Chromatography Hardware Technology Guide

Robust and Economic Purification Platforms Through the Selection of Optimal Hardware
The ongoing evolution of biotech manufacturing technology multiplies the choices relating to the best approach to processing.

Where once process choices may have been limited to the selection of the critical consumables and level of system automation, the maturation and acceptance of single-use technology to meet the changing manufacturing drivers, and the realization of long-awaited continuous processing options, multiplies 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.

Introduction

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 re-usable 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.

Hardware may be dedicated to an individual process operation. However, flexible hardware can be configured to accommodate multiple chromatography stages and support both packed column and membrane based purification technologies. Such systems minimize capital investment and may contribute to greater process agility for multipurpose and multiproduct facilities.

Chromatography hardware is typically sized from the dynamic binding capacity (DBC) of the sorbent selected. A higher DBC will reduce the overall bed volume required, however, choices remain that may have an impact on the process economy. For example, by dividing the culture volume into smaller sub-batches a single, large column may be replaced with a single, or multiple smaller columns and supporting hardware. Or cycling the column several times during the batch leads to the potential for fewer and/or smaller columns with subsequently lower capital investment, but at the expense of extending the process time.

Sorbents and Membrane Adsorbers

Every mAb is unique and may therefore demand the creation of a specific purification process. However, the application of a robust purification platform may fast track this development process. Pall’s model platform is below.

Kaneka KanCapA protein A sorbent
High capacity and highly NaOH resistant for highly productive processes with a long service life.

Mustang® Q membrane adsorber
High flow, high capacity single-use capsules for the efficient removal of high molecular weight species such as DNA.

CMM HyperCel™ CEX mixed-mode sorbent
Unique selectivity for the separation of proteins with similar isoelectric points and hydrophobicity at all conductivities.

Others chemistries that may assist include:

HEA, PPA and MEP HyperCel sorbents
A range of mixed-mode sorbents, each with unique selectivity.

HyperCel Star AX sorbent
High productivity protein capture at moderate or high conductivity.

Journey Choices

Your guide to chromatography using Pall technology.

Whether your preference is to leverage the benefits of a single processing philosophy or to create a hybrid process using elements of single-use or continuous technology to improve productivity, this guide provides a technology overview to rapidly identify the best-fit technology, enable quick selection, and fast-track process development, transfer or process expansion.

On your own unique journey, you have reached capture and purification – the next steps are critical because they involve choices – choices that relate to the best route towards your process optimization, whether it be traditional, single-use or continuous.
Chromatography Hardware Guide for mAb Processes

Identifying the best direction to take for critical downstream purification 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 continuous manufacturing.

Deciding which path to follow

- **Traditional**
  - Chromatography System
  - Increasing prior knowledge
  - Increasing process flexibility
  - Stainless Steel and Plastic Totes

- **Single-Use**
  - Allegro Single-Use Chromatography Systems
  - Increasing process flexibility
  - Decreasing footprint and operating costs
  - Single-Use Concentration and Diafiltration

- **Continuous**
  - Cadence BioSMB Chromatography Systems
  - Concentration and Diafiltration System
  - Inline Concentration

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Cleanable and sanitizable chromatography columns, at all scales, supported by process control and packing systems, are used by the majority of approved manufacturing processes. The strength of prior knowledge and the track record of regulatory acceptance makes this the default approach and is an easy choice for those with a strong track record of process development, technology transfer and facility expansion.

Despite high levels of capital investment for the largest systems and the required cleaning and cleaning validation, this can still be seen as the best fit for large-scale manufacturing and for facilities that may be dedicated to the production of a single product.

The Pall Resolute range of columns, process control and packing systems support all process scales and processing choices from manual packing and operation to the fully automated packing and precision controls of the Resolute Linear column designs.

These columns are designed for large-scale pilot and full scale production, and offer a unique combination of active multi-axis piston control, precision linear actuation and fully automated unit operations that deliver:

- Fully scalable technology
- Quiet, clean operation
- Reduced operator involvement and error
- Predictable, time efficient packing

The Autopak system is an integral part of every Resolute Linear chromatography column and can save 30% on labor time while also maximizing sorbent utilization to reduce process costs.

Column Sizing

The column size will be a function of the operating binding capacity (OBC) and the number of sub-batches per column. Smaller columns may reduce sorbent volume and reduce capital investment but will lead to longer process times.

**Flowchart**

- Best fit for large-scale, single-product manufacturing facilities
- Manual and fully automated options to fit every budget and every scale
- 200 mm to 2000 mm column diameter
The adoption of a single-use manufacturing philosophy 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 in general include faster turnaround times and increased productivity due to the elimination of cleaning.

The Allegro single-use chromatography system extends these benefits to chromatographic operations allowing greater adoption of the single-use philosophy throughout downstream processing.

Improved Process Economy and Flexibility
Using a single-use chromatography system can reduce long term processing costs by up to 18% and deliver flexibility to support all scales of clinical manufacture.

The disposable product contact flow path also means that a single system can manage multiple chromatography stages in the purification process to minimize capital investment and maximize productivity.

Working with traditional packed columns, prepacked columns or membrane based chromatography products, the flexible process options make the use of single-use chromatography systems the ideal choice for multi-product facilities and for the manufacture of small volumes of clinical material.

Single-Use Alternative Chromatography Hardware

Allegro Plastic Totes
Collapsible, stackable and mobile totes for the handling of buffers and intermediates.

Mustang Capsules
Single-use membrane adsorbers can streamline the purification process and when coupled with the right platform these can integrate easily to accelerate production and reduce overall process costs.

Cadence Inline Concentrator
Reduce process times and extend performance in dilute feeds using inline concentration to reduce process volumes before column loading.

Allegro Single-Use Chromatography System
Multiple chromatographic processes from a single system.

Allegro Single-Use TFF Systems
Automated concentration and diafiltration for 500 L to 2500 L batch volumes using Cadence single-use ultrafiltration modules.

• Best fit for small-scale and multi-product facilities
• One versatile platform for all chromatography stages
• Works with prepacked columns and traditional columns

The Single-Use Alternative

Chromatography Hardware

System Flow Rates

Costs per Batch
Based on 6000 L at 5 g/L and 20 batches per year

* Calculations based on nominal 2 hour load time
* Biologe Process analysis and economic model
The potential of continuous processing has been discussed for several decades. However, the technology necessary to realize these benefits in bioprocessing has, until recently, been slow to match the expectation.

Whether you plan for a fully continuous process, or choose to extract the value from individual technologies by including a hybrid solution, Pall’s range of Continuous Ready technologies gives you access to these benefits to reduce cost and maximize process agility and facility utilization.

Cadene BioSMB systems support multicolumn and multi-stage chromatography steps to maximize sorbent utilization and integrate multiple operations to support both batch and continuous purification.

When coupled with other Continuous Ready technology the Cadence BioSMB system becomes the heart of continuous downstream purification to deliver purified, virus free drug substance ready for final formulation.

Minimizing Chromatography Operating Costs
When benchmarked against traditional chromatography methods, using the Cadence BioSMB system for downstream purification can save 34% through significant reductions in capital and labor costs. These savings can be multiplied when integrated into a fully continuous downstream process, significantly reducing footprint and maximizing facility utilization.

Example
Merck presented data at BPI 2016 to show how a single Cadence BioSMB 350 system purified a 400 L batch at 5.8 g/L using 80% less Protein A sorbent than a traditional single-column solution. Just as impressive, the time taken from PD to this scale (x150) was just 3 weeks and all product quality attributes and system performance remained the same.
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 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.

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.

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