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Resolute® Linear AutoPak Columns: A Fully Automated, Cost-Saving Solution for Column Packing and Operation

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Abstract

Large-scale column packing is a technically challenging, expensive, and time-consuming necessity in biopharmaceutical manufacturing. Resolute® Linear columns with AutoPak technology address each of these issues by combining a proven flowpath with simple, repeatable, and robust automation, ensuring consistent, accurate packing every time. Operating expenses are dramatically lower compared to conventional column technology thanks to reduced buffer consumption, 100% resin utilization, and the elimination of additional packing hardware and manual interventions that can lead to error traps. Suite utilization and safety are also improved by largely automating column maintenance in a hoist-free vertical space, avoiding full disassembly and an increased footprint.

Here, we present a comprehensive case study to showcase the benefits of automated, error-free column packing. A detailed packing trial utilizing MabSelect SuRe™, Fractogel® SO3, and Phenyl Sepharose Fast Flow was completed at Sartorius' Customer Interaction Center in Marlborough, Massachusetts. Multiple successful packing iterations were performed, meeting all customer and manufacturer parameters. Washout and distribution efficiency were also demonstrated via a dye study of a packed bed. Resolute® Linear AutoPak columns eliminate failed packs, and the savings in operating expenses easily offset the initial capital expense, making this technology a game-changer in the purification space.

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Introduction

For decades, column chromatography has been synonymous with the time-consuming and procedurally complex task of column packing. If not performed correctly, packing requires costly and lengthy remediation. Its complexity, ambiguity, formation, and infrequency often lead to a small core group of skilled end users who are experienced enough to pack columns confidently and properly. Unfortunately, the statement “Column packing is equal parts science and art” still rings loudly in chromatography suites across the globe.

Even if inherent challenges are addressed, packing traditional columns remains a time-, resource-, and labor-intensive activity. Cleaning and sampling of packing systems, the costly volumes of packing buffers, and incomplete resin utilization, combined with hundreds of operator touchpoints, result in an expensive, lengthy process rife with potential for errors. Expensive rework from failed packs unexpectedly impacts production batches, leading to avoidable added operating expenses. Traditionally, a column is fully unpacked into a cleaned | sampled slurry vessel, and the column and packing systems themselves must be re-cleaned, rinsed, and sampled. A recalculation of slurry concentration | volume must then be performed, and the slurry resampled to account for any lost resin. The plant time lost to these activities can easily span days.

A fully automated approach to column packing, unpacking, repacking, and cleaning-in-place (CIP) could remove user error, ensure reproducibility, fully-utilize all resin, and remove the need for a technical expert’s knowledge and presence to complete successful packs.

Introducing Sartorius Resolute® Columns With AutoPak Technology

The Sartorius Resolute® AutoPak is a fully automated column that uses 100 % of calculated resin volume, with a hardware flow path design that drives process efficiency and reduces operating expenses. The Resolute® AutoPak technology cuts resin requirements by eliminating the need for overage, which subsequently reduces buffer and plant water requirements. These reduced operating expenses (OPEX), coupled with time and facility savings driven by a lower incidence of failure, optimize plant utilization, reduce process risk, increase productivity in the manufacturing environment, and support the attainment of corporate sustainability goals (Table 1).

The Resolute® flowpath has been the gold standard in the industry for nearly thirty years, providing optimized flow distribution along with minimal pressure drop across the fully scalable range of columns (from 400 - 2,000 mm diameter). Sartorius' Resolute® Linear AutoPak line of columns builds on this leading technology by incorporating a novel method of fully automated column packing. Column packing is accomplished without external systems or pumps, using precision control driven by simple, proven recipes developed by Sartorius across the range of currently available chromatography resins. Combined with the flowpath, AutoPak technology delivers repeatable, successful packs requiring no operator intervention.

Table 1: *Cost Savings Comparison: Resolute® AutoPak – Automated | Reproducible Packing vs. Conventional Manual Packing*

	Success Rate [%]	# of Packing Events Per Year	Plant Time Impact	Annual Labor Savings	Annual Resin	Buffer Savings
Manual	~ 75	8	3.75 days saved	$19,200 saved	$413,224 saved	
Resolute® AutoPak	> 95	6				

OPEX Savings

Column packing operating expenses can be classified into three categories: consumables, plant time, and labor costs. Tables 1 - 4 compare packing scenarios performed by traditional column packing methods and by AutoPak technology.

- Increased packing success rate, coupled with resin and buffer savings, contributes to substantial time and cost savings due to the fully automated and repeatable, programmable packing (Table 1).
- Auto-repacking functionalities eliminate the need to remove resin from the column, as the entire resin bed is fully resuspended inside the column tube, requiring a only few column volumes of packing buffer. Preparation, cleaning, and sampling of tanks or packing systems are not required, nor is there a need for resin volume make-up or re-calculation of slurry percentage (Table 2). The same cost savings and efficiencies can be applied to auto-packing—unpacking buffer requirements are reduced compared to conventional column unpacking (Table 2).
- The proven Resolute® flow design of the columns can provide very low pressure drop and high-resolution chromatography over a wide range of normal operating flow rates (typically from 30 to 800 cm/h). Flow efficiency reduces buffer volumes required for processing and cleaning the columns as well as reducing plant utilization time.
- Resolute® flow design also delivers savings in process solutions and cycle time, supporting the achievement of sustainability goals (Table 3).
- Quicker and safer automated hoist-free maintenance mode does not require tools or disassembly of major column elements, reducing component changeover time by 75%. Maintenance within the column footprint by vertically raising the column tube (rather than rotating components laterally) significantly reduces floor space demand while still ensuring user safety (Table 4).

Auto RePack:
- Resin stays in column
- No prep day and <1 hour total re-packing time
- Total buffer: 1 bed volume (BV) for RePack | 2 BVs for UnPack

Auto UnPack:
- No pre-priming
- 1 hour total unpacking time after 2 hours prep
- Total buffer: 2 BVs for Pack | 2 BVs for UnPack

Table 2: *Cost Savings Comparison: Resolute® AutoPak – Automated | Reproducible Packing vs. Conventional Manual Packing*

Activity	Repack and Unpack Events/Year	Materials Impact	Plant Hours Impact	Labor Impact (min 2 operators)	Plant Utilization Impact
Auto-RePack | Auto-Unpack	6	$1.7M resin savings $23,940 buffer saved	16 day/yr saved	$69,735 saved	2 additional batches/year

Table 3: *Cost Savings Comparison: Resolute® AutoPak – Automated | Reproducible Packing vs. Conventional Manual Packing*

Process Phase	Performance of Enhanced Washout Efficiency	Buffer Consumption Impact	Annual Material Impact
Equilibration	3 (vs. 4) BV	**Assumptions** ▪ Protein A, hydrophobic interaction chromatography (HIC), ion-exchange chromatography (IEX) each at 1,200 x 200 mm bed geometry at 25 batches per year ▪ Buffer cost $3/L **Calculation:** ▪ Volume = 125 cycles x 1 BV x 5 phases x 226 L/BV	
Wash	2 (vs. 3) BV		
Elution	2 (vs. 3) BV		
Regeneration	2 (vs. 3) BV		
CIP	4 (vs. 5) BV		
Annual Total		**141,250 Liters**	**$423,740**

Table 4: *Resolute® AutoPak - Integrated Hoist-Free Maintenance*

Activity	Feature	Total Cost of Materials	Change-Over Events | Year	Plant Time | Impact	Labor Cost Impact (Min. Two Operators)
Change-out of bed supports, major seals, nozzle valve elastomer sets	Safe, rapid hoist-free access to top and bottom consumable elements allowing Preventative Maintenance to be reduced from 2 x 8 h shifts to only 4 h.	$50,000 in spare parts (x 6 events) = $300,000	6	4.5 days saved	$11,200

Case Study:
Qualified, Repeatable, Automated Packing

Ease of operation is only impactful if the results meet qualification parameters. The following summarizes the results of a comprehensive packing trial using a 1,000 mm Resolute® Linear AutoPak column. The study was performed at the request of a Sartorius client at the Sartorius Customer Interaction Center of Excellence in Marlborough, Massachusetts, with three commonly used resins.

The trials were performed using packing recipes developed by Sartorius experts utilizing key parameters confirmed by the client. The resins packed were donated by the client and were considered fully life-cycled and at the end of production use: Fractogel® SO3 (Millipore, Bedford, MA USA), MabSelect Sure™, and Phenyl Sepharose Fast-Flow (Cytiva, Uppsala, Sweden). To assess packing performance and efficacy, Sartorius and the client agreed on acceptance criteria prior to initiating any packing studies (Table 6).

A total of three sets of three packs were executed within the acceptance criteria. All resins were packed using AutoPak technology. The first and second packs of each resin were performed from a fresh start, with resin suspended outside of the column in a slurry tank, whereas the third pack of each resin was performed from a packed state, using the Auto-RePack feature to resuspend the resin in-column and re-pack. This method of repacking is unique to AutoPak columns and occurs completely inside the column, eliminating the need for column CIP or any external storage | re-slurry of resin. Qualified pack results are detailed in Table 5.

After packing qualification, a dye migration test was performed to demonstrate three benefits of the Resolute® flow distribution design: Cleanability of the packed bed, full utilization of resin, and decreased buffer usage resulting in higher eluate pool concentrations. The bed was saturated with phenol red dye by one BV upflow, followed by recirculating 2 BVs of downflow. The bed was then washed with pH 8.5 buffer in three BVs of upflow followed by three BVs of downflow. Separate bands of phenol red dye were injected, and the packed bed was then sectioned to demonstrate efficiency.

MabSelect SuRe™ and Phenyl Sepharose Fast-Flow were packed multiple times with no issues. Fractogel® — the most challenging of the three resins to pack — met qualification standards at two different bed heights.

This study yielded proof of the performance of the Resolute® Linear AutoPak 1,000 mm column for three resins, achieving results within consensus criteria for chromatography efficiency and peak asymmetry for packed bed height of either 20 or 25 cm.

Sartorius' Resolute® Linear AutoPak columns offer a solution to the core challenges of column packing, simplicity, reproducibility, and hands-off packing. Furthermore, AutoPak technology introduces significant savings in three categories of operating expenses: Material cost, plant productivity, and labor (Table 7).

Table 5: *Packing Study Results*

Pack	Sorbent	Slurry Concentration [%]	Compression Factor	HETP [cm]	Plate Number [m^{-1}]	Asymmetry
1	MabSelect Sure™	63.5	1.18	0.021	4754	1.05
2	MabSelect Sure™	66.1	1.18	0.025	4330	1.05
3	MabSelect Sure™	66.1	1.18	0.026	3959	1.07
4	Phenyl Sepharose 6 Fast Flow	52.0	1.15	0.023	4004	1.03
5	Fractogel® SO3	70.0	1.28	0.028	3599	0.97
6	Fractogel® SO3	69.5	1.28	0.029	3450	1.23
7	Fractogel® SO3	69.5	1.28	0.029	3410	0.70
8	Fractogel® SO3	57.4	1.28	0.024	4219	0.70

Table 6: *Acceptance Criteria for Packing Performance*

	MabSelect Sure™	Fractogel® SO3	Phenyl Sepharose FF
HETP	≤ 0.10	≤ 0.08	≤ 0.10
Asymmetry Factor	0.7 - 1.4	0.7-1.4	0.7-1.4

Table 7: *Summary of Consumables, Plant Time, and Labor Costs*

Activity	Performance Comparable to Traditional | Competitor	Impact – Annual	Impact – 10 years Life of Columns Assets
Packing | Unpacking	Materials, time, and labor savings	Material savings (>$1.7M) 10 days plant time saved	100 plant days saved = >12 additional batches
Full Automation Prevents Packing Failures	Improved success rate from 75 % to 100 %	3.75 days plant time saved	38 plant days saved = >five additional batches
Ease of Service	Preventative Maintenance shortened from 2x 8 h shifts to only 4 hours	4 days plant time saved	40 plant days saved = five additional batches
Flow Distribution	Reduced buffer at each phase (equil-wash-elute-regen-CIP)	Material savings ($423,740) 7.8 days plant time saved	$4.2M One additional batch per year
Combined Totals	Time, and labor savings, as well as productivity gains	>25 days plant time saved >$2M material saving vs. traditional pumped slurry packing	10% productivity gain Resin and buffer savings that support client sustainability initiatives

Conclusion

Column packing continues to remain a thorn in the side of biopharmaceutical manufacturers; traditionally a highly complex, manual operation, it is beset by potential error traps. Failed packs can cost facilities in labor, safety, consumables expenses and plant time. Resolute® Linear AutoPak's fully automated, reproducible packing all but eliminates the possibility of failed packs as demonstrated in this case study. Furthermore, as shown here, its intelligent design and automation reduce operating expenses in packing, unpacking and CIP operations that can easily counter the capital expense of the column itself.

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