

Advanced Downstream Bioprocessing Solutions



Inspiring advances in bioprocessing



Repligen is a trusted partner in upstream process intensification and downstream pre-packed disposable chromatography. Focused on cost and process efficiencies, our people and our technologies help meet critical bioproduction demands worldwide. As the recognized global leader in Protein A manufacturing, Repligen's Protein A affinity ligands are routinely used to purify most of the world's monoclonal antibodies.



Leadership.

- Most of the world's monoclonal antibodies are purified using native and recombinant Protein A manufactured by Repligen
- Products are used in multiple clinical and commercial applications
- 20 of the Top 25 Pharma companies use Repligen products



Innovation.

- Leader in pre-packed chromatography column technology
- Leader in cell culture process intensification/optimization technology
- Products focused on improving process efficiency and process economics



Quality.

- Multi-site ISO 9001certified manufacturing
- Secure supply chains, stringent inventory management
- Complete regulatory support packages
- Focus on business continuity, quality systems and risk mitigation



Support.

- Consistent, predictable deliveries
- Field applications team
- Worldwide service and support

Setting new standards in bioprocessing

Upstream solutions



XCell™ ATF System

Simplify and intensify upstream bioprocessing.

The XCell™ ATF System, available in single-use or stainless steel format, is a cell retention device attached to a bioreactor that delivers high cell density and process intensification.



Cell culture supplements

Recombinant and animal-free, LONG® R³ IGF-I and LONG® EGF provide the benefits of serum-derived supplementation while maintaining an animal-free process.

Downstream solutions



OPUS® Pre-packed Chromatography Columns

Leader of the Pack.

From bench-scale to production-scale, OPUS® columns are ready-to-use pre-packed alternatives to self-packed columns.



Protein A Affinity Resins

Protein A resins from the leading manufacturer of rProtein A ligands.

Captiva® and Immobilized Protein A (IPA) affinity resins from Repligen help you optimize process economics while maintaining industry-standard performance.



Protein A Ligands

Leader in Protein A ligand manufacturing since 1985.

Most of the world's commercial monoclonal antibodies are purified using native and recombinant Protein A ligands manufactured by Repligen.

Analytics



ELISA Kits

ELISA Kits deliver fast, reliable, and reproducible quantitation of leached Protein A, MabSelect SuRe™ ligand and LONG® R³ IGF-I.

The value choice in Protein A resins

CaptivA® Protein A Affinity Resin



CaptivA® Protein A Affinity Resin is the most cost-effective chromatography media available today.

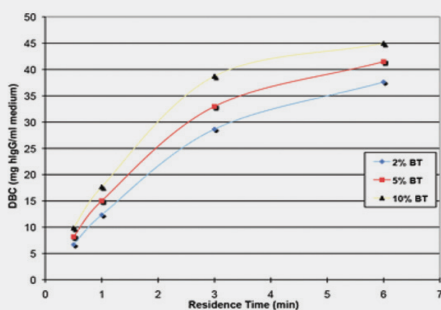
CaptivA® resin delivers excellent binding capacity, caustic stability and low leaching at a fraction of the cost of traditional resins. CaptivA® resin combines an industry standard agarose bead with recombinant native Staphylococcal Protein A (rSPA) manufactured by Repligen, the world's leading manufacturer of recombinant Protein A.

- **Industry- accepted**, in 3 commercial processes and an expanding pipeline of Phase 1-3 processes
- **High dynamic binding capacity**, 30-40 mgs / ml
- **Low Protein A leaching**, less than 10 ng/mg IgG
- **Cost-efficient**, one-third the cost of traditional resins, increased savings when pre-packed into OPUS® columns
- **Secure supply**



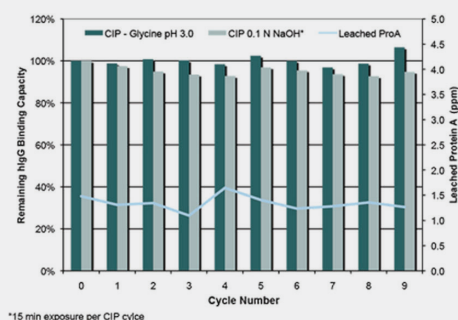
Formulated as a 52% ± 1% slurry in 18.5% ± 1% ethanol, CaptivA® Protein A resin is bottled in volumes from 5 mLs to 1 Liter.

High dynamic binding capacity



Dynamic binding capacity was determined for human polyclonal IgG at four different flow velocities providing residence times ranging from 0.5 to 6 minutes. A 5 x 50 mm column was loaded with a 2 mg/ml hlgG solution in PBS pH 7.4. Capacity was determined and reported at 2, 5, and 10% breakthrough. A column bed height between 10-20 cm, loaded at 200 cm/hr provides 6-12 minutes of residence time.

Low Protein A leaching



The human polyclonal IgG binding capacity was determined following each column cycle. Cleaning was performed between cycles with either extra volumes of Glycine pH 3.0 elution buffer or 0.1 N NaOH with a 15 minute contact time. Leached Protein A was measured in the product elution pool from each cycle using the Repligen Protein A ELISA Kit.

Detect and quantify ligands and Protein A

ELISA Kits



ELISA Kits deliver reliable quantitation of Protein A, MabSelect SuRe™ ligand and LONG®R³ IGF-I.

ELISA Kits deliver the precision, reproducibility, and sensitivity required for the accurate detection and quantitation of leached native and recombinant Protein A, MabSelect SuRe™ ligand and LONG®R³ IGF-I.

- **Accurate**, most accurate matched standard for MabSelect SuRe™ resin
- **Reproducible**, consistent inter- and intra-kit consistency
- **High specificity**, using polyclonal chicken antibody
- **High sensitivity**, using biotinylated rabbit anti-Protein A detection antibody
- **Optimized**, with three proven sample preparation protocols



Protein A ELISA Kit for MabSelect SuRe™ Ligand

For downstream processes that utilize a MabSelect SuRe™ capture step, this is the only kit on the market that includes the SuRe™ ligand standard.



Protein A ELISA Kit for Native and Recombinant Protein A

For downstream processes which utilize a non-MabSelect SuRe™ Protein A capture step, this kit contains native and recombinant Protein A ligand variants.



LONG®R³ IGF-I ELISA Kit

For both cell culture and drug substance samples, this is the only commercially available kit for the quantitation of LONG®R³ IGF-I.

Assay Recovery & Sensitivity: Recombinant Protein A Ligand

Protein A ELISA Kit for Native and rProtein A

Buffer	Protein A Range Tested (ng/ml)	Mean Recovery (%)	High (%)	Low (%)	LLOQ (ng/mL)	LLOQ (ppm)
Citrate	1.6 - 0.05	98	103	91	0.038	0.30
Glycine	1.6 - 0.05	101	102	96	0.067	0.54
Acetate	1.6 - 0.05	97	100	90	0.033	0.26

Assay Recovery & Sensitivity: MabSelect SuRe™ Ligand

Protein A ELISA Kit for MabSelect SuRe™ Ligand

Buffer	Protein A Range Tested (ng/ml)	Mean Recovery (%)	High (%)	Low (%)	LLOQ (ng/mL)	LLOQ (ppm)
Citrate	1.6 - 0.05	101	105	95	0.058	0.46
Glycine	1.6 - 0.05	99	102	94	0.051	0.41
Acetate	1.6 - 0.05	101	103	94	0.046	0.37

*MabSelect SuRe™ and SuRe™ are registered trademarks of GE Health Care.

First and only pre-packed columns for 1000L - 2000L bioreactor harvests

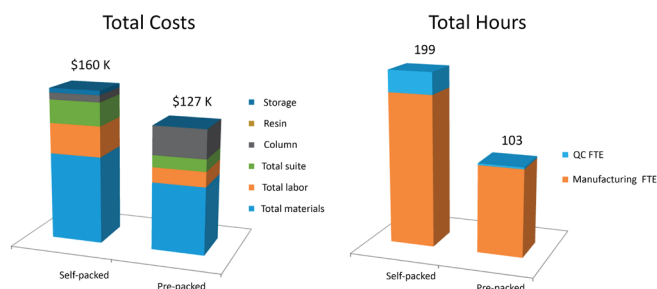


OPUS® 45 cm and 60 cm Columns purify feed streams from production-scale bioreactors.

Specifically engineered to meet the requirements of large-scale bioreactors, OPUS® 45cm and 60cm columns match the performance of traditional self-packed columns while delivering the cost and labor savings expected from ready-to-use pre-packed columns.

Cost and labor savings

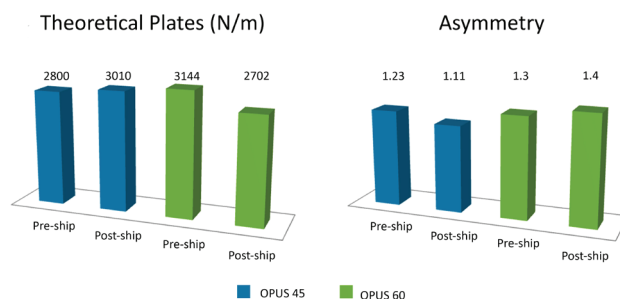
Over 19% cost savings and up to 50% labor savings were achieved when using OPUS® columns compared to self-packed columns.



Assumptions: Glass column amortized over 20 campaigns, OPUS® 60 cm columns over 3 campaigns; 3 batches/campaign; 2 cycles/batch; 0 column repacks.

Performance maintained after shipping

OPUS® columns are shipped in qualified packaging which has passed the International Safe Transit Authority's (ISTA) worst case shipping simulations.

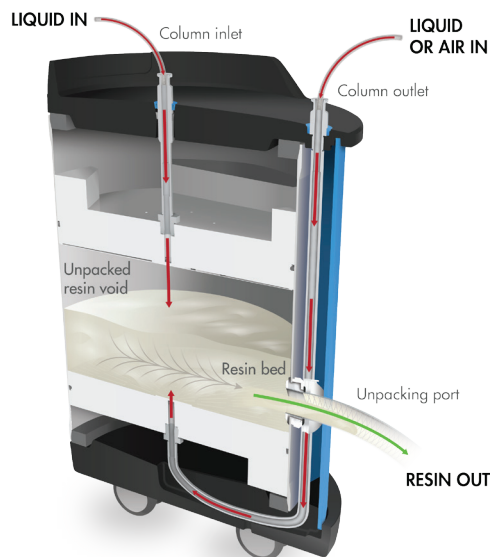


Shipping tests include high temperature (38° C) and high humidity for 36 hours, low temperature (4° C) and low humidity for 36 hours, compression testing (381 kgs on top of crate), 2 hours of random vibrational testing, multiple drop tests.

Physical Attributes

	OPUS® 45	OPUS® 60
Internal diameter	45.7 cm	59.9 cm
Column body pressure rating	3 bar	3 bar
Bed height range	5-30 cm	5-30 cm
Column volume: 20 cm bed height	33 L	56 L
Assembled column height	~ 90 cm	~ 92 cm
Outer diameter (including caps)	54 cm	61 cm
Inlet/Outlet flow path internal diameter	12.7mm (0.5 inches)	19.05 mm (0.75 inches)
Inlet/ Outlet port connectors (per ASME BPE Standards, current ed.)	Fractional tri-Clamp	1 inch tri-Clamp
Estimated weight @ 20 cm BH	68 kg (150 lbs)	160 kg (350 lbs)

Ultimate flexibility from pre-packed to unpacked OPUS® 45R and 60R Columns



Breakthrough technology from the Leader of the Pack in pre-packed columns

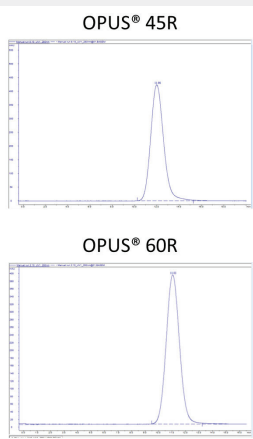
OPUS® 45R and OPUS® 60R columns provide ultimate flexibility in pre-packed column technology without compromising chromatographic performance or cleanability. The innovative side port allows for easy unpacking in <5 CVs. This unique feature not only mitigates risk associated with implementing pre-packed columns within a facility, but it also allows for reuse of the unpacked resin in other columns.

- Innovative side port for simple resin removal
- Performance and cleanability maintained
- Mitigates process risk
- Unpacked resin available for use with other columns



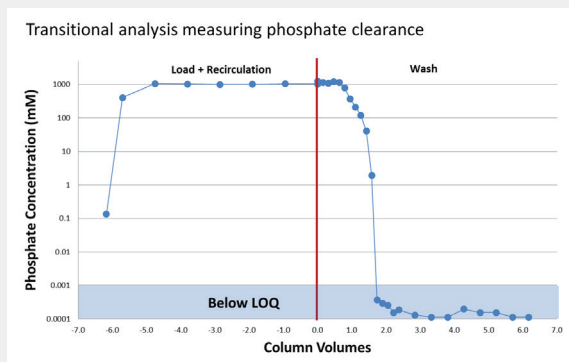
OPUS® R Columns maintain performance
compared to standard columns

Chromatographic performance	N/m	As
OPUS®45	2636	1.1
OPUS®45R	2661	1.2
OPUS® 60	3144	1.3
OPUS®60R	2979	1.1



100 cm/hour with 1% CV of 10% Acetone.

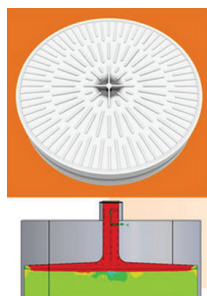
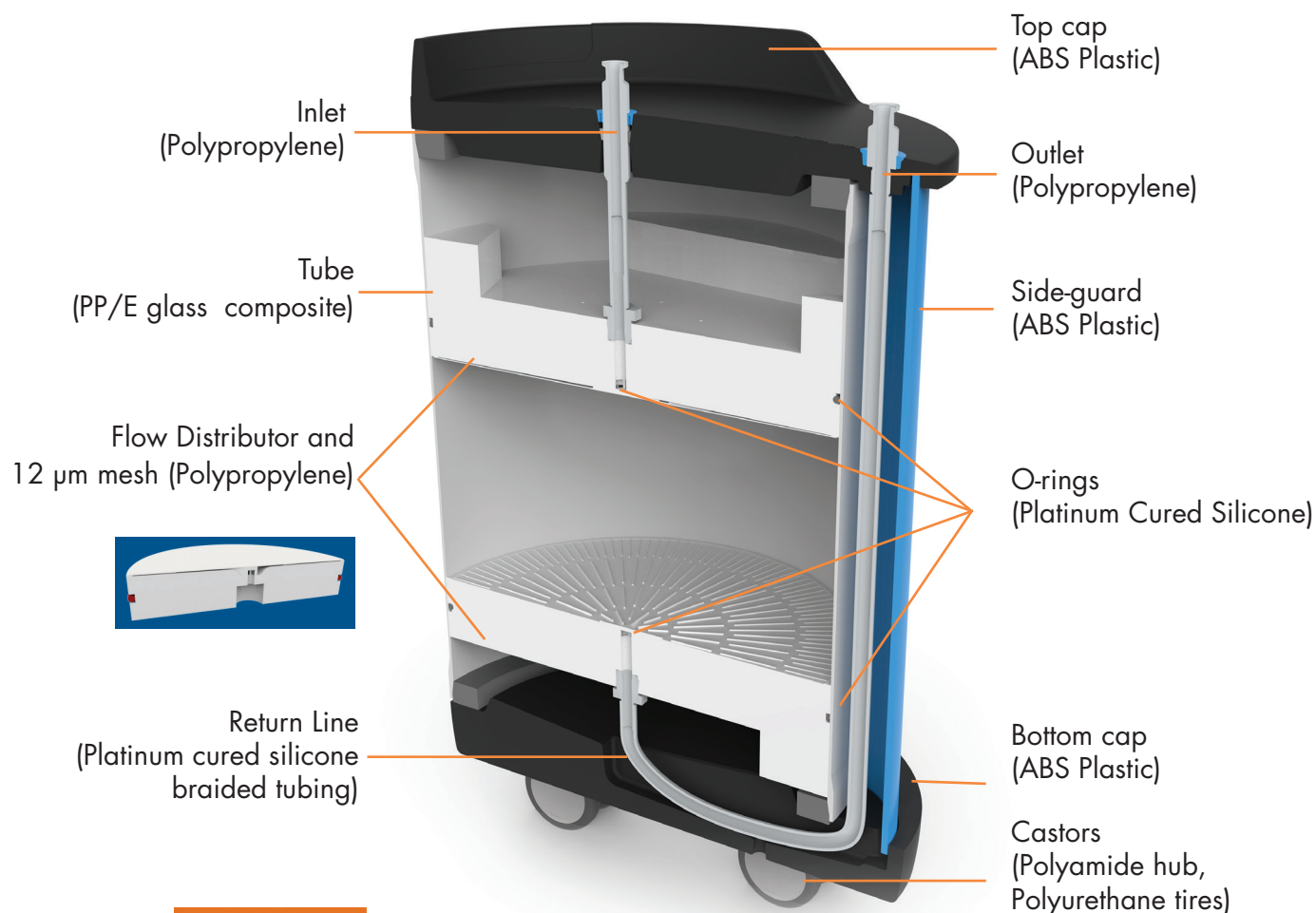
OPUS® R Columns maintain cleanability
compared to standard columns



Lack of dead zones measured by phosphate cleaning confirms the CFD transitional analysis: 6 log reduction of phosphate in <2 CVs.

Proven column design

OPUS® Pre-packed Chromatography Columns



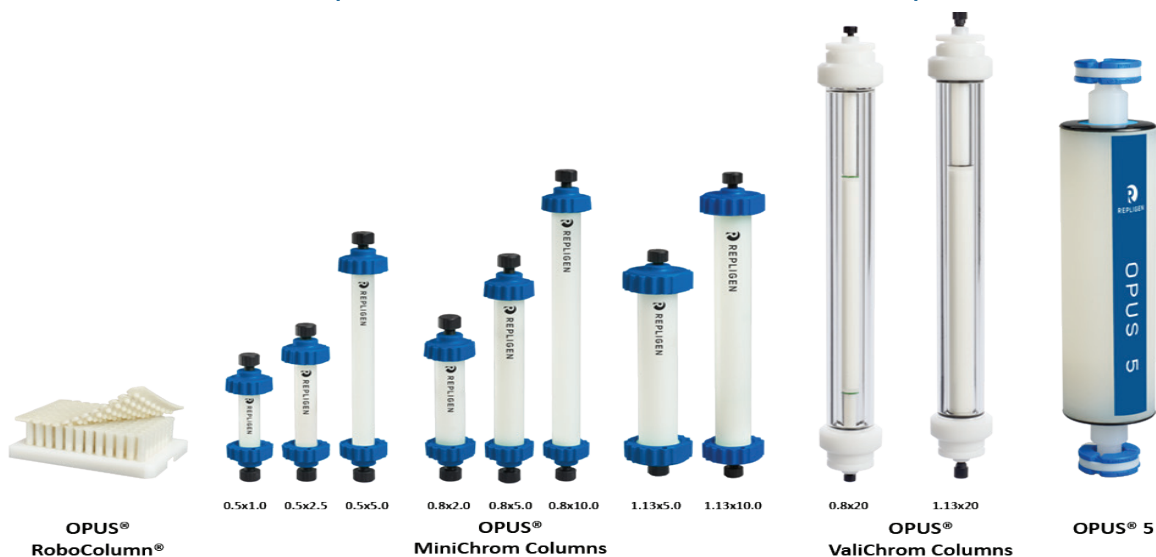
OPUS® Column flow distributors are designed to maintain uniform flow distribution. The design leverages industry accepted column technology, including a radial flow field and anti-jet funnel.

During the development of OPUS® Columns, dispersion as a function of column performance was modeled to confirm critical parameters of the flow distributor. The final design was qualified through computational fluid dynamics modeling and applications case studies performed in the OPUS® applications lab.

OPUS® Columns Materials of Construction	
Component	Material
10 cm – 30 cm column tube	Polypropylene
45 cm – 60 cm column tube	70% w/w E-Glass / PP engineered composite structure
Flow distributors	Polypropylene
Inlet and Outlet	Polypropylene
Bed support screens	Polypropylene
O-rings	Platinum-cured medical grade Silicone
Return line	Platinum-cured medical grade Silicone reinforced with a strong polyester fiber

Leader of the pack in pre-packed chromatography process development

OPUS® Pre-packed Columns for Process Development



**Open platform,
user-specified
resin**

**OPUS®
RoboColumn®**
for sample preparation

**OPUS®
MiniChrom**
for process development

**OPUS®
ValiChrom**
for process validation



OPUS®RoboColumn® is a miniaturized column on a 96-well plate used with robotic fluid handlers for automated, parallel chromatography resin screening and sample preparation.



OPUS®ValiChrom is a glass pre-packed column that is an exact scale-down model of a full-scale column, ideal for process validation, including viral clearance.



OPUS®MiniChrom is a pre-packed column with flexible multiple configurations, designed for bench-scale resin screening, process development, and sample preparation.



OPUS® 5 has an internal diameter of 5 cm, ideal for process development assessment of chromatography scale-up prior to clinical or commercial manufacturing.

Leader of the Pack

OPUS® Pre-packed Chromatography Columns



From bench-scale to production-scale, OPUS® Columns are pre-packed alternatives to self-packed columns.

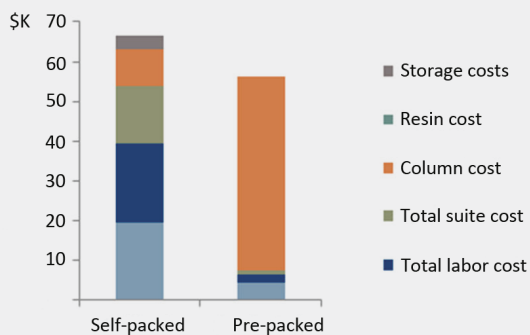
Applying the most advanced pre-packed chromatography column technology available today, OPUS® Columns have unique design features and robust GMP-compliant construction that make them ideal for efficient downstream chromatography processes.

- **Flexible**, from bench-scale to production-scale
 - 0.5 to 60 cm internal diameters
 - 0.25 to 30 cm bed heights
 - Pre-packed with user-specified resin
- **Production-scale**, OPUS® 45 cm and 60 cm Columns meet requirements of larger 1000L-2000L bioreactors
- **Bench-scale**, OPUS® Columns for process development are ideal for screening, validation, sample preparation
- **Cost-efficient**, substantial cost and labor savings compared to self-packed columns
- **Robust**, GMP-compliant construction, ISO certified



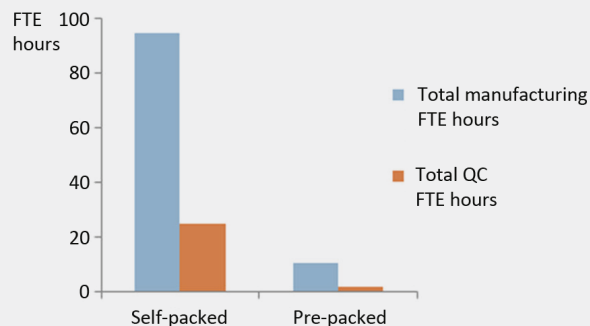
A complete Regulatory Support File includes product specifications, manufacturing procedures, extractables and leachables, shipping qualification, material certificates and example certificates of analysis.

Cost Savings



Case study: Using OPUS® 45 cm pre-packed columns generated over \$10,000 savings compared to self-packed columns.

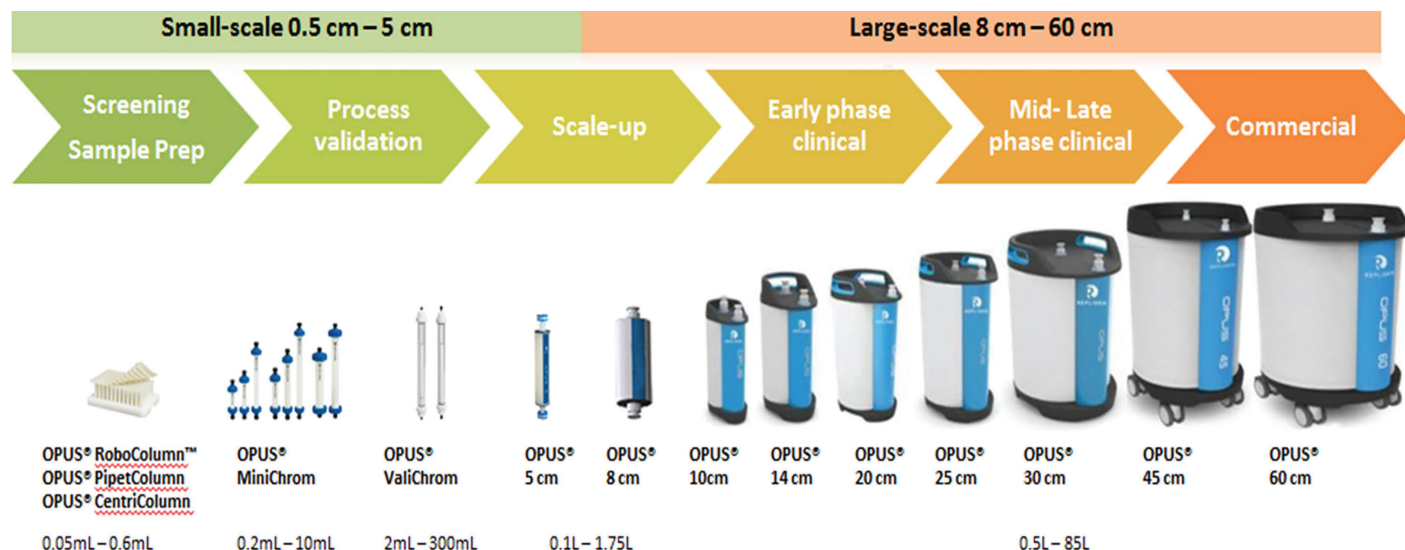
Labor Savings



Case study: Using OPUS® pre-packed columns helped reduce labor usage by over 100 hours, an 89% reduction compared to self-packed columns.

Unparalleled flexibility

OPUS® Pre-packed Chromatography Columns



Partial List of Resins Packed		
Affinity Resin	HIC Resin	IEX/Mixed Mode Resin
Captiva® PriMAB	Butyl Sepharose® FF and HP	Capto™ Impres, SP, Q
Eshmuno® A	Phenyl Sepharose® FF HS	Capto™ Q, S, DEAE, Adhere
MabCapture™ A	Phenyl Sepharose® HP	Ceramic Hydroxyapatite (CHT)
MabSelect SuRe™	Toyopearl® Butyl 600M	Ceramic HyperD®
MabSelect SuRe™ LX	Toyopearl® Butyl 650	DEAE Sepharose® FF
MabSelect™	Toyopearl® PPG 600M	Eshmuno® CPX
POROS® Heparin		Fractogel® TMAE and HiCap
ProSep® UP		POROS® HQ50, HS 50, XS
RMP Sepharose®		Q Sepharose® FF
		SP Sepharose® FF and HP