APPLICATION NOTE

Praesto™ 70 CH1 Pre-clinical Modeling: Technical Insights to Process Economic Benefits

Innovative Solutions for the Biotherapeutic Industry

Introduction

The biotherapeutic industry continually seeks innovative solutions to address the growing complexity of new biotherapeutic molecules. One such solution is Purolite™ Praesto 70 CH1, a high-capacity, high-lifetime resin specifically designed to target CH1 antibody domains. This article explores the challenges faced by the industry, the significance of these challenges, and how Purolite Praesto 70 CH1 offers a promising solution.

The Challenge

New biotherapeutic molecules bring about various challenges, primarily related to the removal of product-related impurities. The complexity of these molecules often results in lower yield and stability, making the manufacturing process economically unviable. Traditional resins lack the capacity and lifetime to efficiently purify these complex molecules, necessitating the development of innovative solutions.

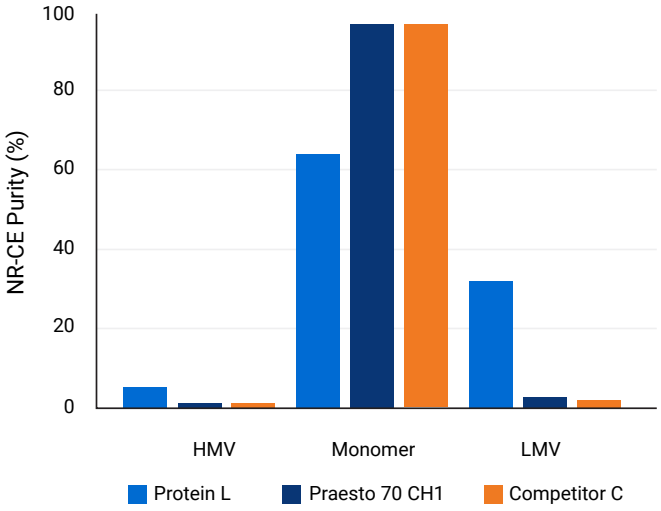
Furthermore, traditional Protein A resins lack selectivity, and in the case of bispecific molecules, typically co-purify homodimers and heterodimers. Alternative resins (Protein L, CH1, Kappa and Lambda, for example) improve selectivity but typically present shorter lifecycles and lower capacities. Here we discuss a novel CH1 resin with higher capacity, extended lifecycle, and superior pressure-flow properties. This study models cost, productivity, sustainability, and facility fit benefits against Protein L and a currently available CH1 resin.

The Study

The aim of this study was to demonstrate the benefits of novel affinity resins which bind Fabs and deliver high-purity products. CH1-binding resins were the subject of this work, as in many cases, when compared to a traditional protein L based resins, impurity removal is substantially higher when using CH1 ligands, as shown in Figure 1.

Figure 1

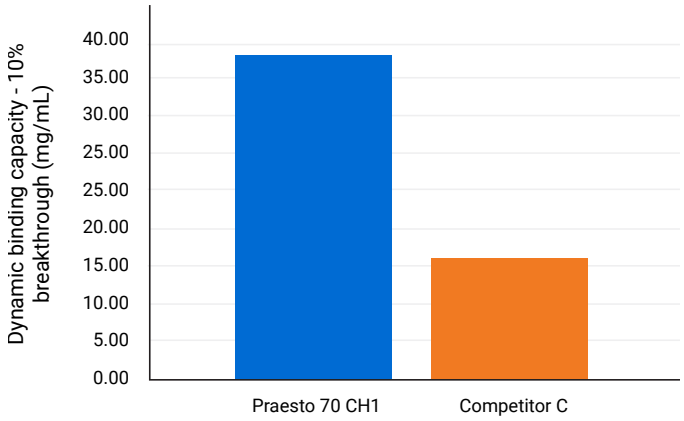
Non-reduced capillary electrophoresis (NR-CE) to analyze the % high molecular weight (HMW), monomer (the target molecule) and low molecular weight (LMW) species in the elution pool from a Fab purification performed with Competitor L, a leading protein L based resin, and two CH1-binding resins: Competitor C and Praesto 70 CH1



Once the need for a CH1-binding resin has been identified, candidate resins must be selected and compared to determine their relative strengths and weaknesses. There are two CH1 resins currently on the market: Ecolab's Praesto 70 CH1 and Competitor C. In response, we need to compare both resins head-to-head. To compare both resins head-to-head, first the dynamic binding capacity was assessed. This was done for an IgG1 based Fab at 10% breakthrough with a 6-minute residence time, and the results are shown in Figure 2. The results show that in this experiment, Praesto 70 CH1 has over double the capacity on the competitor C resin with this Fab.

Figure 2

Dynamic binding capacity at 10% breakthrough of an IgG Fab, 6 min residence time on the two CH1-binding resins, Praesto 70 CH1 and Competitor C

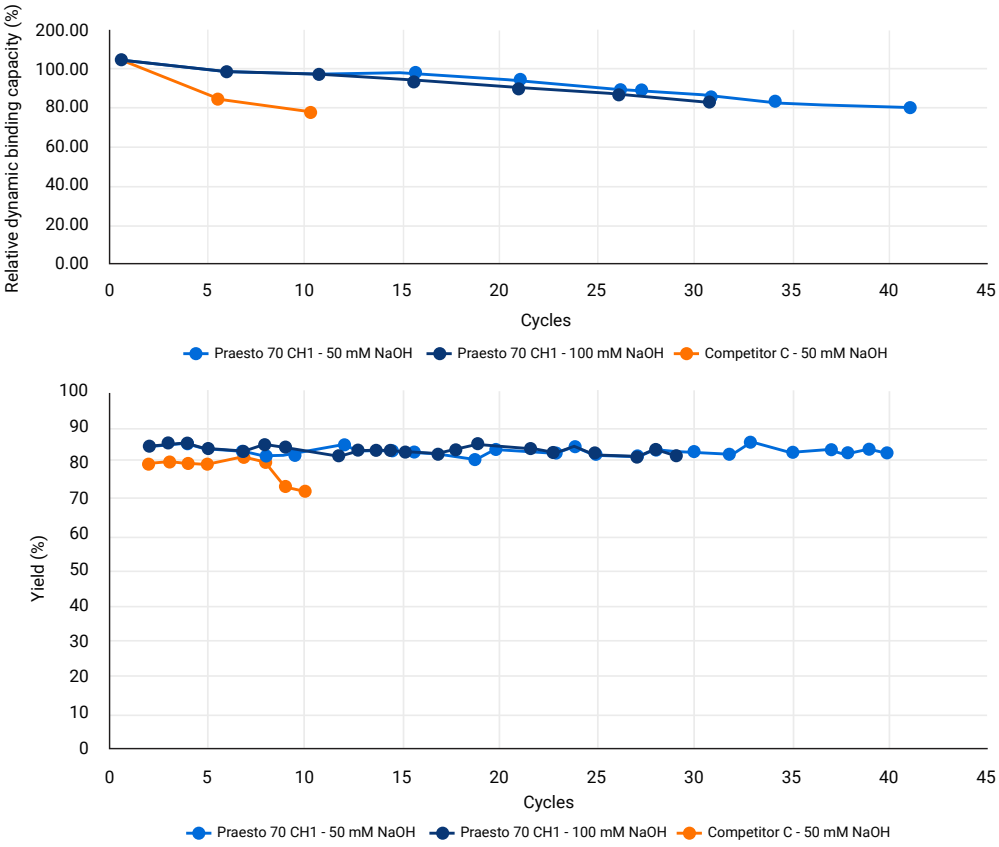


Resin lifetime was then analyzed using both yield and relative dynamic binding capacity. In these experiments the columns were equilibrated with 50mM Tris-Hac, 150mM NaCl, pH7.4 for 5CV and then loaded to 80% of the DBC 10% breakthrough value. After a 4CV wash using the equilibration buffer the column was eluted using 5CV of 50mM NaAc-HAc, pH3.0. The peak collection was initialed by mAu >100 and stopped by mAu <100. Afterwards, the columns underwent a strip using 3CV of 1M Hac, were re-equilibrated for 3CV before cleaning with NaOH (either 50 or 100mM) for 3CV with 15 min contact time. This was cycle 1, after which the protocol was repeated. The results are shown in Figure 3A and 3B. The relative dynamic binding capacity for Competitor C fell below 80% after 11 cycles, and the yield dropped to 72% after 10 cycles. This study could not continue after 11 cycles due to severe pressure problems in the column. Praesto 70 CH1 maintained a relative dynamic binding capacity and yield above 80% for 40 cycles using 50mM NaOH and 31 cycles using 100mM NaOH for cleaning.

Figure 3

Lifetime study for Praesto 70 CH1 and Competitor C

Both studies used a 0.66 x 10cm bed height column. The top graph shows the relative dynamic binding capacity after each cycle, while the bottom graph shows the yield.



The third property investigated was the presence of product-related impurities. For this work, results were analyzed from work carried out and published by Wuxi (CH1-specific affinity resins possess the potential of separating heterodimer from homodimers in asymmetric bispecific antibody purification, Wanyuan Dong, Yifeng Li* Downstream Process Development (DSPD), WuXi Biologics, Shanghai, China. JBM 2024 , 11(3), September 2024). Their work focused on asymmetric bispecific antibody production, where both the target heterodimer and homodimer byproducts can bind to the CH1-specific resin. It was found that the CH1-binding resins, specifically Praesto 70 CH1, can differentiate between these two species, allowing for the separation of the target heterodimer. Removing homodimers at the capture stage reduces the burden on subsequent polishing steps, making the overall purification process more efficient and robust. Thus, the conclusion was that CH1-specific affinity resins can be a better alternative to conventional Protein A for product capture in asymmetric bispecific antibody purification, potentially improving the overall process.

CH1 Pre-clinical Modeling

A model was developed to investigate the potential cost, productivity and sustainability benefits of Praesto 70 CH1 and Competitor C. This model utilized parameters outlined in Table 1 and run conditions shown in Table 2.

TABLE 1 **Parameters for the Pre-clinical Modeling Study**

	Competitor C	Praesto 70 CH1
Bead Size	50 Micron	70 Micron
Bed Height	10 – 22 cm	10 – 22 cm
Column Diameter	20 – 60 cm	14 – 45 cm
Packing Factor	1.15	1.2
Residence Time	6 min	6 min
DBC at 10% BT	15.9 g/L	38.0 g/L
Yield	78%	83%
Lifecycles*	11 at 78% DBC	31 at 80% DBC ** 40 at 80% DBC
Resin Cost	List $/L	List $/L
Column	Pre-packed OPUS	Pre-packed OPUS

Columns were packed using a packing factor of 1.15 (Competitor C) AND 1.2 (Praesto 70 CH1). Columns were prepacked OPUS (Repligen) with pricing in line with standard 2025 list values.
*based on 15-minute CIP contact time in 0.05 M NaOH
** denotes 0.1 M NaOH

TABLE 2 Protocol Used as a Basis for the Modeling Study

Step	Column Volumes	Buffer	Linear Velocity
Equilibration	5	50 mM Tris-Hac, 150 mM NaCl	150 cm/h
Load	-	-	6 min residence time
PLW (Chase)	2	50 mM Tris-Hac, 150 mM NaCl	150 cm/h
Elution	1 – Competitor C 2.2 – Praesto 70 CH1	50 mM NaAc-Hac	150 cm/h
Strip	3	1 M HAc	150 cm/h
Re-Equilibration	5	50 mM tris-Hac, 150 mM NaCl	150 cm/h
Sanitization	3	50 mM NaOH	150 cm/h
Storage*	3	-	150 cm/h

Operational Parameters

A two-batch clinical campaign across a range of titers (1.5, 2.2, 3.5 and 5 g/L) has been explored in a 200 L bioreactor. Column setup and key performance metrics are outlined in Table 3 below.

TABLE 3 Column Setup and Resin Performance for Praesto 70 CH1 and Competitor C Resins

Titer	1.5 g/L		2.2 g/L		3.5 g/L		5 g/L	
Resin	Competitor C	Praesto 70 CH1	Competitor C	Praesto 70 CH1	Competitor C	Praesto 70 CH1	Competitor C	Praesto 70 CH1
Bed Height	15.5 cm	14.5 cm	13 cm	21.5 cm	14 cm	11 cm	19.5 cm	10.5 cm
Diameter	20 cm	14 cm	25 cm	14 cm	30 cm	20 cm	30 cm	25 cm
Resin Volume	5.8 L	2.6 L	7.7 L	3.8 L	11.9 L	4 L	16.5 L	5.9 L
DBC%	79%	89%	77%	88%	77%	89%	76%	86%
DBC	12.6 g/L	33.8 g/L	12.2 g/L	33.4 g/L	12.2 g/L	33.8 g/L	12.1 g/L	32.7 g/L

Assumptions and Constraints

Dynamic binding capacity (DBC) at 10% breakthrough was measured for both CH1-binding resins at a 6-minute residence time. Column dimensions (bed height and diameter) were optimized to meet batch time (16 hours) and cycle number constraints (6 cycles), reflecting resin performance. Lifecycles were modeled using %DBC data. Column setup was designed to minimize cost of goods. Non-loading flowrates were set at 70% of the maximum flowrate for a given bed height, based on pressure-flow characteristics, and are dependent on column diameter and viscosity, varying by project. Campaign cost is based on resin, buffer, labor and waste costs. Pre-packed OPUS column pricing is also accounted for in the resin costs. Facility area is calculated by accounting for GMP floorspace requirements for chromatography equipment and ancillaries, operator space, buffer and waste storage space. Chromatography equipment was selected to meet maximum flowrate used per scenario (L/h) and accounts for around 15% of the total room size. HVAC operation based on a Class-C facility consuming 0.5 kW/m2 (saving energy in cleanrooms). Energy consumption is a function of batch time and is converted into equivalent carbon dioxide (eCO2) emissions based on a 0.235 kg eCO2/kWh. Carbon emissions are based on water, buffer ingredients, HVAC energy consumption and wastewater treatment. Carbon emissions per buffer ingredients are based on Ecoinvent database [Ecoinvent - Data with purpose]. Water for Injection (WFI) is used for the processing, with a water to WFI conversion ratio of 1.43, in line with prior publications [Water related impact of energy: Cost and carbon footprint analysis of water for biopharmaceuticals from tap to waste - ScienceDirect]. Purified water assumes an input of 100 kW h/m3 and wastewater decontamination an input of 90 kW h/m3. [Streamlined life cycle assessment of single use technologies in biopharmaceutical manufacture - ScienceDirect]. PMI is a metric used to define the process mass intensity. Here, it is limited to the CH1 capture step (denoted by PMICH1) and comprises water, buffer ingredients and resin. A more thorough definition is available in the glossary.

Results

The following section outlines the performance, cost, sustainability and facility fit data for Praesto 70 CH1 versus Competitor C.

Cost and Productivity

Resin cost of goods (COGs) and productivity are key metrics in assessing the performance of a resin. This has been modeled across titer range for each CH1 resin scenario. The result of this modeling is in Table 4 below.

TABLE 4 CH1 Resin Performance Data Across 1.5 – 5 g/L Titers

Titer		1.5 g/L		2.2 g/L		3.5 g/L		5 g/L	
Scenario		Competitor C (5.8 L)	Praesto 70 CH1 (2.6 L)	Competitor C (7.7 L)	Praesto 70 CH1 (3.8 L)	Competitor C (11.9 L)	Praesto 70 CH1 (4.0 L)	Competitor C (16.5 L)	Praesto 70 CH1 (5.9 L)
Resin COGs ($/g)	Campaign	366.8	169.4	323.2	154.5	297.6	109.8	277.6	108.8
	Lifetime	350.6	65.7	295.1	56.1	278.8	64.2	258.9	52.7
Productivity		4.7 g/L/h	7.9 g/L/h	5.8 g/L/h	7.9 g/L/h	6.3 g/L/h	14.6 g/L/h	5.2 g/L/h	17.2 g/L/h
Cost		$170,576	$84,364	$220,451	$112,866	$322,933	$127,583	$430,234	$180,653
Throughput		27.7 g/h	20.3 g/h	44.4 g/h	29.9 g/h	75.3 g/h	58.0 g/h	86.3 g/h	101.7 g/h
Batch Time		10.8 h	14.8 h	9.9 h	14.7 h	9.3 h	12.1 h	11.6 h	9.8 h
Cycles		5	4	6	4	6	6	6	6
Resin Utility		96%	39%	91%	36%	94%	58%	93%	48%

Note that COGs refers to resin costs in pre-packed columns only; non-resin costs were a relatively small fraction. Lifecycle data for Praesto 70 CH1 is based on 0.1 M NaOH (31 cycles at 80% DBC) versus 0.05 M NaOH per cycle for Competitor C (11 cycles at 78% DBC).

Notably, these results are based on a cleaning-in-place strategies of **0.1 M NaOH per cycle** Praesto 70 CH1, versus **0.05 M NaOH** for Competitor C. Several key benefits emerge when comparing Praesto 70 CH1 to Competitor C under the specified conditions:

Higher Productivity:
1.3 to 1.7 times higher at 1.5–2.2 g/L, and 2.3 to 3.2 times higher at 3.5–5 g/L*.

*It is worth noting that a non-loading linear velocity of 150 cm/h was used for both resins. This could be improved at a greater magnitude for Praesto 70 CH1 as it has superior pressure flow properties.

Substantial Cost Savings:
50-60% cost savings, translating to $86,000-$250,000 in reductions across the modeled titers.

Lower COGs:
100-200 $/g versus 275-370 $/g , equating to savings as high as 60% for two-batch clinical campaigns.

Extended Resin Utility:
More cleaning cycles are tolerated, potentially increasing savings to over 80%. Resin utilization is 36-58% for Praesto 70 CH1 versus 91-96% for Competitor C, indicating that a further reduction in COGs to 50-70 $/g could be obtained versus 250-350 $/g for Competitor C when the full lifecycle of the resin is required.

Amortized Resin Costs for CH1 Resins

When evaluating the cost-effectiveness of Praesto 70 CH1 in fragment purification processes, it is helpful to use a Protein A-based standard monoclonal antibody (mAb) process as a benchmark. Currently, the total cost of goods (COGs) for a commercial process can be as low as $50 per gram. Of this, commercial modeling suggests that Protein A resin would account for just 3%, or $1.50 per gram with $48.50 per gram allocated to non-Protein A steps.

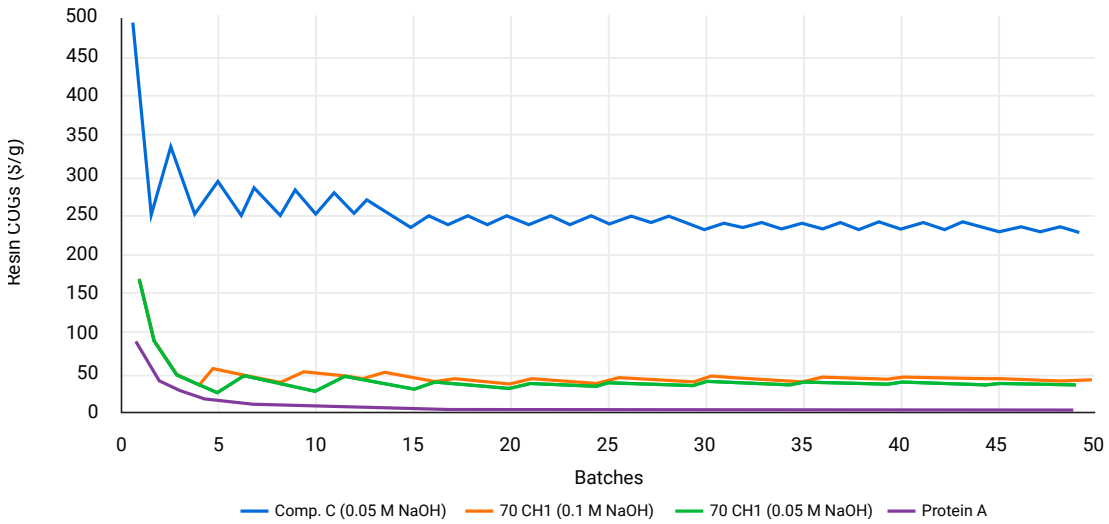
Figure 4 shows how Praesto 70 CH1 cost of goods are more closely aligned to Protein A across multiple batches, versus Competitor C. Note that the values for Competitor C are volatile across the throughput range due to the shorter lifetime of the resin.

Using Competitor C in the current clinical setup and deducting pre-packed column costs, the loose resin cost is $228.9 per gram. When added to the same non-capture step costs, the total COGs reach $277.4 per gram, more than 5.5 times higher than the standard Protein A process.

Praesto 70 CH1 offers a more economical alternative. Depending on the cleaning strategy used, resin COGs are $39.8 per gram with 0.1 M NaOH and $32.4 per gram with 0.05 M NaOH. This gives total COGs of $88.3 and $80.9 per gram respectively with numbers that are only 1.6 to 1.8 times higher versus the standard Protein A benchmark.

Figure 4

Amortized resin costs for CH1 resins (Praesto 70 CH1 and Competitor C) versus a standard Protein A resin over 15 batches



With additional optimization, we believe these numbers could be reduced further via the following:

- Bulk purchasing of resin could enable pricing discounts
- NaOH concentration alignment for Praesto 70 CH1 with that of Competitor C (0.05 M) would extend resin lifetime
- Accounting for the CH1 ligand's superior impurity clearance versus standard Protein A could highlight savings associated with the removal of an intermediate chromatography step or reduced processing demands
- Increased lifecycles: early customer feedback suggests that with further development, Praesto 70 CH1 could exceed 100 cycles
- Optimization of the setup to account for facility and capital costs
- Operation with a multi-column chromatography setup, which would increase productivity and potentially lower COGs via more efficient resin usage

Taken together, these improvements suggest that Praesto 70 CH1 could further reduce fragment process costs to levels more closely aligned with standard Protein A, making it a compelling option for cost- and time-sensitive clinical campaigns and a viable alternative to Competitor C.

Sustainability & Facility Fit

Beyond cost and productivity, resin performance plays a critical role in shaping sustainability and facility fit metrics. Superior binding capacity and pressure-flow characteristics directly influence productivity, enabling lower resin volumes and short batch times. These improvements can support more compact chromatography equipment, thus lowering floorspace and buffer volume requirements to allow for smaller GMP facility footprints and lower emissions.

In comparing Praesto 70 CH1 with Competitor C, the data (presented in Table 5) shows that Praesto 70 CH1 supports a more compact setup. Chromatography hardware requirements can be reduced from 1.2 m² to 0.6 m², excluding additional space considerations. This translates into a smaller facility footprint, with Praesto 70 CH1 delivering reductions in total buffer volume (58-62%), elution volume (17-24%), and equipment footprint compared to Competitor C.

Note: minimum room size is based on the minimal estimated requirements for equipment, ancillaries, operators and liquids (buffer) and operator space. Equipment size is based on the maximum flowrate used. For context, equipment size represents around 15% of the total room size. Waste is defined as spent buffer volume plus resin volume. Whilst not accounted for in the prior section, savings in floorspace would also translate to lower COGs via reduced capital costs – particularly in new facilities if a more compact design could be accounted for.

TABLE 5 Data Associated with Facility Fit

Scenario	Competitor C (5.8 L)	Praesto 70 CH1 (2.6 L)	Competitor C (7.7 L)	Praesto 70 CH1 (3.8 L)	Competitor C (11.9 L)	Praesto 70 CH1 (4.0 L)	Competitor C (16.5 L)	Praesto 70 CH1 (5.9 L)
Total Buffer Volume	297 L	122.3 L	459.5 L	181.4 L	712.5 L	273.7 L	992.4 L	408.2 L
Elution Volume	24.3 L	19.6 L	38.3 L	29.1 L	59.4 L	45.6 L	82.7 L	68.0 L
Equipment Size	1.2 m²	0.6 m²	1.2 m²	0.6 m²	1.2 m²	0.6 m²	1.2 m²	0.6 m²
Minimum Room Size	7.7 m²	5.4 m²	8.4 m²	5.7 m²	9.4 m²	6.1 m²	10.5 m²	6.7 m²
Water	425 L/batch	175 L/batch	657 L/batch	259 L/batch	1019 L/batch	391 L/batch	1,419 L/batch	584 L/batch
Buffer Efficiency	1.28 L/g	0.49 L/g	1.35 L/g	0.50 L/g	1.31 L/g	0.47 L/g	1.28 L/g	0.49 L/g
Waste	609 kg/ campaign	251 kg/ campaign	938 kg/ campaign	372 kg/ campaign	1,455 kg/ campaign	557 kg/ campaign	2,026 kg/ campaign	831 kg/ campaign
PMI	312 kg/kg	128 kg/kg	481 kg/kg	190 kg/kg	746 kg/kg	285 kg/kg	1,038 kg/kg	425 kg/kg

Given the high cost per square meter in bioprocessing facilities, reducing footprint is economically advantageous. Although direct cost savings are not calculated here, Praesto 70 CH1 could reduce space requirements by up to 30%, potentially lowering facility costs or allowing for greater product throughput. These spatial efficiencies also contribute to improved sustainability metrics, particularly in terms of energy consumption and carbon emissions.

Resin volume is another important consideration. Praesto 70 CH1 enables a 50-60% reduction in resin volume relative to Competitor C, which has implications for column diameter and scalability, especially in commercial production. Since resins are mass-intensive to produce, they carry their own carbon footprint, so reductions here could further lower emissions.

Process Mass Intensity (PMI), which measures the mass of inputs relative to outputs, is a useful metric for evaluating the sustainability of a process. Whilst traditional bioprocessing averages around 7,700 kg/kg, newer continuous approaches have achieved values below 1,500 kg/kg. For the CH1 step, Praesto 70 CH1 achieves a 60% reduction in PMI compared to Competitor C, driven primarily by lower buffer consumption, especially water. Buffer usage, which contributes significantly to PMI, is reduced by 50-60%, and elution volume is 20% lower. These reductions can either shrink facility size, lowering HVAC energy demands, or increase capacity within existing setups.

Further improvements in PMI could be realized by increasing resin utility. As mentioned previously in the Cost and Productivity section, Praesto 70 CH1 currently achieves 36-58% utility, compared to 91-96% for Competitor C. Extending resin lifecycles, potentially through milder cleaning agents like 50 mM NaOH or through process optimization, could help amortize the environmental impact of resin use. Industry feedback suggests lifetimes exceeding 100 cycles may be achievable.

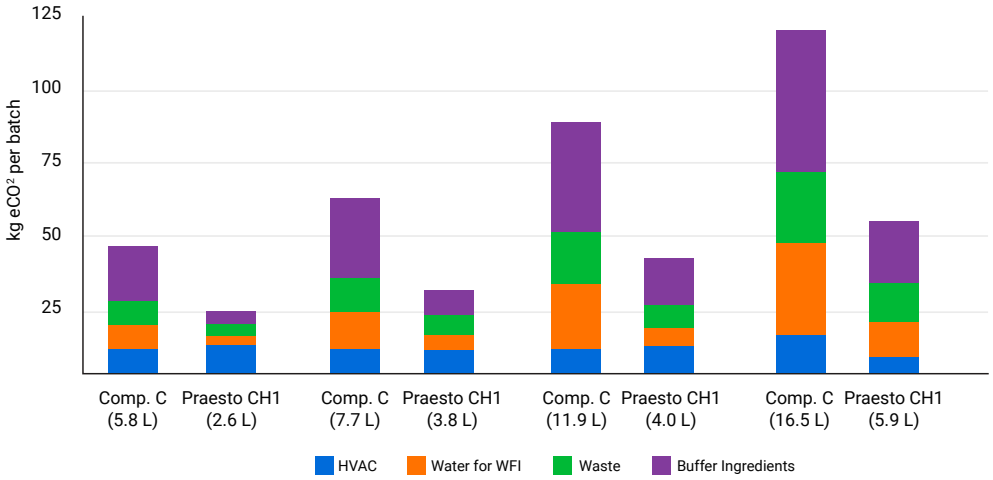
From a process design perspective, multi-column chromatography offers additional benefits. Studies using Praesto Jetted A50 have shown savings of 40% in buffer volume and 30% in resin volume. These formats also reduce floorspace and batch times due to their compact and efficient hardware.

Reducing buffer usage is particularly attractive, as buffer ingredients (e.g. salts) have their own carbon footprints. Moreover, producing water for injection (WFI) and disposing of liquid waste are energy-intensive processes that contribute to emissions.

Estimated carbon emissions data (Figure 6) highlights the impact of HVAC, WFI, waste, and buffer ingredients. Buffer usage is the primary driver of emissions, and Praesto 70 CH1 shows a 42–57% reduction in total eCO_2 compared to Competitor C. These savings are enabled by the higher capacity, superior pressure-flow properties, and longer lifecycle of Praesto 70 CH1, which support a more compact and efficient processing setup.

Figure 5

Praesto 70 CH1 versus Competitor C eCO_2 per batch



Conclusion

This report presents modeled data based on an IgG1 Fab fragment, highlighting the performance of Praesto 70 CH1 resin compared to the current Competitor CH1 resin. Across all measured metrics and a range of titers, Praesto 70 CH1 consistently demonstrates superior performance. Its enhanced binding capacity, improved pressure-flow characteristics, and extended lifecycle contribute to notable gains in cost reduction, productivity, facility fit, and sustainability.

One of the most compelling advantages of Praesto 70 CH1 is its potential to simplify the purification process. Its improved impurity clearance, better than that of Protein A resins, may allow for the removal of intermediate chromatography steps such as hydrophobic interaction chromatography (HIC) or ion exchange (IEX). This streamlining not only intensifies the process but also reduces complexity and operational burden.

Further optimization is possible through lifecycle management and process intensification strategies. For example, rapid cycling approaches tailored for clinical applications or the adoption of multi-column chromatography can enhance throughput and efficiency. These strategies, when combined with the inherent strengths of Praesto 70 CH1, offer a pathway to more cost-effective, scalable, and sustainable bioprocessing.

Glossary

PMI (Process Mass Intensity)

A measure of process efficiency, PMI calculates the total mass of materials used (inputs) relative to the mass of product generated (output). In bioprocessing, it reflects how resource-intensive a process is, with lower values indicating more sustainable and efficient operations.

Buffer Efficiency

Refers to how effectively buffer solutions are used during purification steps. High buffer efficiency means less buffer is required to achieve the desired separation or purification, reducing costs, waste, and environmental impact.

WFI (Water for Injection)

Highly purified water used in pharmaceutical manufacturing, especially for injectable products. It meets strict quality standards and is costly to produce and dispose of, making its usage a key factor in sustainability and cost metrics.

Cost of Goods (COGs)

The total cost to produce a unit of product, including raw materials, consumables, labor, and overheads. In bioprocessing, COGs often focus on resin, buffer, and facility-related expenses, and are critical for evaluating process economics.

Productivity

The amount of product generated per unit of time, volume, or resin. Higher productivity indicates a more efficient process, often linked to better resin performance and shorter batch times.

Throughput

The volume of material processed over a given time period. It reflects the capacity of a system or facility to handle production demands and is influenced by equipment size, resin performance, and process design.

Utility [Resin]

The proportion of resin that is actively used during a campaign.

- Resin used: The fraction of resin that contributes to product capture and purification.
- Resin unused: The portion that remains idle or underutilized, often due to process limitations or conservative design.

HVAC (Heating, Ventilation, and Air Conditioning)

Systems that regulate air quality and temperature in GMP facilities. HVAC contributes significantly to energy consumption and carbon emissions, especially in cleanroom environments.

Amortization

The process of spreading the cost of an asset, such as chromatography resin, over its useful lifecycle. In sustainability terms, amortizing resin cost and emissions over more cycles improves economic and environmental efficiency.

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