LEADER OF THE PACK:

6-8 Week OPUS® Lead Times, OPUS® R Pre-packed Columns

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Vice President – Product Management and Field Applications
March 28, 2017
Leader of the pack: Broadest range of pre-packed columns from bench to production scale: 50µl - 85L
OPUS® Pre-packed Columns

<table>
<thead>
<tr>
<th>Process Development</th>
<th>Manufacturing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small-scale 0.5 cm – 5 cm</td>
<td>Large-scale 8 cm – 60 cm</td>
</tr>
</tbody>
</table>

- **Screening**
  - Sample Prep
- **Process validation**
- **Scale-up**
- **Early phase clinical**
- **Mid- Late phase clinical**
- **Commercial**

**OPUS® RoboColumn™**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 0.2mL – 10mL
- Resin: 2mL – 300mL

**OPUS® PipetColumn**
- Diameter: 0.1L – 1.75L
- Bed Height: 0.2mL – 10mL
- Resin: 0.1L – 1.75L

**OPUS® CentriColumn**
- Diameter: 0.5L – 85L
- Bed Height: 0.2mL – 10mL
- Resin: 0.1L – 1.75L

**OPUS® MiniChrom**
- Diameter: 0.5L – 85L
- Bed Height: 0.2mL – 10mL
- Resin: 0.1L – 1.75L

**OPUS® ValiChrom**
- Diameter: 0.5L – 85L
- Bed Height: 0.2mL – 10mL
- Resin: 0.1L – 1.75L

**OPUS® 5 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 8 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 10 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 14 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 20 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 25 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 30 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 45 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**OPUS® 60 cm**
- Diameter: 0.05mL – 0.6mL
- Bed Height: 2mL – 300mL
- Resin: 0.2mL – 10mL

**Platformable**
Leader of the Pack:
OPUS® Pre-packed Chromatography Columns
Any resin, any application, any size

Pre-packed chromatography columns with unparalleled flexibility in media choice, application and size

- Expert in packing manufacturing-scale columns
- >100 45s and 60s shipped since 2015
- >400 8-60cm columns shipped since 2013
- 1000s of pre-packed columns shipped globally each year (>0.5cm ID)

- >100 Phase 1-3 campaigns and 1 commercial process since launch in 2012
- >100 different resins packed (8-60cm IDs)

Increase process efficiency
- Most flexible in resin choice, application and size (0.5-60 cm IDs)
- Ready-to-use and disposable – no cleaning validation process
- Faster campaign turnarounds

Optimize process economics
- Up to 35% cost savings over self-packed columns
- Up to 150 FTE hours savings per campaign
- No upfront capital expense

Quality and risk mitigation
- No column packing failures
- ISO 9001 quality manufacturing
- Complete documentation package for GMP use
Scalable Diameters from 0.5 to 60 cm ID
14 industry standard diameters

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Process Development (cm)</th>
<th>GMP Manufacturing or Production Scale (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OPUS® RoboColumn</strong></td>
<td>0.5</td>
<td><strong>OPUS® Pre-GMP</strong></td>
</tr>
<tr>
<td><strong>OPUS® MiniChrom</strong></td>
<td>0.5, 0.8, 1.13</td>
<td><strong>GMP Run Ready</strong></td>
</tr>
<tr>
<td><strong>OPUS® ValiChrom</strong></td>
<td>0.5, 0.8, 1.13, 1.6, 2.5</td>
<td></td>
</tr>
<tr>
<td><strong>OPUS® PD</strong></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Configurable bed heights from 5 to 30 cm

<table>
<thead>
<tr>
<th>Bed Height</th>
<th>GMP Manufacturing or production scale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Process Development (cm)</strong></td>
<td></td>
</tr>
<tr>
<td>OPUS® RoboColumn: 0.25 - 3.0</td>
<td>OPUS® Pre-GMP</td>
</tr>
<tr>
<td>OPUS® MiniChrom: 1.0 - 10.0</td>
<td>OPUS® GMP Run</td>
</tr>
<tr>
<td>OPUS® ValiChrom: 10 – 60</td>
<td>Ready</td>
</tr>
<tr>
<td>OPUS® PD: 5 - 30</td>
<td>5 – 30 cm</td>
</tr>
</tbody>
</table>
Packed with any resin

>100 resins packed

<table>
<thead>
<tr>
<th>Partial List of Resins Packed: OPUS® 8 - 60</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affinity</strong></td>
</tr>
<tr>
<td>CaptivA®</td>
</tr>
<tr>
<td>MabSelect SuRe™ LX</td>
</tr>
<tr>
<td>MabSelect SuRe™</td>
</tr>
<tr>
<td>MabSelect™</td>
</tr>
<tr>
<td>MabCapture™ A</td>
</tr>
<tr>
<td>Eshmuno® A</td>
</tr>
<tr>
<td>Amsphere A3</td>
</tr>
<tr>
<td>KanCap A</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>IEX/Mixed Mode Resin</td>
</tr>
<tr>
<td>POROS® HQ50, HS50, XS</td>
</tr>
<tr>
<td>Capto™ Impres, SP and Q</td>
</tr>
<tr>
<td>Capto™ Impres, Adhere, MMC</td>
</tr>
<tr>
<td>Capto™ Q, S, DEAE, Phenyl</td>
</tr>
<tr>
<td>Capto™ Adhere, MMC</td>
</tr>
</tbody>
</table>
Regulatory support file includes fit for purpose information to support GMP use

- Product specifications
- Manufacturing and quality systems
- Manufacturing procedures
- Packing environment
- Shipping qualification
- Extractables and Leachables
- Material Certificate Information
- Example Certificate of Analysis

Download at http://www.repligen.com/resources/quality-documents/
Certificate of analysis delivers critical incoming release specifications for end users

Regulatory / quality compliance

**Product Identification**
- Column specifications (ID, BH, lot #, serial #, PN)
- Resin type and lot number
- Shipping solution
- Pack date

**Quality Control Release Data**
- Theoretical plates / meter result
- Asymmetry result
- Bioburden and Endotoxin (GMP Run Ready only)
- Chromatogram and test method (page two)

**Quality Assurance Information**
- ISO 9001 certified
- Product Contact Material Statement
- Manufacturing environment
- Chromatography resin control

**Attachments**
- Resin Manufacturer’s CoA
Savings Delivered: 150 FTE hours, 2 suite days, and $25k saved per campaign per column

Self pack vs. pre-pack cost comparison for multi-product facility supporting phase I/II projects

COST COMPARISON
OPUS® Pre-packed Columns vs. Self-packed Columns

Proprietary Repligen model calculates savings per campaign and assumes the pre-packed column is used 1 campaign, and self-packed column is used for many campaigns over a period of many years.
Many different value drivers for pre-packed columns

Economic & operational benefits magnified as more columns are required more frequently

**Why Use Pre-Packed Columns**

- **Economics**
  - ~100 - 150 hours per column
  - ~$19,000 per column
- **Manufacturing strategies**
  - Multi product/Geo-Political
  - Disposable facilities
- **Manufacturing flexibility**
  - Accommodate different processes & titers
  - Smaller footprint vs. self-pack
- **Operational excellence/Lean**
  - Eliminate packing suite space, equipment
  - Simpler manufacturing process
- **Reliable packing / performance**
  - Eliminate packing risks
- **Product safety**
  - Well established benefits of disposables

**Buying process**

**Rational**

**Value**

**Emotional**

**Political**
OPUS® R
Pre-packed Columns
OPUS® 45R and 60R with unpacking capability
Ultimate flexibility from pre-packed to unpacked

- OPUS® 45/60cm column with a side port to enable resin unpacking in <5CVs
  - Tubing accessories included
  - Supporting (non-supplied) equipment includes a quaternary flow pump and slurry tank
- Port designed to have no impact on chromatographic performance or cleanability of packed bed
  - No new product contact components
- Use unpacked resin for process development or as a back-up strategy for manufacturing in the event of a deviation
OPUS® R column design
Class VI, EMEA 410/01 compliant materials of construction

OPUS® 45R cm Column

OPUS® R Unpacking Port Assembly Drawing

| Product Contact Component | Material of Construction
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Inside port</td>
<td>polypropylene</td>
</tr>
<tr>
<td>2: Inner gasket</td>
<td>silicone</td>
</tr>
<tr>
<td>5: Outer gasket</td>
<td>silicone</td>
</tr>
<tr>
<td>6: Plug o-ring</td>
<td>silicone</td>
</tr>
<tr>
<td>7: OPUS® R plug</td>
<td>polypropylene</td>
</tr>
</tbody>
</table>

| Non-Product Contact Component | Material of Construction
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3,4: Outer nut and washer</td>
<td>ABS plastic</td>
</tr>
<tr>
<td>8: 1” TC BioClamp</td>
<td>Glass filled Nylon</td>
</tr>
</tbody>
</table>
Resin removal in < 5CVs with Sepharose 6FF and POROS resin
Simple unpacking methods

**OPUS® 45R (45.7 x 20 cm)**

Tubing set configuration and diagram for unpacking

<table>
<thead>
<tr>
<th>Pre-packed Resin</th>
<th>Resin Yield (45.7 x 20 cm)</th>
<th>Residual Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepharose 6 FF</td>
<td>99% (39.1L of 39.4)</td>
<td>3 CV (95L)</td>
</tr>
<tr>
<td>POROS</td>
<td>99% (39.1 of 39.4)</td>
<td>3.25 CV (104L)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step</th>
<th>Step Description</th>
<th>CVs (POROS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Resin flush, flow into inlet and outlet</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Slurry flush, air sparge/purge</td>
<td></td>
</tr>
<tr>
<td>3, 4</td>
<td>Column Rinse 1, fill (buffer), slurry flush</td>
<td>0.75</td>
</tr>
<tr>
<td>5, 6</td>
<td>Column Rinse 2, fill, slurry flush</td>
<td>0.75</td>
</tr>
<tr>
<td>7, 8</td>
<td>Column Rinse 3, Fill, slurry flush</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Total Volume 3.25 CV

Play Video
OPUS® R columns maintain chromatographic performance: no impact on efficiency or asymmetry
Sepharose 6 Fast Flow, 20cm bed height

<table>
<thead>
<tr>
<th>Chromatographic performance</th>
<th>Plate Count (N/m)</th>
<th>Asym</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPUS 45 cm</td>
<td>2636</td>
<td>1.1</td>
</tr>
<tr>
<td>OPUS 45R</td>
<td>2661</td>
<td>1.2</td>
</tr>
<tr>
<td>OPUS 60 cm</td>
<td>3144</td>
<td>1.3</td>
</tr>
<tr>
<td>OPUS 60R</td>
<td>2979</td>
<td>1.1</td>
</tr>
</tbody>
</table>

100 cm/hour with 1% CV of 10% Acetone
Computational fluid dynamics shows unpacking port has no impact on performance

Laminar flow maintained in OPUS® 45 R and 60 R columns

Unpacking port has no impact when purging the column compared to a column purged with no port

Lack of volume change of the non-binding pulse indicates presence of a port at the side wall does not create “band broadening”

Uniform, laminar flow through the packed bed is maintained
Bioburden challenge shows columns are cleanable and easily sanitized

Bioburden incubation

- **Method:**
  - OPUS® 45R (20cm bh) and OPUS® 60R (20cm bh) Sepharose 6FF columns packed and qualified
  - Columns saturated with 1CV *E. coli* (absorbance 0.1 @600nm) and incubated overnight at room temp
  - Flushed with 3CVs water and sampled column effluent
  - Sanitized:
    - Flush with 1 M sodium hydroxide in **up-flow** at 100 cm/h for 30 minutes then **down-flow** at 100 cm/h for 30 minutes
    - Recirculate 1 M sodium hydroxide for 2 hours in **up-flow** at 100 cm/h
    - Incubate the column in 1 M sodium hydroxide for 1 hour (static sanitization for complete removal of endotoxins)
    - Flush with water until neutral pH is achieved
  - Incubated at room temperature overnight
  - Samples collected and tested for bioburden and endotoxin

<table>
<thead>
<tr>
<th>Bioburden Challenge Data</th>
<th>OPUS® 45R</th>
<th>OPUS® 60R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleaning Step/Measurement</td>
<td>Bioburden (CFU/mL)</td>
<td>Endotoxin (EU/mL)</td>
</tr>
<tr>
<td>Water effluent after overnight <em>E. coli</em> incubation</td>
<td>TNTC</td>
<td>&gt; 0.25</td>
</tr>
<tr>
<td>Water effluent post sanitization effluent</td>
<td>0</td>
<td>&lt; 0.25</td>
</tr>
</tbody>
</table>
OPUS® R Columns maintain performance after shipping
OPUS® 60R shipping study

During the ISTA test (procedure 2B) the column was subjected to the following conditions:

- High temperature (38º C) and high humidity for 36 hours
- Low temperature (4º C) for 36 hours
- Compression testing (2836 lbs, or 1286 kgs on top of crate)
- 2 hours of random vibrational testing
- 6 drop tests
- 4 incline impact tests

**Asymmetry**

<table>
<thead>
<tr>
<th></th>
<th>Pre-shipping</th>
<th>Post-shipping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymmetry</td>
<td>1.03</td>
<td>1.04</td>
</tr>
</tbody>
</table>

**Plate Count (N/m)**

<table>
<thead>
<tr>
<th></th>
<th>Pre-shipping</th>
<th>Post-shipping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plate Count (N/m)</td>
<td>3367</td>
<td>3373</td>
</tr>
</tbody>
</table>
Ultimate flexibility from pre-packed to unpacked

OPUS® 45R and 60R Columns

Unpacking port design maintains chromatographic performance and cleanability

OPUS® R Column design allows for easy unpacking in < 5 CVs

Use unpacked resin for:
- Back-up column packing
- Process development
- Resin end of life studies

Learn more at
www.repligen.com/45R_60R
Investing in Capability and Capacity
Eight fold increase in manufacturing capacity

$3M facilities and human resources investment enables 6-8 week lead times

From 2 to 7 packing rooms in 1 year

January 2016
- 2 clean rooms
- 4 manufacturing associates

September 2016
- 5 clean rooms (ISO 7)
- Expanded prep space (ISO 8)
- 3 new packing stands
- 14 Manufacturing Associates/Engineers
- Increased QA, Engineering, Logistics/Supply Chain and Customer Service support staff
- Process improvements

March 2017
- 7 clean rooms (ISO 7)
- 4 new chromatography test skids
State of the art packing facility in Waltham, MA USA
Controlled packing and testing environment

<table>
<thead>
<tr>
<th>OPUS® packing suite capabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automated parts washer</td>
</tr>
<tr>
<td>• Validated cleaning protocols</td>
</tr>
<tr>
<td>1 large ISO 8 classified buffer prep room</td>
</tr>
<tr>
<td>7 ISO 7 classified packing rooms</td>
</tr>
<tr>
<td>• Capacity for &gt;800 columns per year (1 shift operation)</td>
</tr>
<tr>
<td>7 custom-configured packing stands</td>
</tr>
<tr>
<td>• 1 multi-diameter packing stand per room</td>
</tr>
<tr>
<td>• Axial compression and/or flow packing</td>
</tr>
<tr>
<td>4 custom-configured chromatography skids</td>
</tr>
<tr>
<td>• Plate count, asymmetry, pressure-flow testing</td>
</tr>
<tr>
<td>• Improved process monitoring and documentation</td>
</tr>
</tbody>
</table>
Commitment to column packing excellence

>$3M investment in facility and equipment to expand capacity
  • New clean rooms for column packing and expanded prep space
  • New packing stands
  • New chromatography test skids

Experienced management and leadership
  • R&D, quality, process engineering, operations, logistics/supply chain, customer service

Continuous process improvements
  • Quote to order
  • Packing process and batch record
  • Greater standardization of procedures
  • Shipping and logistics