Implementing Disposable Chromatography: Technology Fit in Downstream Purification

Fletcher Malcom, Dana C. Pentia, William J. Wilde, James R. Peyser
Repligen Corporation, Waltham, MA, USA

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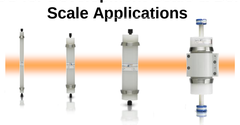
Summary

Disposable and single-use technologies have become standard in many of the world's leading biopharmaceutical companies. Faster product changeover, favorable economics, and improved safety have driven this paradigm shift. As with any paradigm shift, overcoming barriers to implementation is critical to the success of pre-packed disposable columns in GMP manufacturing.

In 2012 Repligen conducted proprietary market research[1] to validate the most important barriers and found column size, chromatographic performance, economics, and documentation were the most commonly referenced barriers to implementing pre-packed disposable columns. OPUS® (Open Platform User Specified) columns by Repligen have been intelligently designed and developed for GMP Manufacturing to offer the following:

- **Column Size**: 9 industry standard diameters available in bed heights ranging from 5 – 40 cm
- **Chromatographic Performance**: OPUS columns maintain critical purification parameters throughout extensive cycling experiments simulating >100 process cycles
- **Economics**: An economic model developed with BioProcess Technology Consultants (BPTC) shows OPUS columns save on average $20,000 USD for a small scale clinical campaign
- **Documentation**: OPUS columns are manufactured under a certified ISO 9001:2008 Quality Management System and come with a regulatory support file and fully qualified certificate of analysis

Column Size

Two Platforms	Diameter	Bed Height	Any Resin
OPUS for Development Scale & Bench Scale Applications  OPUS for GMP Manufacturing Scale Applications 	Development or Bench Scale: **IDs: 1.2, 2.5, 5, 8 cm**	Development or Bench Scale: **1.2 ID: 5- 25 cm 2.5, 5 ID: 5 – 20 cm 8 cm ID: 5 – 30 cm**	**Examples of Resins Packed** **CaptivA™ PriMab™ MabSelect SuRe™** (PA) **Sepharose® 4 & 6 FF, HP** (PA, IEX, HIC) **Capto™** (IEX) **Toyopearl®** (IEX & HIC) **POROS®** (IEX) **ProSep® UP** (PA) **Fractogel®** (IEX) **CHT** (HIC)
	GMP Manufacturing Scale: **IDs: 10, 14, 20, 25, 30, 45 cm**	GMP Manufacturing Scale: **All IDs: 5 – 30 cm**	

Conclusions:

- Open Platform User Specified Columns offer unparalleled flexibility in a pre-packed column format to deliver the standardized disposable platform the bioprocessing industry requires

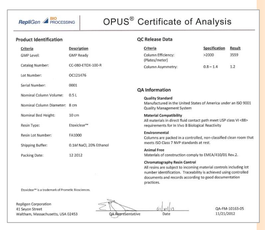
Documentation

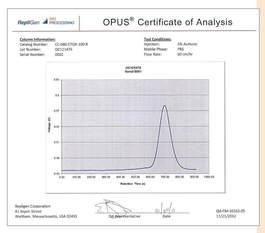
OPUS 10 – 30 cm ID Regulatory Support File

Table of Contents

- Product Specifications
- Manufacturing & Quality Systems
- Manufacturing Procedures
- Extractables & Leachables
- Shipping Qualification
- User Instructions
- Material Certificates
- Example CoAs

OPUS 10 – 30 cm ID Certificate of Analysis





Product Identification
- Column Specifications
- Resin Type & Lot Number
- Shipping Buffer
- Pack Date

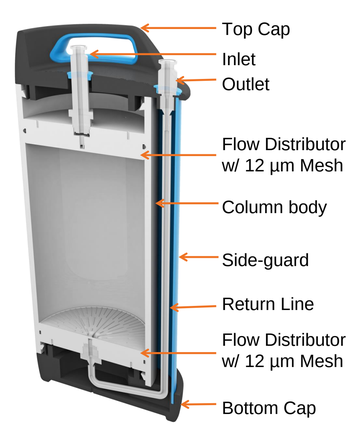
Quality Control Release Data
- Plates / meter Result
- Asymmetry Result
- Bioburden and Endotoxin Results (optional)

Quality Assurance Information
- ISO 9001 Certified
- Product Contact Material Statement
- Manufacturing Environment
- Chromatography Resin Control

Attachments
- Resin Manufacturer's CoA
- Chromatogram

Conclusions:

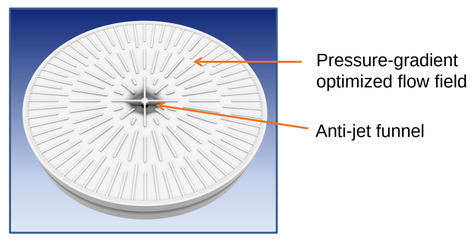
- OPUS columns come with the documentation to support an NDA and CMC package
- Repligen manufacturers OPUS columns under an ISO 9001:2008 certified Quality Management System



Legend:

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

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



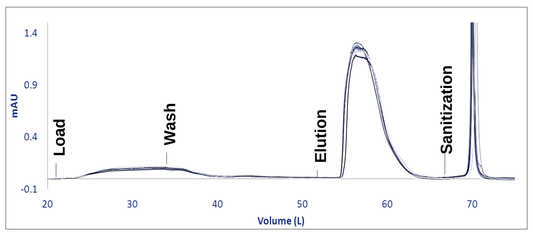
Chromatographic Performance

Method:

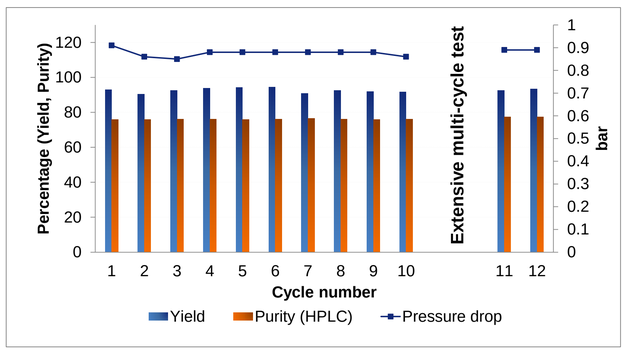
- Purification of a recombinant protein from filtered cell lysate on an OPUS 20 x 20 cm column packed with SP Sepharose® for 10 cycles, and 2 additional cycles after an extensive multi-cycle test[2]
- Extensive multi-cycle test: re-circulate the same OPUS column with high salt buffer for 2 weeks

Results:

Overlay of 10 chromatograms: rProtein purification



Quantitative results for 10 cycles of rProtein purification followed by additional 2 cycles post extensive multi-cycle test



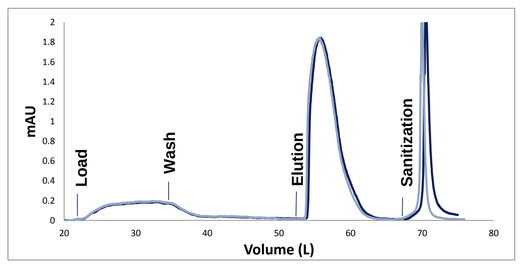
Column quality attributes pre & post-run: rProtein purification

Conditions	Plate count plates/m	Asymmetry
Pre-run	2815	1.3
Post-run	3512	1.2

Column quality attributes: Extensive multi-cycle test

Column volumes of buffer	Plate count (plates/m)	Asymmetry
0	2820	1.1
95	2890	1.0
355	2885	1.2
470	3535	1.1
985	3113	1.3
1225	2840	1.3

Overlay of 2 additional cycles rProtein purification post extensive multi-cycle test



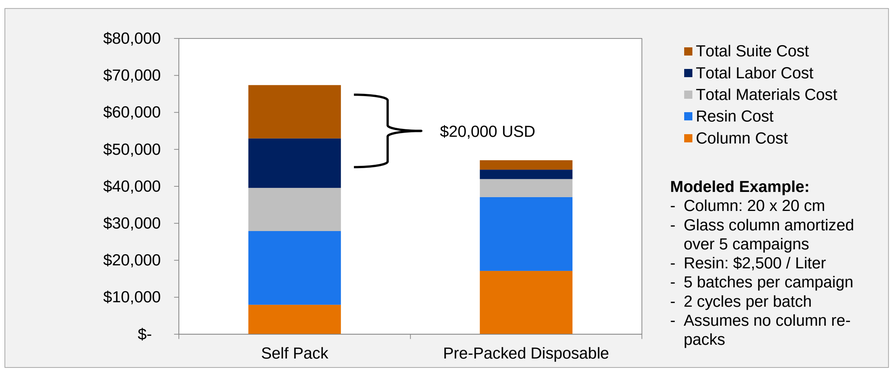
Conclusions:

- Pre-packed columns maintained packing quality attributes (plates/m, asymmetry, pressure drop) and consistent purification results (yield, purity, chromatography)
- Performance characteristics are maintained for simulated equivalent flow of >100 process cycles

Economics

Function	Self Pack - Task List	FTE Hours		OPUS® Pre-Pack – Task List
		1 Procurement	Procurement 1	
Procurement	Specify & Order Column			Specify & Order Column
	Receive & Asset Tag Column	3 QC	2 QC	Receive Column
Documentation & Engineering Prep	Draft & Approve I/OQ Protocol	8 QC/QA	1 QA/QC	QA Inspection, Release Assign RM lot#
	Verify Vendor Documentation	3 QC	3 QC	Verify Vendor Documentation
	Complete & Document IQ	8 Mfg		
	Install new frits O-rings, clean column	8 Mfg		
	Complete & Document OQ	6 Mfg		
Packing	Prep Column Packing Buffers	4 Mfg		
	Prep Resin Slurry & De-Fine	2 Mfg		
	Pack, Test & Document Column	12 Mfg	1.5 Mfg	Test & Document Column
Purification	Purification Process Column Cycling	SAME		Purification Process Column Cycling
Storage	Sanitize Post Use	0.5 Mfg	0.5 Mfg	Sanitize & Store For Next Use
	Unpack Column	8 Mfg		
	Clean & Verify Column, Change Frits, O-Rings	21 Mfg/QA		
	Prep & Store Empty Column	2 Mfg		
	Retire Column & Discard Column		1 Mfg	Discard
Totals	**Self Pack vs. OPUS**	**86.5 h**	**10 h**	**~ 75 hours in savings**

bptc



Modeled Example:
- Column: 20 x 20 cm
- Glass column amortized over 5 campaigns
- Resin: $2,500 / Liter
- 5 batches per campaign
- 2 cycles per batch
- Assumes no column re-packs

Column operation costs not included

Conclusions:

- Pre-packed columns save significant time (~75 h) in small scale clinical manufacturing campaigns
- OPUS columns save an estimated $20,000 USD per column in a typical small scale clinical manufacturing campaign[3]

Conclusions

OPUS pre-packed disposable columns are ideal for the purification of biological molecules and can replace conventional columns in clinical scale GMP manufacturing due to:

- **Available Column Sizes**: Easily platformable disposable column technology with 9 industry standard diameters, a range of bed heights, and configurable for nearly any commercially available bioprocess chromatography resin
- **Fit for Purpose Chromatographic Performance**: OPUS columns demonstrate the robust, reproducible, and rugged properties necessary for GMP manufacturing
- **Significant Economic Gains**: OPUS columns save on average $20,000 USD and an estimated 75 hours of FTE labor per column for a typical small scale clinical campaign
- **Adequate Documentation Package to Support CMC and NDA Submissions**: OPUS columns are manufactured under a certified ISO 9001:2008 Quality Management System and come with a regulatory support file and fully qualified certificate of analysis

Visit www.repligen.com/opus to learn more, or configure your own column at www.repligen.com/configure-a-column.

References:
1. 2012 Proprietary Market Research, The Latham Group
2. *Multi-Cycle Performance of OPUS Columns*, © Repligen Corp. 2012
3. Malcom, F. *Implementing Disposable Chromatography: Process and Technology Fit*, BDP Week: Huntington Beach, CA 2013. IBC Life Sciences

Repligen Corporation, 41 Seyon Street, Waltham, Massachusetts 02453, U.S.A.
www.repligen.com, +1-781-215-0111