

# SARTORIUS

## Customer Case Study

# Merck Process Transfer and Scale-Up of Batch Protein A Chromatography to 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/](http://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 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 BioSMB Applications Specialists, Merck developed a 5-column process utilizing 5 mL columns on the 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 BioSMB Process 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

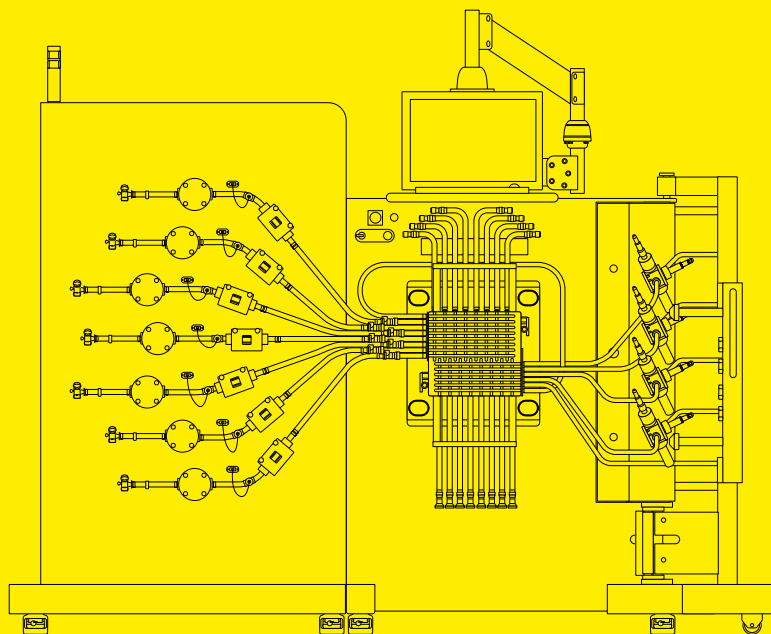
Process Steps:  
Affinity Chromatography

Process Scale:  
BioSMB PD: PD | Bench Scale  
BioSMB Process 80: Production  
Scale (400 L @ 11 h)

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

Used Products | Solutions | Services:

- BioSMB PD
- BioSMB Process 80

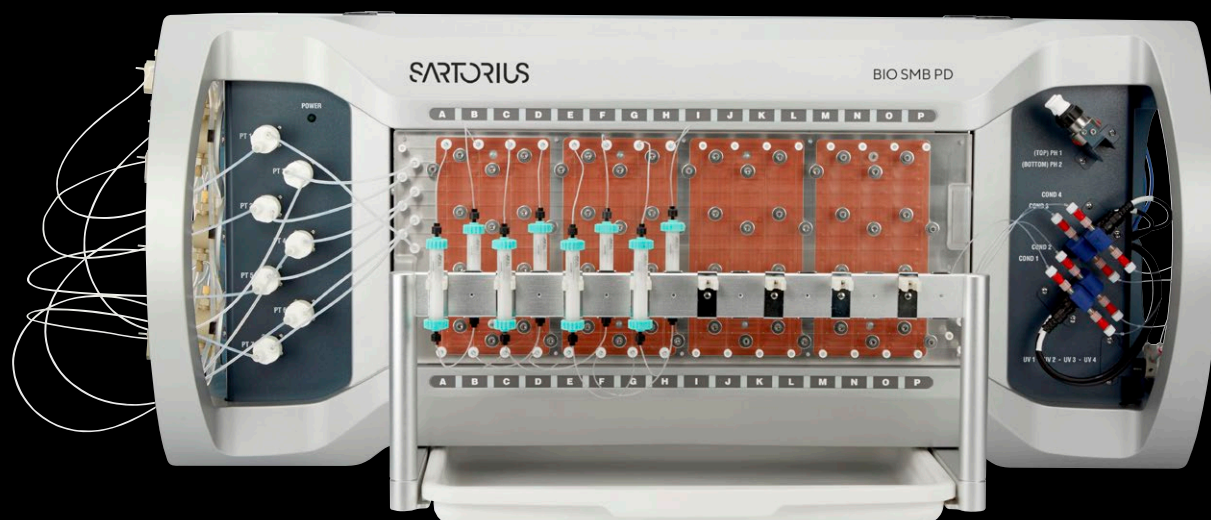


# Outcome

A process comparison between batch and 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 BioSMB system.

	Batch	BioSMB PD	BioSMB Process
Elution titer	9.54 gm/L	13.84 gm/L	13.85 gm/L
Product yield	98%	97%	97%
<b>Specific Productivity</b>	<b>16 gm/L/hr</b>	<b>56 gm/L/hr</b>	<b>56 gm/L/hr</b>

Process Comparison	Batch	BioSMB Process
Cycles	3	13
Column diameter	40 cm	14 cm
Column height	16 cm	5 cm
<b>Protein A volume</b>	<b>20 L</b>	<b>3.85 L</b>



# 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: BioSMB Process

- 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: 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: BioSMB Process

- 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

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