Design Features of Pre-Packed Disposable, Development to Production Scale Chromatography Columns Confer Reliable Flow and Chromatographic Characteristics

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Summary

Disposable manufacturing has been a developing trend in biopharmaceutical manufacturing for the last two decades. In a 2011 Survey of Biopharmaceutical Manufacturing Capacity and Production[1] the authors note "we are on the verge of the first approvals of mainstream biopharmaceutical products manufactured using single use/disposable systems" and "Single use and disposable chromatography units will be the most important trend in the next five years"[2].

Disposable technologies have been adopted by biopharmaceutical industry as a mean for faster product changeover, favorable economics, and improved safety. Until now there has not been a broadly applicable solution for disposable chromatography steps.

Repligen's OPUS™ (Open Platform User Specified) pre-packed columns are disposable and can be packed with almost any bioprocessing resin, at internal diameters ranging from 0.5 cm to 60 cm, and column heights from 5 cm and up, offering a broad, scalable solution for the purification of biological products.

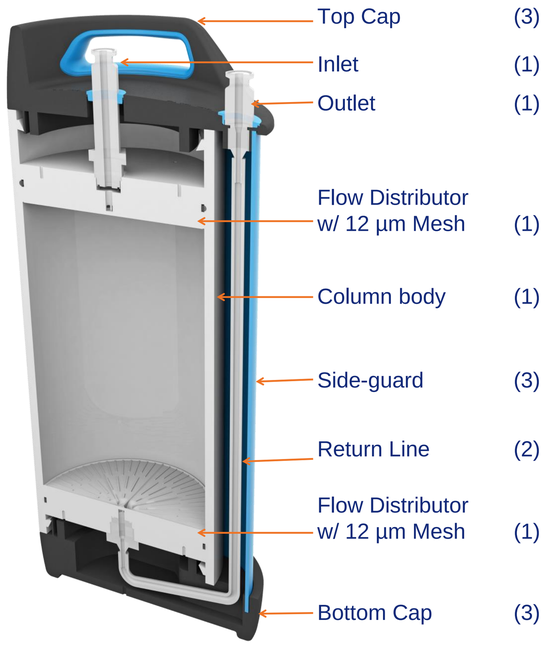
Design of the flow distribution permits even flow for all column sizes.

OPUS™ columns characteristics are maintained during various transportation conditions, making them suitable for use at different manufacturing sites.

Design and Materials of Construction

Objective: Design of a simple, clean, robust and functional pre-packed disposable chromatography column

Figure 1: Cross-section of a large scale OPUS™ column



Legend:

Product Contact Material:
1 = Polypropylene
2 = Platinum Cured Silicone

Non-product Contact Materials:
3 = Acrylonitrile Butadiene Styrene (ABS) copolymer

Figure 2: Design features of the flow adaptor

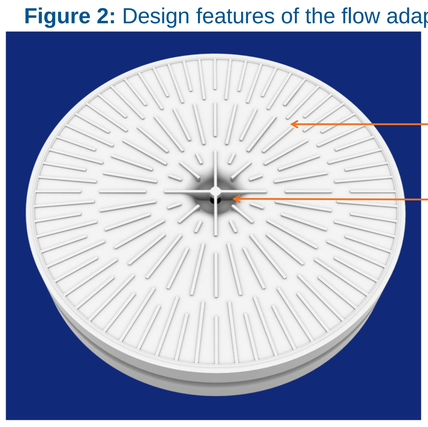


Figure 3: Cross-section of the flow adaptor

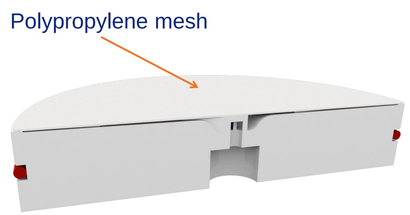
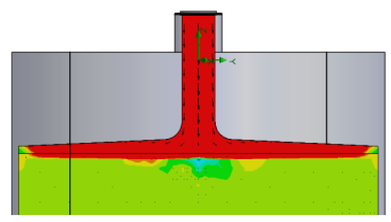


Figure 4: Computational flow mapping



Conclusions:

- Engineered design enables even flow distribution of the mobile phase
- Ease of use is conferred by simplicity of construction
- Regulatory compliance is addressed by the use of USP class VI certified product contact materials

Assessment of Chromatographic Performance

Objective: To experimentally demonstrate flow uniformity of OPUS™ columns through size exclusion performance

Method:
- Determination of plates number and asymmetry for different sizes of OPUS™ columns. Columns are injected with 1% of CV of 2% acetone solution at a linear flow rate of 100 cm/h. Columns are pre-packed with Sepharose® 6FF resin. Columns are all 20 cm height, and IDs of 1.2, 2.5, 8 and 20 cm
- Measuring separation resolution of molecular weight markers on different sizes OPUS™ columns. 1% of CV of 2mg/mL solutions of molecular weight markers injected into the columns at a linear flow rate of 30 cm/h

Acceptance Criteria:
- Column quality attributes pass acceptance test: Plates/m: >1500, Asymmetry: 0.8-1.6
- Resolution of molecular weight markers is consistent for all column scales

Results:

Table 1: Column properties for OPUS™ columns pre-packed with Sepharose® 6FF

Column ID	Plates/m @ 100cm/h	Asymmetry @ 100 cm/h
1.2 cm	3010	1.1
2.5 cm	3465	1.2
8 cm	2959	1.2
20 cm	3295	1.2

Figure 5: Chromatogram for separation of molecular weight markers

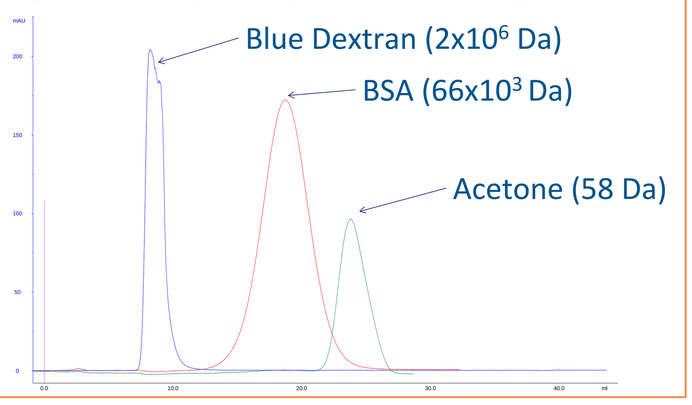


Table 2: Separation resolutions for various sizes OPUS™ columns

Column ID	Resolution Dextran/BSA	Resolution Blue Dextran/Acetone	Resolution BSA/Acetone
1.2 cm	2.2	4.6	0.9
2.5 cm	2.6	6.1	1.1
8 cm	2.3	6.1	1.2
20 cm	2.8	7.1	1.2

Conclusion:
- Consistency of separation resolutions and column properties proves flow uniformity
- Chromatographic performance is demonstrated and maintained over a range of OPUS™ column diameters

Transportation Validation

Objective: To demonstrate that a GMP-ready pre-packed disposable OPUS™ column can be shipped without compromising performance.

Method:
- A 20 cm diameter by 10 cm bed height OPUS™ column was subjected to a rigorous shipping study using the International Safe Transit Association's (ISTA) Procedure 1A
  Tests included:
  - Fixed displacement vibration test: a total of ~ 15000 vibrational impacts over 64 min
  - Shock-drop test: drop tests on corners, edges, and faces of the packing box from 70 cm (24 inches) height
- A 20x20 cm column packed with SP Sepharose® was shipped 6000 miles by truck and air. The column was assessed for chromatographic efficiency by measuring plates number and asymmetry

Acceptance criteria:
- Intact column upon visual inspection
- Packed bed chromatographic quality attributes (plates number and asymmetry) are preserved

Results:
- Visual Inspection: Minor abrasions caused by vibration testing, some minor damage to the external package cause by drop test on the angles. Column found undamaged and intact. **The package passed ISTA 1A testing**

Figure 6: Column quality testing pre and post shipping; 20x10 cm OPUS™ column

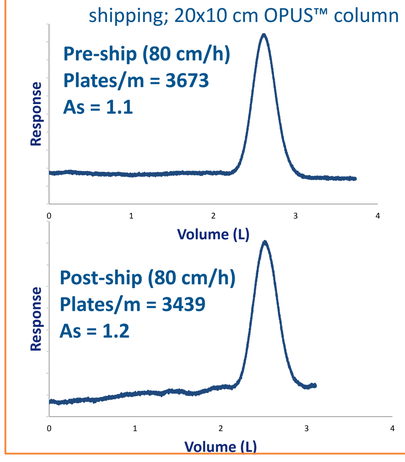
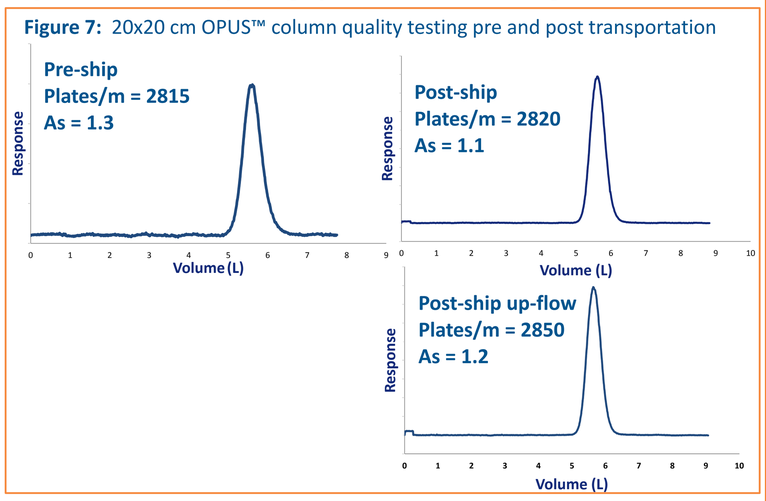


Figure 7: 20x20 cm OPUS™ column quality testing pre and post transportation



Conclusion:
- Packaging withstood the rigors of a commercial shipping environment
- Chromatographic performance maintained after shipping

Conclusions

- Design and selection of construction materials ensures OPUS™ columns are suitable for manufacturing of biological products
- Engineered design of the flow distributor confers even flow dispersion of the mobile phase
- Outstanding design is confirmed by consistency of size exclusion resolution and column quality attributes for various scales of OPUS™ columns
- Transportability and ruggedness of OPUS™ columns is demonstrated by rigorous tests
- OPUS™ columns offer unparalleled flexibility in regards to column size and choice of chromatographic resin packed, while maintaining the highest standards of quality

References:
1. 8th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production
2. Dr. Stefan Schmidt, CSO, ERA Biotech

Company Info

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