

Customer Case Study

Merck Process Transfer and Scale-Up of Batch Protein A Chromatography to Resolute® BioSMB Multi-Column Platform



Customer Profile

Company Name:
Merck & Co., Inc.

Company Location:
Kenilworth, NJ, USA

Company Type:
Large Biopharma

Industry:
Health Care

Company Size:
71K Employees

Company Revenue:
\$46.84 Billion

Company Profile:
www.merck.com/company-over-view/

Customer Challenge

The driver for the study was an exploratory evaluation of the impact and benefits of multi-column chromatography. Product quality consistency was considered, as well as the possible cost and resin savings associated with transitioning from batch to continuous. There was also another goal of executing the process transfer and scale-up in as short a time as possible.

Background Information

Merck's key driver for this study was to reduce the operating costs of existing purification steps with high resin costs. The Resolute® BioSMB multi-column chromatography system was used to demonstrate enhancements in productivity and efficiency compared to batch mode. Performance data indicated that product yield and quality were consistent throughout the process's 150 × scale-up and comparable to the batch benchmark.

Provided Solution

The harvested cell culture fluid (HCCF) with target mAb product was purified using Protein A resin with a dynamic binding capacity of ~45 g/L. With support from Resolute® BioSMB Applications Specialists, Merck developed a 5-column process utilizing 5 mL columns on the Resolute® BioSMB PD system to conduct a continuous chromatography proof of concept at the bench scale (4 mL/min). This was later scaled up roughly 150 × to the Resolute® BioSMB 80 system using 5 × 0.77 L columns (14 cm i.d. × 5 cm) operating at a flow rate of 37 L/h – which was roughly 10% of the system capacity.

Under these conditions, 400 L of HCCF containing 2.3 kg of expressed mAb (5.8 g/L) was processed in 13 cycles over 11 hours.

Project Key Indicators

Molecule type: mAbs, Biosimilars

Process Steps:
Affinity Chromatography

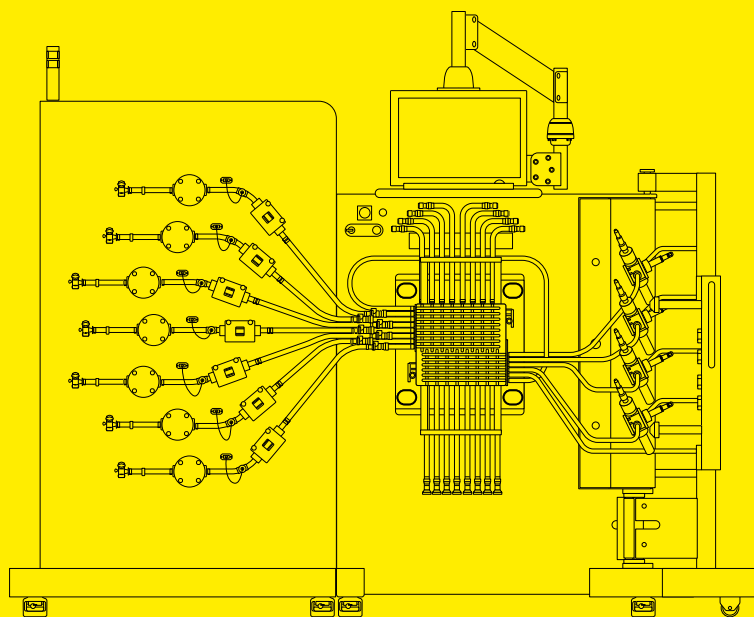
Process Scale:
Resolute® BioSMB PD:
PD | Bench Scale

Resolute® BioSMB 80:
Production Scale (400 L @ 11 h)

Project Duration:
3 weeks for tech transfer and scale-up

Used Products | Solutions | Services:

- Resolute® BioSMB PD
- Resolute® BioSMB 80

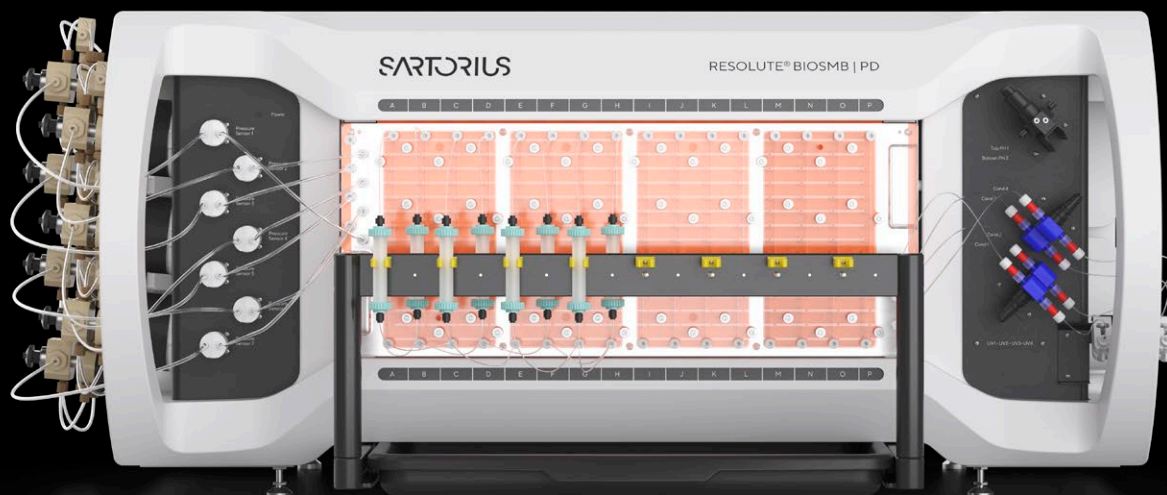


Outcome

A process comparison between batch and Resolute® BioSMB showed that similar processing times were possible between both technologies and different media requirements. While the batch process required a 20 L Protein A chromatography column processing over three cycles, the multi-column process required just 3.85 L of Protein A resin packed into 5 columns each of 0.77 L volume, operated over 13 cycles. This equated to a 16.15 L resin savings (greater than 80%) using the Resolute® BioSMB system.

	Batch	Resolute® BioSMB PD	Resolute® BioSMB 80
Elution titer	9.54 gm/L	13.84 gm/L	13.85 gm/L
Product yield	98%	97%	97%
Specific Productivity	16 gm/L/hr	56 gm/L/hr	56 gm/L/hr

Process Comparison	Batch	Resolute® BioSMB 80
Cycles	3	13
Column diameter	40 cm	14 cm
Column height	16 cm	5 cm
Protein A volume	20 L	3.85 L



At a Glance

3.5× higher productivity
than the batch mode

80% reduction in
chromatographic resin cost

Process scaled up
150×
from PD to Process

Process Comparison

Before: Batch

- Baseline yield: 98%
- Baseline impurity removal: 2.4 LRV HCP, 0.45% aggregate
- 20 L Protein A resin

After: Resolute® BioSMB

- Comparable yield: 97%
- Comparable impurity removal: 2.5 LRV HCP, 0.65% aggregate
- 3.85 L Protein A resin, 81% reduction

Scale Up Comparison

Before: Resolute® BioSMB PD

- 46.4 g/L binding capacity, 56 g/L/hr specific productivity
- 4.2 LRV DNA, 2.6 LRV HCP, 0.72% aggregate
- 4.0 mL/min flowrate

After: Resolute® BioSMB 80

- 46.4 g/L binding capacity, 56 g/L/hr specific productivity (same process metrics)
- 5.0 LRV DNA, 2.5 LRV HCP, 0.65% aggregate (product quality unaffected by scale-up)
- 37 L/hr flowrate, 150× larger process

Germany

Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

USA

Sartorius Stedim North America Inc.
565 Johnson Avenue
Bohemia, NY 11716
Toll-Free +1 800 368 7178

 For more information, visit
www.sartorius.com