Millipore®
Preparation, Separation,
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Technical Brief

ProSep®-vA Ultra Media 300 Cycle Lifetime Study

Introduction

The selectivity, recovery and productivity benefits of protein A affinity chromatography now make it the most widely used technique for initial capture in the commercial purification of monoclonal antibodies (mAbs).

While overall process economics are dependent on a number of factors, including buffer, utility, labor and capital depreciation costs, media cost can also have a significant impact. As protein A affinity resins are typically more expensive than other media, they may be viewed as less attractive for process selection. However, media cost is directly related to the lifetime of the resin and an extended resin lifetime may well compensate for a higher initial cost. Together with the other benefits of purity and yield, protein A resins can result in a favorable overall process cost and contribute to reduced cost of goods.

This Technical Brief presents data on a study illustrating the extended lifetime capability for ProSep®-vA Ultra resin.

Study Details

Sample	mAb containing clarified Chinese Hamster Ovary (CHO) feedstock at a mAb concentration of 1.5 g/L
Column	0.66 x 5.15 cm (1.8 mL)
Flow rate	Loading: 0.7 mL/min (RT 2.5 min) All other steps: 2 mL/min (RT 0.9 min)
Dynamic binding capacity of ProSep®-vA Ultra media	50 mg/mL (determined at 10% breakthrough)
Column load	21 mg/mL
Cleaning	Cycle run after every fifth cycle

Step Description	Buffer	Step Length
Column equilibration	PBS pH 7.4	9 CV
Sample load	CHO/mAb feedstock	12 CV
Wash	PBS pH 7.4	10 CV
Elute	0.1 M glycine/HCl pH 3.0	7 CV
Regenerate	Phosphoric Acid pH 1.5	4 CV
Cleaning every fifth cycle	6 M Urea in PBS	6 CV
Re-equilibrate	PBS pH 7.4	12 CV

PBS – Phosphate Buffered Saline
CV – Column Volumes

Results

Consistent performance of the ProSep®-vA Ultra media over the 300 cycle duration of the study is demonstrated by the following figures.

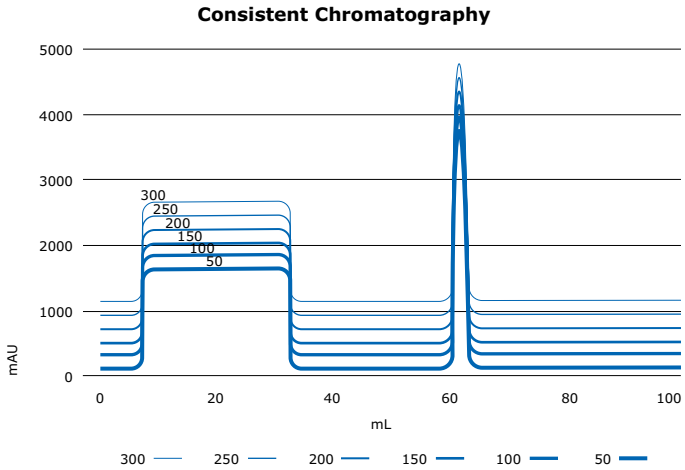

Figure 1.

Consistent chromatographic performance is demonstrated by the overlay of chromatograms through cycles 50 to 300.

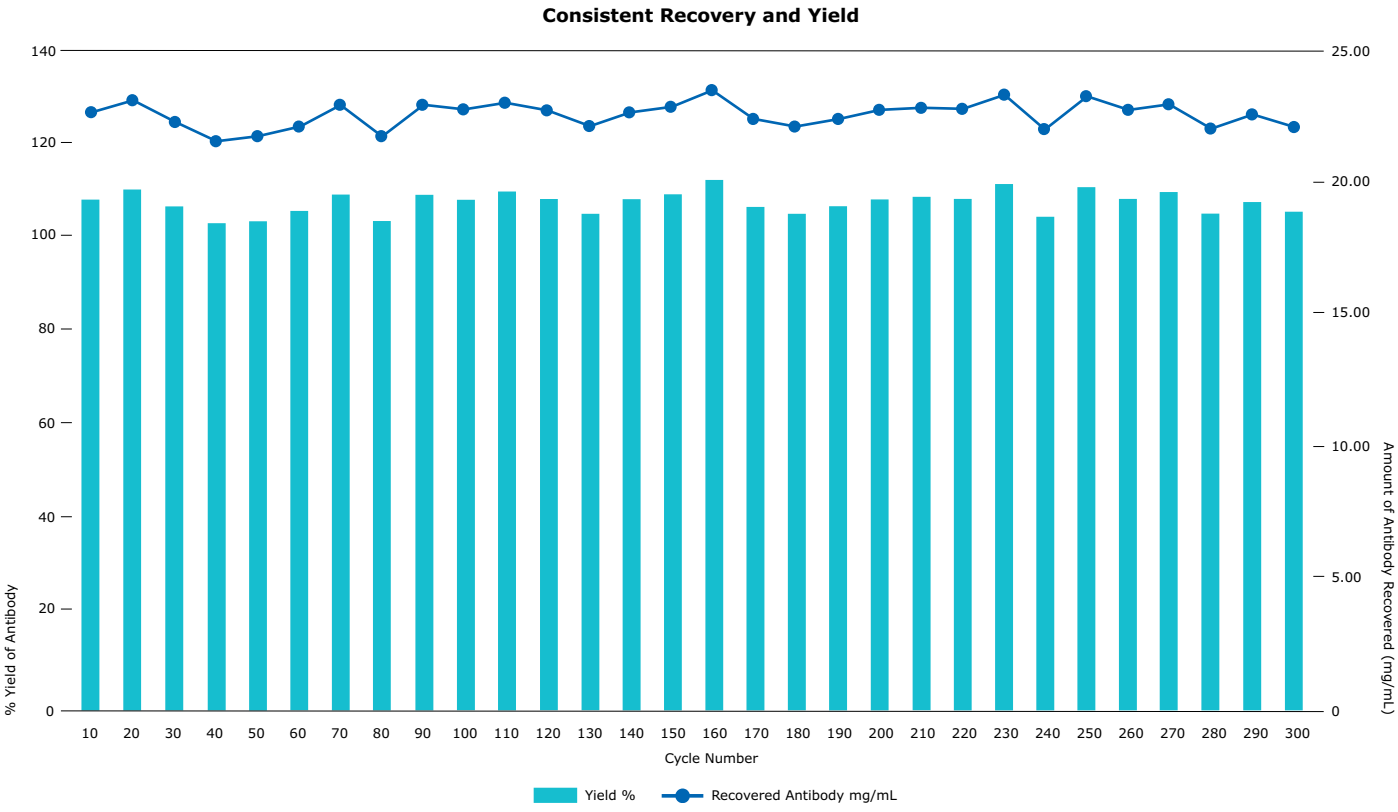

Figure 2.

Comparing the antibody recovery and yield data for every tenth cycle demonstrates consistency of performance with values being within +/-4% of the mean and no indication of loss of performance with repeat cycles.

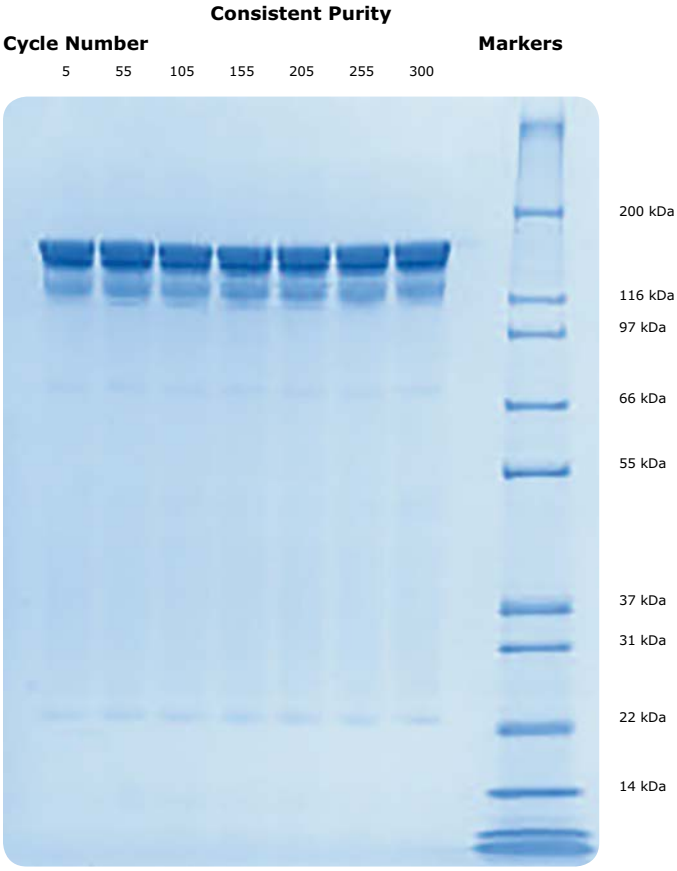

Figure 3.

The equivalent SDS-PAGE (non-reduced) profiles of elution fractions from selected cycles demonstrates consistent purity is maintained during repeated use.

Conclusion and Discussion

The results show the extended lifetime capability of ProSep®-vA Ultra media, demonstrating consistent yield and purity out to 300 cycles, with no indication of declining performance.

The impact of extending lifetime on process economics is illustrated in Figure 4. The relative media cost per gram of mAb produced is shown as a function of achievable cycles. By increasing media lifetime to 300 cycles, the media cost component is reduced fivefold compared to a media with a lifetime of only 50 cycles. As buffer costs remain essentially constant irrespective of the number of cycles achieved, the relative media contribution to the overall process cost is significantly reduced.

Therefore, the lifetime of the media is a critical component in determining the cost-effectiveness of the media.

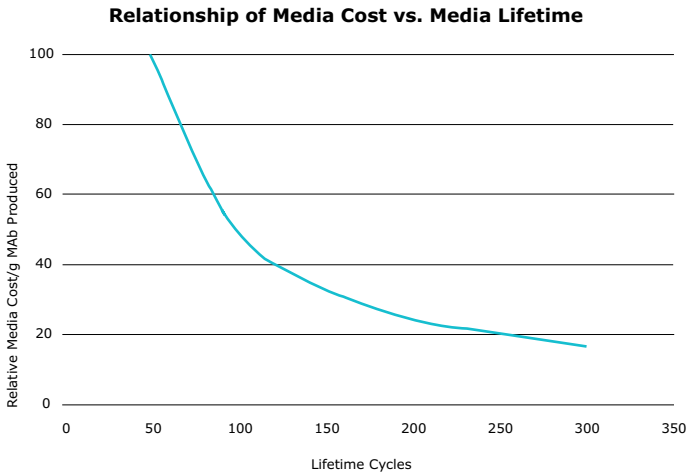

Figure 4.

Increasing the lifetime of the media significantly reduces its contribution to overall processing costs.

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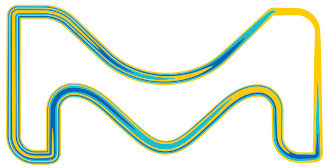

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