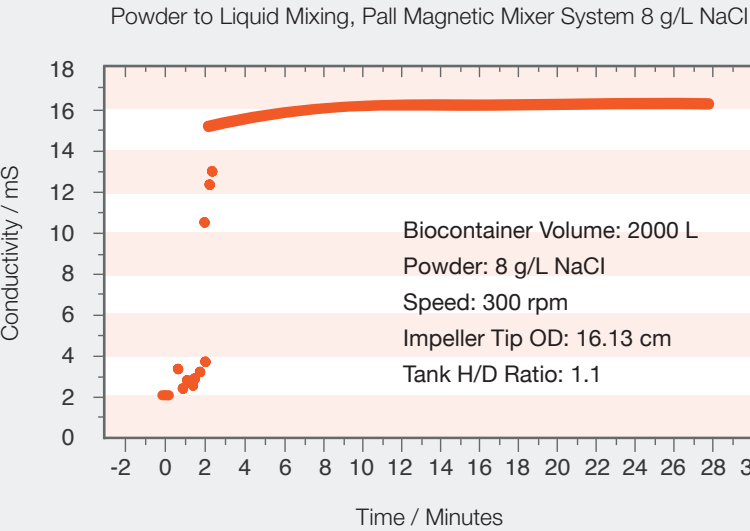
Magnetic Mixer System
Tank volumes range from 30 L to 3000 L and each can be driven by a single, interchangeable, mobile drive unit. Tanks are fitted with single-use mixing systems containing a magnetically-driven impeller for exceptional robustness and cleanliness

Supor Filters



Allegro Stainless Steel Totes and Allegro Biocontainers
Where buffer preparation takes place off site, the range includes transportable totes qualified to meet International Safe Transit Association (ISTA) 3H, and United Nations Economic Commission for Europe (UNECE) standards to assist in the safe movement of fluids

Effective Solid-Liquid Mixing at Large Scale



Efficient mixing of buffer components with low mixing times using controlled mixing parameters assure repeatable performance to support unit operations that depend upon the availability of large volumes of process buffers.

Preparation of 2000 L of 8 g/L NaCl. Solid addition (16 kg NaCl) made in a single addition. 95% conductivity established after 6 minutes with equilibrium established at 15 minutes.



Reference: USD3028 -
Preparing 2000 L of an
8 g/L Salt Solution using a
Pall Magnetic Mixer System

- Best fit for **large-scale** manufacturing looking to access the benefits of single-use
- Supporting **hybrid solutions** that take the first step to access the benefits of single-use
- Scalable products to establish strong platform solutions for future process evolution

Palltronic Flowstar IV Instrument
User-friendly, compliant instruments for the simple testing of critical filters



The Single-Use Alternative

Buffer and Media Preparation

The adoption of a single-use manufacturing philosophy at all points throughout a typical process is rapidly developing as the go-to strategy to increase the productivity of existing facilities and to allow greater flexibility to meet changing demands on these facilities.

The most visible process benefits associated with the adoption of single-use technology include faster turnaround times and increased productivity due to the elimination of cleaning. As preparative vessels outnumber product contact vessels these benefits are quick to be seen in the preparation and storage of buffers.

As average process volumes reduce, establishing compact and effective single-use platforms that work well in highly productive, small footprint manufacturing facilities requires more than just a single product.

Pall's unique breadth of portfolio, coupled with a long standing knowledge that has evolved with the industry, allows the selection of optimal technology that works together to create an intuitive, flexible yet robust process.

Reducing Footprint

Adopting technology that is designed to work with smaller manufacturing areas reduces the amount of non-productive space to improve productivity and work flow. Simple features such as mixer drive units that work with multiple mixing vessels and stackable, collapsible plastic totes result in an increase in the available, usable facility space. Such an increase, however small, can open opportunities for greater efficiency, increased facility utilization and can give a new life to existing manufacturing environments.

Single-Use

The Pall Magnetic Mixer Range

Compact single-use mixing systems incorporating an innovative bottom-mounted magnetically-driven impeller to provide efficient high-torque mixing for powder-liquid and liquid-liquid mixing applications



Kleenpak Presto[®] Sterile Connectors
Intuitive and secure sterile connections to add process flexibility



Kleenpak Disconnectors
Secure disconnections made simple



Allegro Bioprocessing Workstations
Flexible workstations with trays and totes for storage of aliquots and small volumes from 20 L to 100 L



Allegro Transportation Totes
For the safe transport of buffer between sites



Allegro Single-Use Systems

From simple filter and tubing sets to complex systems to support sampling or *in situ* wetting and integrity testing, Pall can help you design a system that is perfect for your needs

Fluorodyne EX EDT 0.1 µm Filtration

High mycoplasma control for the filtration of non-chemically defined media formulations

Supor ECV or EKV 0.2 µm Filtration

High flow, scalable filtration for the highest bioburden controls in buffer and chemically defined media

Allegro Plastic Totes and Allegro Biocontainers

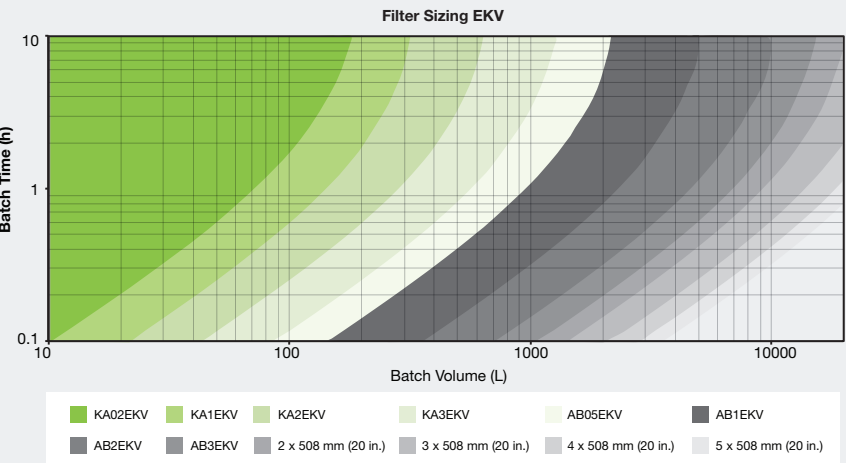
From 50 L to 500 L Allegro plastic totes are engineered to provide support for single-use systems in fluid management applications. The stackable, maneuverable and collapsible totes carry Allegro 3D single-use systems that require no operator intervention for filling and can be integrated with filtration systems to reduce set-up times to further improve process economics

Palltronic Flowstar IV Instrument

User-friendly, compliant instruments for the simple testing of critical filters



Sizing Your Sterilizing Grade Buffer Filter



Calculations assume high fluid filterability fluid ($V_{max} > 10,000 \text{ L/m}^2$) and a low average processing differential pressure of 500 mbar. For other conditions, please contact Pall for guidance or filterability trials to optimize filter selection and sizing for your process.

Simple buffers are typically highly filterable and filter sizing is normally driven by the desired process time. As such, high flow rate filters that are available in a wide variety of sizes, such as Supor EKV sterilizing grade filters, represent the perfect combination and deliver sterilizing grade filtration to achieve the highest degree of bioburden control. Sizing of filters for more complex media formulations may be more difficult with a significant variation in the filterability of the fluid having an impact of filter sizing where filter capacity is likely to be the critical sizing factor.

As a result we recommend that you contact Pall to assist. However, Fluorodyne II EX EDT 0.1 µm filters represent the gold standard for non-chemically defined media, where high mycoplasma removal is desirable to assure contaminant free cell culture media.

- Best fit for small to medium-scale and multi-product facilities
- A flexible platform of products for every process volume
- Simple, low-footprint buffer preparation and storage

Combining Automation with Single-Use Buffer and Media Preparation

Increasing product titers (>3 g/L) being achieved in bioreactors are outpacing current downstream processing capabilities - buffer preparation and delivery must increase in proportion with total process buffer volumes ≥ 8000 L per batch.

Older manufacturing plants have too much facility area dedicated to buffer storage tanks and buffer storage, which reduces the footprint available for value adding production. New facilities being constructed need to accommodate increasing manufacturing capacity to meet the expected growth in global therapeutic requirements, by maximizing commercial footprint and reducing storage area.

Automation combined with single-use technologies can help with evolution of more agile and multi-product manufacturing of biotherapeutics. Especially with the increasing volumes of buffer required for unit operations such as chromatography, SUTFF and cell harvest to ensure maximal yield and purity of the target molecule.

Automation with Single-Use

Allegro Plastic Totes and Allegro Bioprocessing Workstations

Allegro Single-Use Systems
From simple filter and tubing sets to complex systems to support sampling or *in situ* wetting and integrity testing, Pall can help you design a system that is perfect for your need

Analytics
pH, load cells, conductivity, temperature

Kleenpak™ Filter Capsules
Available from 200 cm² to more than 3 m² there is a filter capsule size to match perfectly with your process

Allegro Bioprocessing Workstation
For the storage and easy access of small volumes of buffers, ready for purification and formulation processes

Palltronic Flowstar IV Instrument
Integrating filter integrity testing into system design and recipe development



Control Software
DCS, SCADA & Islands of automation (PLC) work to integrate multiple systems and ensure seamless communication, control and reporting to good automated manufacturing practice (GAMP) guidelines



Allegro MVP System and Magnetic Mixer System
Combining the power of the Magnetic Mixer system with the control of the Allegro MVP system automates pH and conductivity adjustments through configurable recipes that deliver the same result at the touch of a button



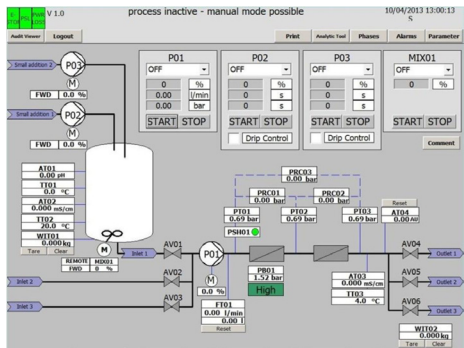
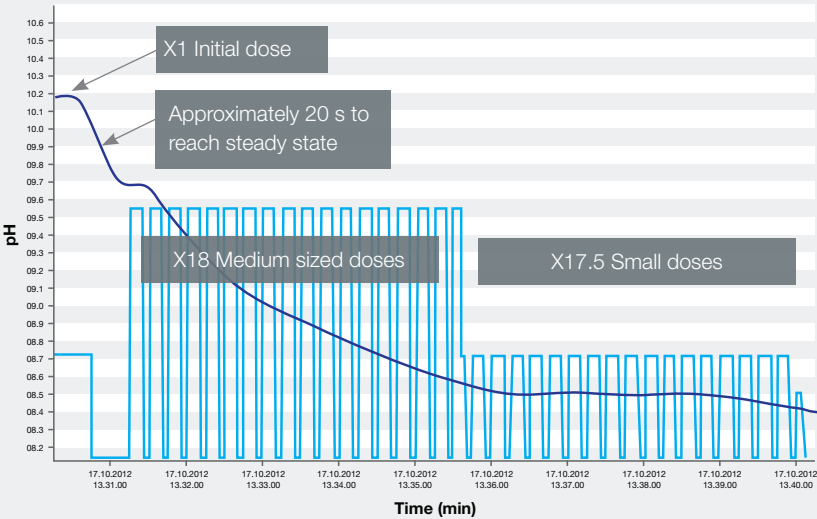
Allegro MVP System
This multipurpose system adds additional control and reporting to simple tasks such as filtration to ensure trouble free, reproducible operation



Allegro Plastic Totes and Allegro Biocontainers
Allegro Single-Use Systems
Integrating operations through good system design

Kleenpak Sterile Connectors and Disconnectors
Simplifying connectivity to deliver robust, flexible solutions

Controlling Preparation by Combining Single-Use Mixing and Automation



Main HMI operating screen of Allegro MVP system

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.

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 minimize 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.

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.

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.



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