InPlace[™] Chromatography Columns

- Automated methoddriven packing
- Scalable design, 20 cm - 200 cm
- Compatible with all resin types, including hydroxyapatite
- Ergonomic operation
- Compact footprint: ~50% lighter than other columns of similar capability
- Compact footprint: ~17% shorter than other columns of similar capability
- On-site packing
 support
- Custom designs to meet your process requirements
- 21 CFR Part 11 and USP VI Compliant
- Complete documentation for regulatory submission

Precise automated packing with reproducible scalability from pilot scale to commercial manufacturing

InPlace[™] Chromatography Columns are designed and manufactured for GMP process scale downstream operations (Figure 1). VERDOT first introduced motorized axial compression columns more than 25 years ago. The innovative design provides reproducible scalability from pilot scale through clinical trials to commercial manufacturing.

With InPlace Columns, the packing, unpacking, and clean-in-place features do not interfere with the flow distribution system, offering optimum performance not only for packing but also during routine processing.

The column is compatible with any chromatography resin. VERDOT[®] has compiled an extensive technical library to provide guidance on packing parameters for every type of commercial chromatography resin including hard-topack and incompressible resins. VERDOT offers on-site technical packing assistance with our experts to further support our customers.

InPlace Columns have a compact footprint (17% shorter) and weigh less (50% lighter) than other columns of the same capacity, making it a more



VERDOT

Figure 1. InPlace[™] Chromatography Column

sustainable option with reduced impact on cleanroom space and facility planning.

The columns are configurable and can be customized to specific application requirements. VERDOT engineers have designed specialty columns for applications ranging from biopharmaceutical to clinical diagnostics and food ingredient manufacturing.

Configurable to your process

Columns are compliant with all cGMP guidelines and can be configured to your specific process requirements, including:

- Column tube heights up to 90 cm.
- Column diameters from 20 200 cm.
- Column tubes are available in borosilicate glass, stainless steel, or acrylic.
- For stainless steel parts, 316L is the standard material of construction; however, columns can also be manufactured with AL-6XN or Hastelloy depending on chemical resistance specifications.
- For top and bottom column filters (also called a frit), the standard mesh nominal pore size is 20 μm. Additional pore size options can be proposed to correlate with the resin bead diameter for your process.

The VERDOT difference

InPlace Columns have several innovative design features that optimize column packing operations.

The InPlace Column (Figure 2) design enables precise reproducible packing, efficient unpacking, and easy slurry collection in <2.5 column volumes. These design features include:



Figure 2. InPlace Chromatography Column schematic

Motorized axial compression since 1999

VERDOT has been manufacturing cGMP chromatography columns since 1999 and was among the first to use a motor for moving the upper headplate adaptor. Motorized axial compression promotes uniform bed consolidation as well as complete slurry transfer in syringe mode. When paired with the Control Console or Automated Packing Station, the packing motor controls the speed and position of the top adaptor for axial compression packing, which makes packing easier, faster, and more reproducible.

Tilting Mechanism

A tilt mechanism assists with the quick and simple removal of residual air during column packing. The air-actuated tilt mechanism is also used during unpacking to support the efficient removal of resin slurry from the column.

Slurry Valves

The patented slurry valves are positioned on the perimeter of the column, and not in the fluid path, which allows for optimal flow distribution during normal operation. When opened, the slurry can be transferred in or out of the column (Figure 3).



Figure 3. Open slurry valve

When closed (Figure 4), the slurry manifold can be flushed with a sanitization agent which cannot contact the packed bed. The CIP port is closed when the slurry valves are in the open position to provide unidirectional flow for the resin slurry.



Figure 4. Slurry valve closed

Flow Distribution System

InPlace Chromatography Columns are designed using computational fluid dynamics (CFD) to ensure optimal and uniform distribution across the bed and through the column. The rigid top and bottom stainless steel filter design allows for uniform flow distribution even if a small headspace is required (e.g., with hydroxyapatite resins).

Inflatable Seal

The inflatable seal design provides added security against leakage and inefficient packing by ensuring uniform pressure against the column wall. Combined with the hydropneumatic pump, the inflatable seal is filled with liquid (usually 20% ethanol) and can be quickly inflated/ deflated by using compressed air. Once inflated, the column seal will be maintained indefinitely or until the resin is unpacked.

Control console options

Motorized columns must be accompanied by either the Control Console or the Automated Packing Station (APS), see Table 1 for comparison of the two console types.

Table 1. Console Comparison

	Control Console	Automated Packing Station
Control speed and position of the adaptor	Automated	Automated
Column priming Column degassing	Manual	Automated
Slurry transfer	Manual	Automated
Axial compression packing	Automated	Automated
Automatic bed detection	No	Yes
Equilibration and HETP testing	No	Automated
Resin reslurry in place	Manual	Automated
Clean-in-place (CIP) Column rinsing	Manual	Automated

The Control Console precisely regulates the speed and position of the top flow adaptor for accurate bed consolidation and compression. The variable height adaptor position is controlled with millimeter accuracy.

Simple methods can be used to automate slurry transfer, packing, and bed compression. The method editor guides operators through each step of the packing process. The graphical interface is intuitive and easy to use, and conforms to 21 CFR Part 11 regulations with full audit trail. The compact Automated Packing Station is a complete solution that fully automates column packing, conditioning, HETP testing, unpacking and system cleaning activities. It synchronizes all fluidic, pneumatic and mechanical elements to provide simple operator interaction. An extensive library of resin packing protocols and unpacking methods are pre-loaded. Full GMPcompliant reports can be generated for all runs.

Regulatory support and quality assurance

VERDOT manufacturing procedures mandate full documentation of each step and every component in compliance with U.S. and European regulations. Chromatography columns are inspected by regulatory bodies and CE certified according to the European Pressure Equipment Directive. All equipment is manufactured in compliance with directives and regulatory standards related to:

- the safety of products and equipment
- the quality of equipment and automated systems
- the quality of product contact materials

The manufacturing facility is certified according to ISO 9001:2015 standards.

Optional accessories and services

Hoist-Free Column Lifter

The lifter provides additional safety and ease of use capabilites during column maintenance activities. Using servomotor linear actuators, the Hoist-Free Column Lifter lifts the top portion of the column for operations on the upper adaptor, or the entire column can be raised for easy access to the bottom process valve.

Onsite Packing Support and Preventive Maintenance Service

VERDOT packing experts have extensive experience in packing all types of commercially available chromatography resin and are available worldwide to assist with packing your InPlace Column.

Regular preventive maintenance (PM) helps to keep columns in the best possible working condition and is important to prolong the working lifespan. During a PM, all gaskets and seals are replaced, along with the top and bottom frits. The column is also inspected for damage or corrosion.

VERDOT recommends PM intervals of up to two years. For columns that are used frequently, preventive maintenance should be performed annually.

InPlace Chromatography Columns simplify packing procedures for any resin type

VERDOT InPlace Columns are designed for scalability and flexibility to fulfill packing needs from pilot to manufacturing scale. Every type of chromatography resin from highly compressible to rapidly settling, rigid, noncompressible beads can be easily packed.

The packing procedures for InPlace Columns are directly scalable because the resin bed is consolidated uniformly using axial movement of the top adaptor, independent of flow rates or pressure endpoints. The piston position is controlled with millimeter accuracy, allowing for precise bed consolidation based on recommended compression factors. Reproducible column packing performance is thus ensured at any diameter from 10 - 200 cm.

VERDOT has extensive experience packing columns with resins that require unusual or innovative packing techniques due to parameters such as compression factor (ranging from 1.0 - 1.7), resin settling rate, backpressure requirements, swelling/shrinking of beads, etc.

Automated methods for column packing are available with the Control Console and Automated Packing Station. Protocols are based on proven packing experience and can be applied to the attributes of the resin base matrix.

The following procedure (Table 2) is a general outline for the majority of column packing protocols. Some methods may require modification depending on the manufacturing environment (e.g., space constraints, equipment limitations, etc.) and/or the physical properties of the media (e.g., settling rate, compression factor, etc.).

Table 2. Packing Protocol Overview

Step	Description		
Column preparaton	Prime column and transfer lines with packing buffer.		
Slurry transfer	Use top adaptor as syringe.		
Bed consolidation	Lower top adaptor at a controlled speed.		
Final compression	Use packing factor to calculate final bed height. Reduce top adaptor speed for controlled compression.		
Qualify packing	Condition packed bed and test for Asymmetry and HETP.		

Column Preparation

- Ensure that the column is level.
- Connect the column to the Control Console or the Automated Packing Station.
- Connect the buffer tank and the slurry tank to the slurry manifold with reinforced tubing as shown in Figure 5.
- Connect a drain line from the top process connection.
- After sanitizing the column, lower the top adaptor to a height of 10cm and inflate the seal.
- Fill the column with packing buffer from the bottom process valve. The slurry manifold and slurry transfer lines should also be primed with packing buffer.
- Open and close the slurry valves several times to remove entrapped air.
- Residual air in the column can be removed by tilting the column, deflating the seal, and lowering the top adaptor into the packing buffer. Then reinflate the seal and return the column to its upright position.
- With the bottom valve closed and the top valve open, lower the piston to remove air from the top process connection.
- Reverse the procedure to remove entrapped air from the bottom process connection: close the top valve and open the bottom valve, then lower the top adaptor.
- When all lines have been primed, lower the top adaptor to approximately 5 cm height with the seal inflated.
- Close the top and bottom process valves.



Figure 5. Column preparation and priming

Slurry Transfer

The InPlace Column slurry transfer valves are designed for minimal shear during transfer of the resin. The syringe-style method for slurry transfer is ideal for chromatography resins that settle slowly (e.g., a resin with small bead size) and for resin slurries that may foam during transfer through a diaphragm pump (e.g., some types of methacrylate-based beads). The syringe transfer method is also useful for thicker resin slurries (>50% v/v).

- The slurry concentration should be close to 50% (v/v).
- With both the top and bottom process connections closed, open the slurry valves and raise the adaptor at a speed of 200 – 300 cm/hr to create suction for slurry transfer (Figure 6).
- Continue to raise the top adaptor until the calculated volume of slurry has been transferred. If performing a complete slurry transfer with no overage, use reserved packing buffer to rinse the slurry vessel and transfer lines. Monitor the transfer closely to avoid introducing air into the column.
- Once all slurry has been transferred, close the slurry valves and initiate bed consolidation.



Figure 6. Slurry transfer

Bed Consolidation & Packing with Axial Compression

Consolidation is the process where the resin beads are no longer in suspension and have migrated to the bottom of the column due to the influence of downward piston movement.

For soft resins, additional compression is applied until the recommended compression factor or packing factor is reached. This factor is influenced by the attributes of the resin's base matrix. Consult the resin manufacturer's protocols for additional guidance.

- The compression factor is defined as gravity-settled bed height divided by packed bed height.
- The packing factor is slightly different. It is calculated by measuring the bed height of a resin under a given flow divided by the packed bed height. The packing factor will vary with different adaptor speeds.
- In terms of the effect on bed compression, the linear speed of the piston is equivalent to a linear flow rate from a chromatography system.

The speed and position of the top adaptor can be precisely regulated to consolidate and compress the resin bed.

- In general, VERDOT recommends lowering the adaptor at an initial speed of 200 - 300 cm/hr (Figure 7).
- If the pressure starts to approach 3 Bar, reduce the speed of the piston.
- When the adaptor is within 2 cm of the top of the consolidated bed, reduce the speed to 60 cm/hr for final compression according to resin packing specifications.

After the packing is complete, the slurry manifold can be rinsed and sanitized.



Figure 7. Bed consolidation and packing

Reslurrying Resin in a Column

Air sparging is used to form a homogeneous slurry, which requires less buffer and reduces the risk of mechanical shear to the resin.

- First, perform a buffer exchange to condition the column with unpacking buffer.
- Initiate downflow from the VERDOT Automated Packing Station or a chromatography system.
- Raise the adaptor at a slower speed than the flow rate to maintain a net positive downflow. For example, apply downflow at 200 cm/hr while raising the piston at 100 cm/hr to maintain a net downflow of 100 cm/hr.
- When a headspace of 5 10cm has formed between the adaptor and the resin bed, change the flow direction to upflow.
- Continue to alternate between upflow and downflow every few minutes until the bed collapses. This process may take 2 - 4 cycles.
- After the bed has collapsed, continue to add unpacking buffer from the bottom process valve until the slurry concentration is approximately 50% (i.e., the total height of the slurry should be at least 2x the packed bed height).
- Stop the buffer flow, open the top process valve and raise the piston to create a headspace of approximately 10cm above the slurry level.
- Apply clean process air at 4 psi (0.3 Bar) to the bottom process valve to mix the slurry by sparging. Continue until the slurry is uniformly mixed.
- During air sparging, the top process valve should be open for more vigorous agitation.
- The time to reach homogeneity will vary depending on the resin type and column size; approximately 30 minutes should be sufficient. Some resin types may require alternate forms of reslurrying without air sparging. If the resin does not reslurry after attempting the above procedure, please contact VERDOT or the resin manufacturer for assistance.

Once the slurry is homogeneous, the column can be repacked without removing the slurry. Contact VERDOT for more information.

Column Unpacking

Unpacking InPlace Columns can be completed with less than 2.5 column volumes (CV). To initiate unpacking of the homogeneous slurry:

- Connect the slurry manifold to a tank or container with a transfer line (Figure 8).
- Tilt the column and open the isolated slurry valve.
- Close the top process valve.
- The pressure from the air sparging will transfer the slurry out of the column.
- Rinse the column several times by injecting unpacking buffer through the bottom or top adaptor, followed by air sparging and transfer to remove traces of resin from the column.



Figure 8. Reslurry column and unpacking

Conclusion

Axial compression column packing provides consistent and reproducible chromatography bed performance. Methods can easily be transferred from lab to pilot to process scale using simplified slurry transfer and bed consolidation protocols.

VERDOT experts can assist with onsite column packing and provide solutions for unique procedural and environmental challenges so that even the most challenging chromatography resins can be packed into a well-distributed and stable bed.

Specifications

		Maximum pressure at 30°C (Bar)		
Nominal ID (cm)	Packed Volume with 20 cm bed height (L)	Calibrated Borosilicate Glass	Stainless Steel 316L	Acrylic
20	6.3 L	4.7	6.0	6.0
25	9.8 L	3.8	6.0	6.0
30	14.1 L	3.6	6.0	6.0
35	19.2 L		6.0	6.0
40	25.1 L		6.0	6.0
45	31.8 L	2.4	6.0	6.0
50	39.3 L		6.0	6.0
60	55.9 L		6.0	6.0
70	77 L		3.0	3.0
80	100.5 L		3.0	3.0
100-200	157.1-628 L		3.0	3.0

Dimensions

Nominal II (cm)	D Dimensions (W x D mm)	Working height at 20 cm bed height*	Total column weight empty (kg)*	
20	694 x 682 mm	1269±20 mm	136	
25	744 x 732 mm	1290±20 mm	184	
30	790 x 647 mm	1599±20 mm	220	
35	844 x 814 mm	1599±20 mm	271	
40	856 x 856 mm	1587±20 mm	317	
45	906 x 906 mm	1587±20 mm	358	
60	1085 x 1051 mm	1725±20 mm	629	
70	970 x 880 mm	1725±20 mm	725	
80	1350 x 1350 mm	1770±20 mm	1143	
100	1350 x 1350 mm	1817±20 mm	1405	
120	1767 x 1610 mm	2350±20 mm	2672	
140	1982 x 1982 mm	2350±20 mm	3885	
160	2182 x 2182 mm	2350±20 mm	4800	
200	2430 x 2430 mm	2822±20 mm	7400	
Intermediate column sizes available. Inquire for more information.				

*Dimensions based on InPlace Chromatography Column with a standard acrylic tube of 60 cm height

