Millipore®
Preparation, Separation,
Filtration & Monitoring Products

Tech Brief

# Consistent and Predictable Process Scale-up with QuikScale® Biochromatography Columns

When introducing a new drug product to market, the scale-up of chromatography separations from the laboratory through process development and on to the purification suite is among the most challenging transitions to achieve. The challenge lies in the complexity of achieving consistent chromatographic performance when moving from small to larger size columns. Even after the separation process has been quantified, columns of different sizes can exhibit differences in the flow cell pattern, seal design, and interior band spreading, which can continue to affect the overall performance of the separation. Significantly reducing column performance variation will result in improved yields and better product purity. A broad range of column diameters providing consistent and high performance under a variety of process conditions would solve many of the difficulties associated with scaling up the purification of new drug entities from the discovery phase.

## Consistent Chromatographic Performance Across a Broad Range of Column Sizes

QuikScale® columns offer a broad range of performance capabilities—a greater than 400 to 1 range in processing capability with each column size designed to provide proven and consistent performance. To further expand the performance capability provided by the QuikScale® column range, each column height may be extended using one of three available tube lengths.

To illustrate the fast scalability of the QuikScale® column, a separation of soy trypsin inhibitor and ovalbumin was performed with a 22 mm Vantage™ L column packed with Q Sepharose™ media. The separations process and operating parameters were then scaled up to a 450 mm QuikScale® column. The scale-up factors are 418X by volume and 20X by diameter. The separation employing the 450 mm QuikScale® column exhibited excellent resolution and an elution profile similar to the chromatogram observed with the 22 mm Vantage™ L column. The separations obtained with the two columns are presented in Figure 1.

Figure 1 demonstrates that the two peaks eluted from each column have similar relative size and retention time. This is supported by the nearly identical selectivity values that were calculated. These values also indicate that both columns were loaded with similar feed solutions and that the anion exchanger partitioned the analytes comparably in both runs. With the larger column, resolution, retention factors, and HETP were obtained that were comparable to or better than the results seen with the smaller bench scale separation.

## Proven Design and Performance Save Cost and Time

QuikScale® columns provide the user with the tools to develop new separations and transfer them to the production suite fast. The columns also provide comparable separation results when scaling up from small to large columns. This predictable performance allows users to quickly move a process optimized in the laboratory to the production suite, avoiding the cost of unsuccessful scale-up attempts.

## Quick and Reliable Scale-up

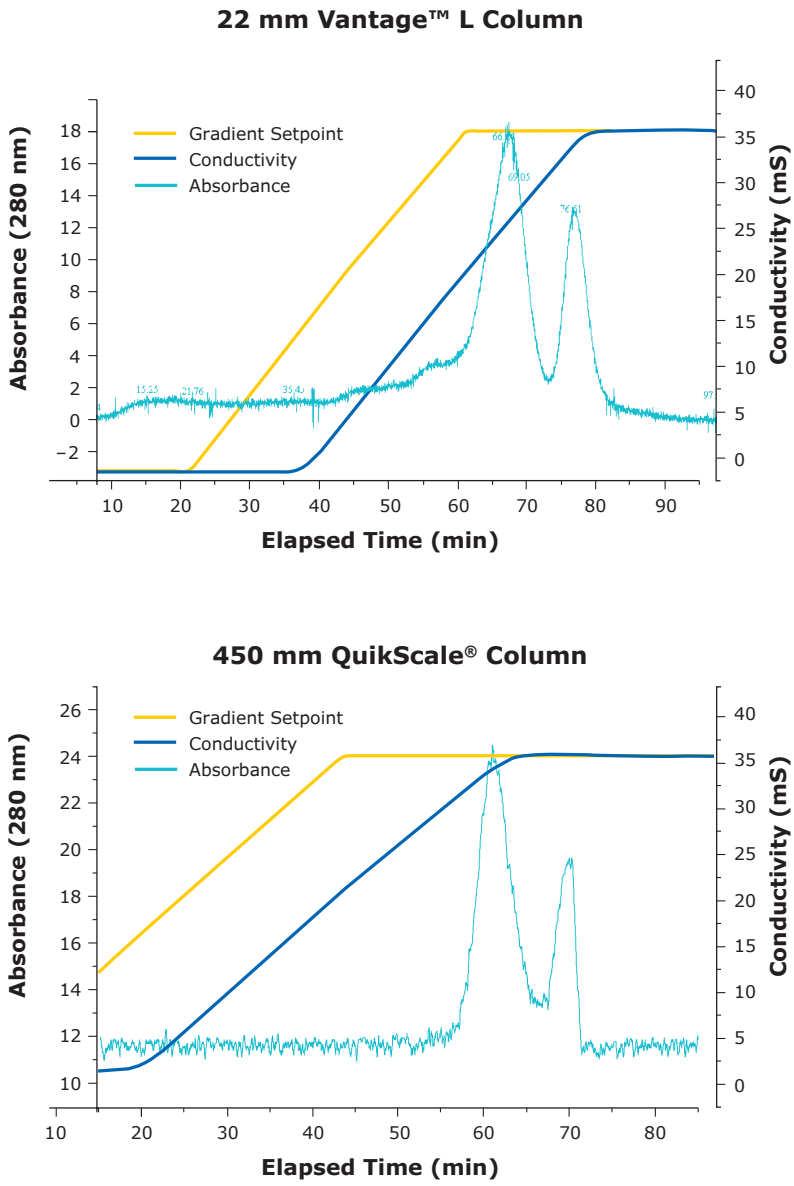


**Figure 1.** Separation of ovalbumin from trypsin inhibitor was scouted on a Vantage™ L column (22 mm). The process was then linearly scaled up (418X by volume, 20X by diameter) to a 450 mm QuikScale® column with highly comparable results.

**Table 1.** Packing Parameters

| | Vantage™ L Column 22 mm | QuikScale® Column 450 mm |
|---|---|---|
| **Media** | Q Sepharose™ FF | Q Sepharose™ FF |
| **Bed height** | 20.0 cm | 18.0 cm |
| **Sample composition** | Ovalbumin/trypsin inhibitor | Ovalbumin/trypsin inhibitor |
| **Gradient** | 100%–0%; 40 min | 100%–0%; 40 min |
| **Equilibration buffer** | 0.01 M Tris | 0.01 M Tris |
| **Elution buffer** | 0.01 M Tris/0.35 M NaCl | 0.01 M Tris/0.35 M NaCl |

**Table 2.** Comparison of Separations with a 22 mm Vantage™ L Column and 450 mm QuikScale® Column

| | Vantage™ L Column 22 mm | QuikScale® Column 450 mm |
|---|---|---|
| **Peak A** | | |
| **$T_r$** | 67.56 min | 60.62 min |
| **Width** | 11.76 min | 8.17 min |
| **Height** | 0.018 AU | 0.016 AU |
| **HETP** | 0.031 cm | 0.015 cm |
| **Peak B** | | |
| **$T_r$** | 77.28 min | 69.67 min |
| **Width** | 6.76 min | 4.67 min |
| **Height** | 0.011 AU | 0.014 AU |
| **HETP** | 0.008 cm | 0.005 cm |
| **$T_m$** | 14.62 min | 15.15 min |
| **∂** | 1.18 | 1.20 |
| **$R_s$** | 1.10 | 1.39 |

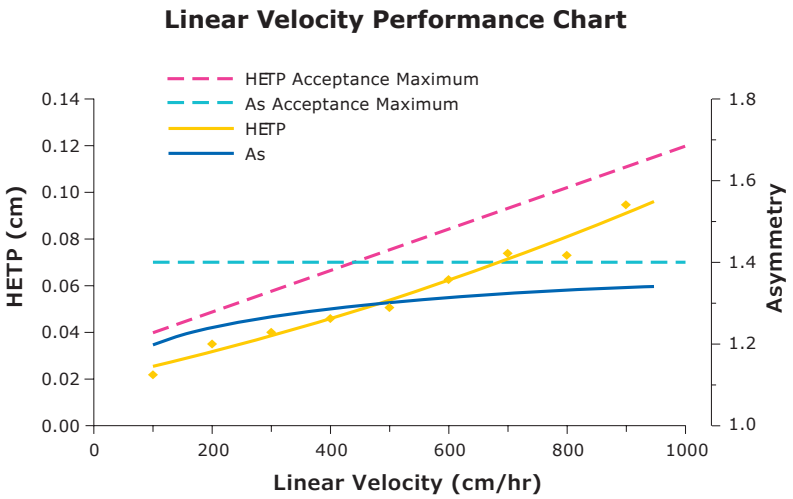


**Figure 2.** HETP/Linear Velocity/As curve for a 450 mm QuikScale® column packed with ProSep® media.

## Superior Separation Performance Improves Product Purity and Increases Production Yields

The separations employing the 22 mm Vantage™ L column and 450 mm QuikScale® column revealed comparable results for both columns. The main difference between the separations was in the resolution achieved. The 450 mm QuikScale® column achieved a much higher resolution than the smaller column. This ability to improve product purity during scale-up allows for increased production yields. Tables 1 and 2 illustrate a statistical comparison of the two separations.

## Scale up Super Fast Media Applications over a Broad Flow Range

The QuikScale® column is optimally designed for use over a very broad range of linear velocities. The unique design of the column leads to predictable chromatographic performance during scale up from low to very high linear velocities (up to 1000 cm/hr), thereby allowing today's 'super fast' media to be utilized at maximum capacity (Figure 2).

## Summary

QuikScale® columns provide a reliable solution to the consistency problems usually encountered when scaling up from the discovery phase to the purification suite. QuikScale® column users can proceed with confidence, knowing that their separation results will remain consistent when moving from small to large scale equipment.

MilliporeSigma
400 Summit Drive
Burlington, MA 01803

For additional information,
please visit **www.EMDMillipore.com**

To place an order or receive technical assistance,
please visit **www.EMDMillipore.com/contactPS**



MS_TB20010000 Ver. 1.0
36181
09/2021