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Customer Case Study

Protein A Resin Reduction Achieved With Process Transfer From Batch to Resolute® BioSMB

Customer Profile

Company Name:
Sanofi-Aventis

Company Location:
Frankfurt am Main, Germany

Company Type:
Large Biopharma

Industry:
Health Care

Company Size:
>100K Employees

Company Revenue:
€36.126 Billion

Company Profile:
www.sanofi.com/en/about-us

Customer Challenge

Sanofi's key driver for this study was to reduce the operating costs of existing purification steps with high resin costs. Regulatory concerns were to be tested by determining product quality consistency through process transfer and scale-up. The feasibility of extended purifications at production scale was also determined by evaluating Resolute® BioSMB system robustness.

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Background Information

The aim of this study was to explore the benefits of multi-column chromatography and application to a perfusion based process. Resin savings and the capability of continuous chromatography to run for long process times were important decision factors in the selection of the technology.

This case study centred on transferring an existing batch chromatography process into a multi column format and then scaling up that process to an continuous perfusion run. The bioreactor was a 50 L single-use perfusion setup where the maintenance of aseptic conditions and flow path robustness were key to meet the target of a 10 day run time that ultimately processed a feedstock volume of approximately 800 L.

Provided Solution

Sanofi used the Resolute® BioSMB PD system to conduct a bench-scale proof of concept for continuous chromatography. Four pre-packed columns with Protein A resin, each with a volume of 5.7 mL (1.2 cm ID × 5 cm BH), were used for this set of experiments. They tested three process settings to determine if the continuous mode of operation was robust.

Scale up to the pilot scale was conducted with a Resolute® BioSMB 80 system. Four Protein A columns, each with a volume of ~200 mL (5 cm ID × 10 cm BH), were used, and the same process settings were used to determine if scale-up had any effect on product quality or any other operating results.

The Resolute® BioSMB 80 was also used on an extended 10-day run to test the system's robustness and the aseptic claims of the single-use manifold. Three of the 200 mL Protein A columns were used, leading to a process flowrate of 5 L/h.

Project Key Indicators

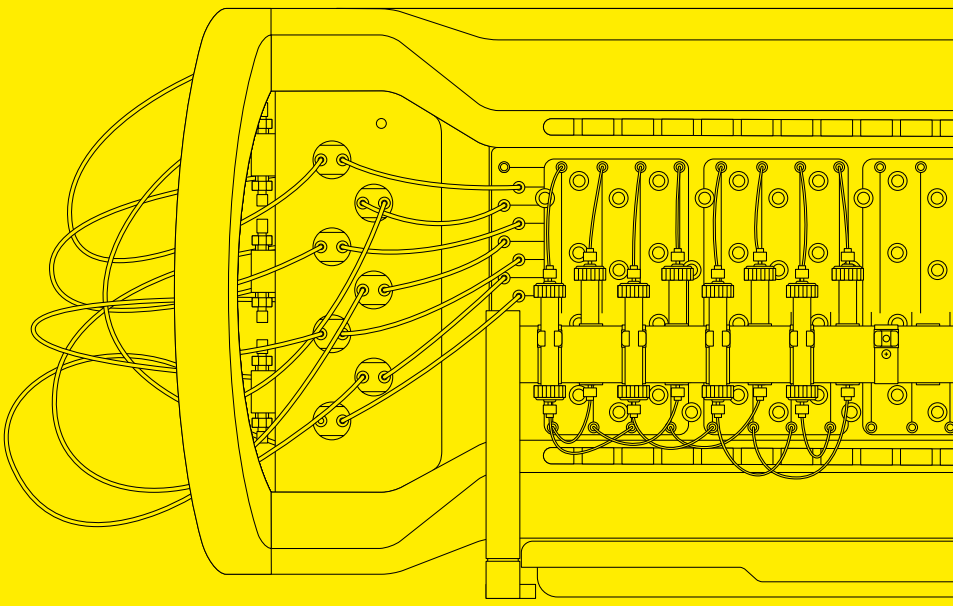
Molecule type: mAbs, Biosimilars

Process Steps:
Downstream
Chromatography

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

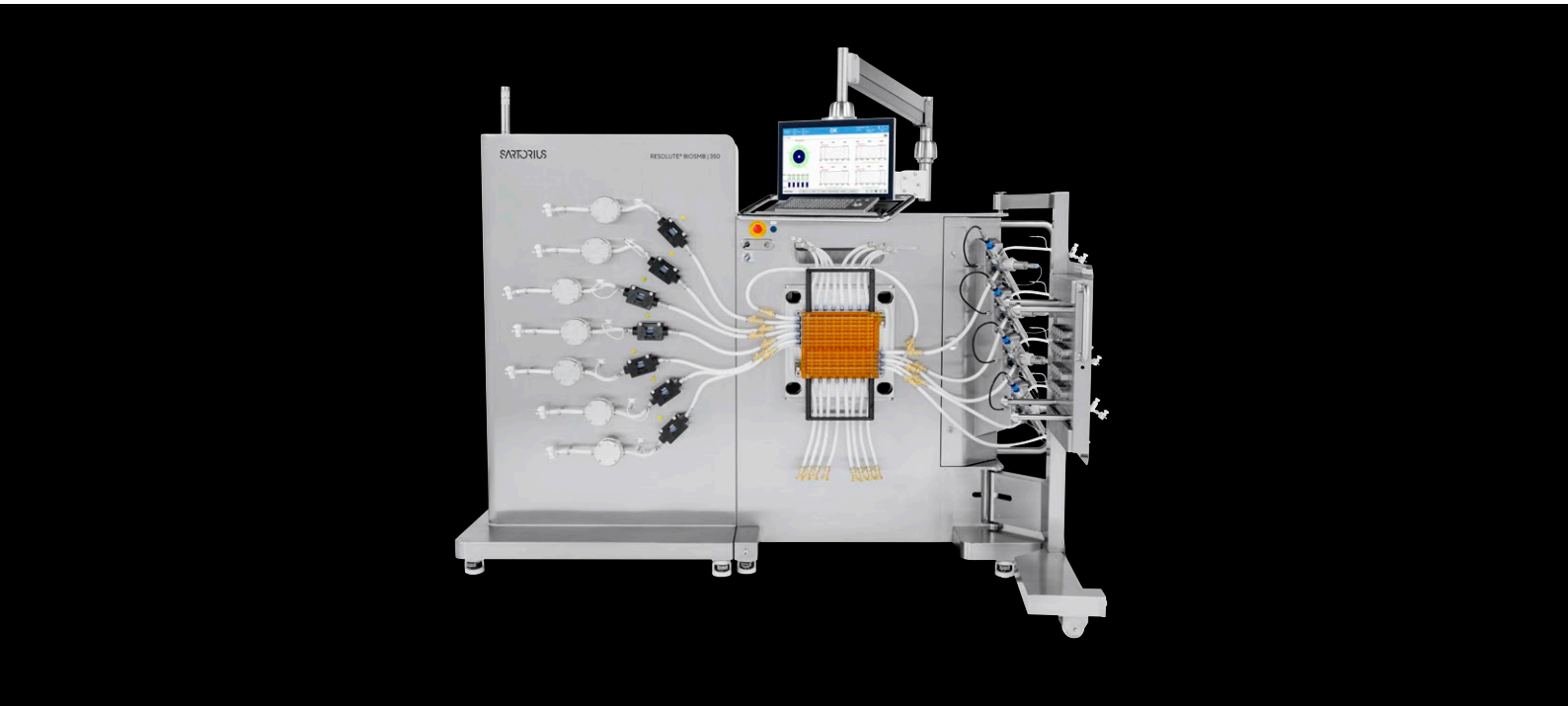
Resolute® BioSMB 80:
Production Scale (Commercial and Clinical)

Used Products | Solutions | Services:
- Resolute® BioSMB PD
- Resolute® BioSMB 80



Outcome

By transferring their existing Protein A step to the Resolute® BioSMB platform, Sanofi saw consistent process performance and product quality compared to batch mode and benefited from a 400 – 500% increase in productivity and greater than 80% reduction Protein-A resin requirement. The standard process architecture between the Resolute® BioSMB PD and Resolute® BioSMB 80 enabled seamless scalability from bench to production-scale. The perfusion optimized single-use manifold of the Resolute® BioSMB 80 system allowed for a robust, 10-day continuous purification process indicating that the functionally closed, single-use, gamma-irradiated flow path is robust in design and suitable for single-use manufacturing facilities. Sanofi also demonstrated that Resolute® BioSMB technology could be optimized for commercial (maximizing load capacity) or clinical processing (minimize resin requirement).



At a Glance

400-500%
increase in productivity

80% reduction
Protein-A resin requirement

Seamless scalability
from bench to production-scale

No measurable bioburden
or contamination was observed during the 10-day straight run

Before: Batch

- Load capacity: 30 g/L @ 4 min contact time
- 14 g/L/hr specific productivity
- 100 L Protein A resin

After: Resolute® BioSMB Clinical

- Load capacity: 32 g/L @ 1 min contact time, higher capacity at faster flowrates
- 65 g/L/hr specific productivity, significantly more productive
- 11 L Protein A resin, 89% reduction in resin usage

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