



Resolute™

Chromatography Columns



Contained column packing

Hi-Resolution flow path for optimal efficiency, capacity and peak symmetry

True linear scale-up

Suitable for use at high linear velocities

Common design from 180-2000mm diameter

Operating pressure 3bar

Choice of durable acrylic or stainless steel tubes

Validated performance for most media types

Process columns for fast, contained and reproducible operation

Resolute™ columns are ideally suited for process purification in the biopharmaceutical industry. A patented* nozzle valve provides all column functions required for packing, unpacking and running of the column in a closed system. Based on established and well proven Euroflow designs, the Resolute column provides improved column performance and true linear scalability combined with reproducible column packing methods for today's high performance media. Euroflow, inventor of the "pack in place" sanitary nozzle valve in 1994, continues to work closely with the biopharmaceutical manufacturing industry to advance the state of the art for both chromatographic performance and productivity. The packing process is controlled by a slurry packing system which, combined with a Resolute column, offers a complete solution for process chromatography from development to manufacturing scale.

Optimised for Chromatographic Performance

All columns manufactured by Euroflow are equipped with our proprietary *Hi-Resolution* mobile phase flow path comprising: mobile phase flow path within the nozzle valve body, distribution end cells, and fully swept piston arrangement. The performance of these important column components is essential for optimal process efficiency, capacity and peak symmetry. Resolute columns maintain identical design parameters throughout both the standard column range from 180 to 1200mm diameter, and engineered columns up to 2000mm diameter. Operation at high linear velocities is free from non-linear column effects and assures true linear scalability of column performance, enabling you to scale up simply, without methods redevelopment or a reduction in the reproducibility of the packing process.

Reduced Validation Effort with Scalable Packing Methods

Resolute columns and packing systems maintain identical linear velocities during the packing process up to 2000mm diameter. This reduces the effort required during preparation of SOP's for larger scale manufacturing packing methods. A range of Resolute slurry packing systems generate the required packing velocities for columns up to 2000mm diameter. This results in a packing cycle time of up to 10 minutes for a 30cm bed height column of any diameter from 400mm to 2000mm. Alternative column packing systems may be of insufficient capacity to maintain the same packing velocity when packing larger columns. This often results in the bed being formed under different conditions and represents a change to the packing method and ultimately the column performance.

General Column Description

- Standard column diameters from 180mm to 1200mm
- all with selectable bed heights from 100mm up to 600mm
- Engineered columns from 400mm to 2000mm diameter
- Bed height: fixed or adjustable (200mm adjustment)
- Nozzle valve: choice of manually operated Resolute DM, or pneumatically actuated Resolute DP columns
- Choice of bed supports in polyethylene or stainless steel
- Piston seal and precision bore tube eliminates need for additional mechanical compression or pneumatic activation of adjuster seals



Fig 1. Resolute DM 1000 column

Compatible with a wide range of Chromatographic Media

Increasingly, new types of chromatographic media with challenging packing methods are specified. Packing an efficient column requires a comprehensive understanding of the media characteristics as well as a correctly specified packing system with adequate capacity and control.

Based on extensive testing, Resolute columns and slurry packing systems deliver excellent performance over a wide range of media types and column configurations including axial packing techniques. Control of the Resolute packing process is based on media-specific set values for both the mobile phase packing pressure and the flow rate in order to determine the pack endpoint. For certain media types this method of control is essential for optimal column performance.

Media Type	Column ϕ mm	Bed Height (mm)	Plates / meter	A_f	RPH
Toyopearl® 650M	400	200-250	4,000-7,000	1.0-1.2	2.0-3.0
Fractogel® EMD	400	250	4,300	0.9-1.3	1.9-3.2
Ceramic HyperD®	400	180-220	3,200-4,200	0.9-1.3	1.9-3.2
Sepharose™ 4FF	280-1200	90-300	3,800-5,000	0.9-1.2	2.0-2.5
Sepharose 6FF	280-800	200-300	3,800-4,200	1.0-1.3	2.0-3.0
Sepharose HP	400	150	10,000 - 20,000	0.8-1.8	1.5-2.0
Sepharose Big Beads	400-2000	150	2,500	1.0-1.5	1.9-2.5
Sephacryl™ HP	600	300	7,000-10,000	1.2	2.5-4.0
Phenyl Sepharose 6FF	400	200	7,000	1.0	2.2

Table 1. Column performance with various media

Hi-Resolution mobile phase flow path

- Nozzle valve mobile phase path delivers consistent low pressure drop across column for true linear scale up
- Infinite multi-port distribution with coned end cell channels provides plug flow conditions
- Secondary cone on support ribs provide evacuation route via central nozzle for simple and effective removal of air within column

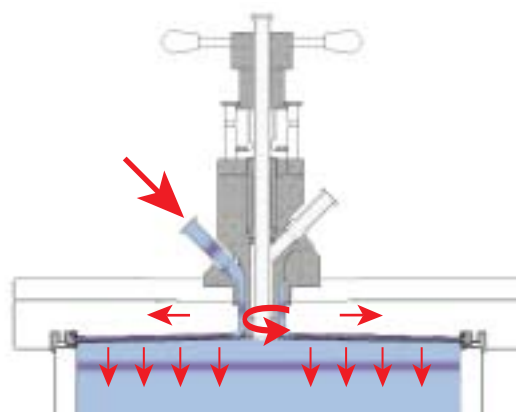


Fig 2. Hi-Resolution flow path

Superior Column Performance

All columns manufactured by Euroflow incorporate a unique *Hi-Resolution* mobile phase flow path suitable for operation at high linear velocities. The flow distribution cells and mobile phase flow path supports plug flow conditions irrespective of column diameter. Figure 3 shows Pressure Flow curves for Resolute columns and alternative vendors' columns. The columns were filled with water, and pressure and flow instruments were used to measure pressure drop across the filled column under process flow conditions. Within the velocity range typical of the majority of process operations Resolute columns exhibit identical Pressure Flow curves, linear up to 1000 cm/hr, at which the pressure is 0.1 bar. Alternative column designs exhibit high, exponential Pressure Flow curves. During normal operations actual pressure drop will be the sum of the value shown below and the additional value from the packed media bed.

Resolute columns support true linear scale up of both the purification performance and column packing methods:

Elimination of non-linear interference from column enables monitoring of actual column pressure resulting from media bed properties.

Pressure versus bed height relationship for a specific media, packed at the same compression, remains constant up to at least 1000 cm/hr linear flow in any diameter of Resolute column.

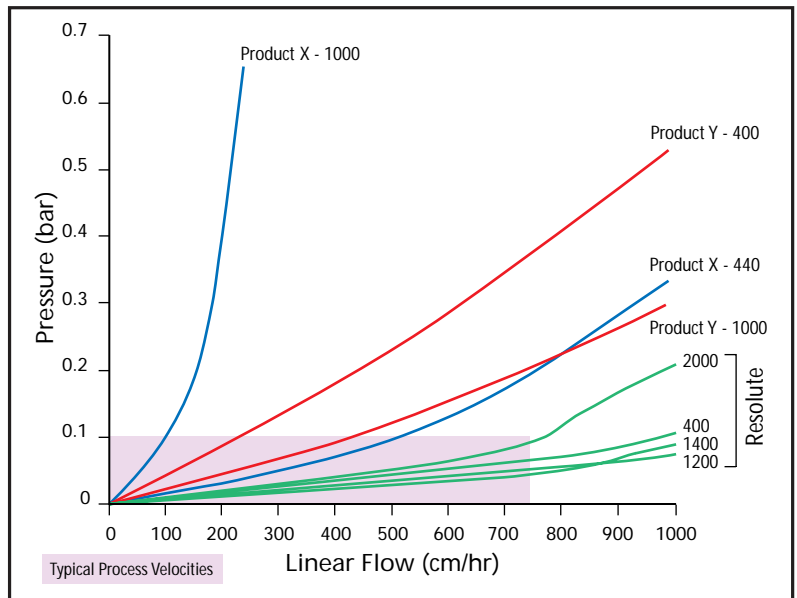


Fig 3. Pressure drop vs Flow for Resolute 400, 1200, 1400 and 2000mm columns and alternative columns fitted with stainless steel mesh bed supports (column Ø mm).

Sanitary Design

- Fully flushed flow path and adjuster seal for clean-in-place (CIP)
- Minimum dead space fixed cell seal arrangement
- Reduced risk of corrosion
 - non metallic nozzle flow path for high salt / low pH conditions
 - forged stainless steel* tube eliminates weld seams on tube wall and flanges (*optional tube material)
- Visible valve flow path aids detection of entrapped air
- Sanitary clamp terminations
- Leachate free acrylic tube – no phthalates
- Peroxide cured seals - no sulphur containing leachate
- Process wetted materials meet regulatory requirements



Fig 4. Top nozzle visible flow path

Effective Column Packing

Complete column packing solutions are available from Euroflow including: Resolute slurry packing systems (SPS) (Figure 5), transfer hose kits, pressure/ flow monitoring kits, media and buffer tanks ready for use with Resolute columns. *Please refer to publication O17PP for further information.*

Contained operation

Because all the column operations are performed in a "closed-system", there is less risk of the operator coming into contact with hazardous materials or the process being exposed to contamination. This results in improved safety and hygienic operation of the column process.

Reproducibility

By eliminating labour intensive column handling operations, the packing parameters can be set and applied within a standard operating procedure. This improves the reproducibility of the packed column performance.

Scalability

All design elements within the mobile phase flow path are maintained throughout the column range up to 2000mm diameter. Unlike conventional columns that are based on different designs as size increases, the Resolute sealing arrangement and flow path follows a single design principle that assures consistent column performance. Resolute slurry packing systems also support large scale operations and maintain identical linear velocities during the packing process up to 2000mm diameter.

Column Options

Standard columns

- Actuated nozzle valve; fits 400 to 1200mm diameter columns
- Bed supports – Polyethylene 10/ 20/ 60 µm
 - Stainless steel 10/ 20/ 50 µm
- Lockable castors* and adjustable feet supplied as standard
 - *280 to 1000mm diameter columns only

Engineered columns

- Operating pressure up to 10 bar
- Certification to ASME or PD5500
- Service frames for piston end cell maintenance
- Actuated nozzle valve
- Hydraulic actuation of column end cell:
 - Positioning of the adjustable piston end cell
 - Axial packing techniques
 - Easier column maintenance

For further information please contact your local representative.



Fig 5. Resolute SPS M



Fig 6. Actuated nozzle valve



Fig 7. Euroflow 2000 mm diameter process column

Principle of Operation

Resolute columns can be packed and unpacked with the column fully assembled. At the centre of the operation is a nozzle valve in both the top and bottom of the column. Process liquids can enter and exit the column via either of these nozzle valves, depending on the characteristics of the chromatographic medium and packing method used.

Top and bottom nozzle valves are identical, making the flow profile the same in either direction. The ability to pack media with the top end cell in place contributes to process hygiene by reducing exposure to the external environment. There are three positions for each nozzle valve: retracted for column run, mid-position for packing and fully extended for unpacking.

Packing position

- Downflow

The top nozzle is extended part way (mid position) into the column. The bottom nozzle is fully retracted. Slurry enters the column via the top nozzle and excess liquid exits via the bottom mobile phase outlet. After packing, the slurry lines are isolated from the mobile phase and can be cleaned independently from the rest of the column.

- Upflow; optional pack direction (not shown)

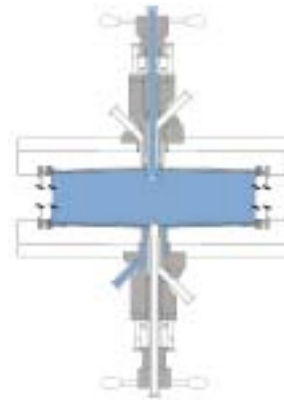
The bottom nozzle is extended part way (mid-position) into the column. The Top nozzle is fully retracted. Slurry is pumped into the bottom and a media bed is formed upon the top bed support.

Running position

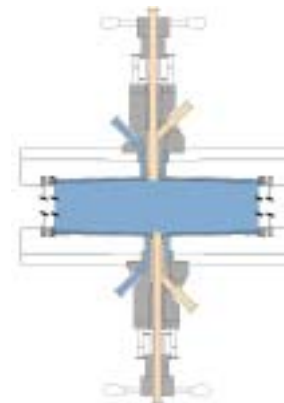
Both nozzles are fully retracted. Mobile phase enters the column through the mobile phase port and flows through the bed support, through the packed bed, through the bed support at the other end of the column and then exits via the opposite mobile phase port.

Unpacking position

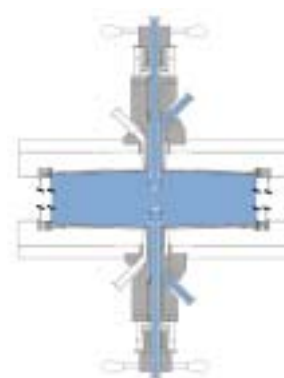
Top and bottom nozzles are fully extended into the column. This makes the slurry waste ports (top and bottom) continuous with the column interior. The chromatography media can exit through these channels as it is mobilised during unpacking. Cleaning solution can be pumped through the nozzle and sprayed into the column. In this way the column is easily and effectively cleaned without exposing the interior or the medium to the external environment, and without dismantling the column.



Nozzle valve in pack position



Nozzle valve in run position



Nozzle valve in unpack position

Column Specifications

Resolute Fixed and Adjustable Columns 180-1200mm diameter								
Operating Pressure	400 - 1200mm 3 bar (44) psi			180 - 280mm 5 bar (73) psi				
Operating Temperature	2-30°C							
Bed Support, type / rating	Stainless Steel Mesh 10, 20, 50 µm Polyethylene Sinter 10, 20, 60 µm							
Stainless Steel surface finish - product flow path	< 0.6 µm Ra, Electropolished							
Stainless Steel surface finish - exterior components	< 0.9 µm Ra, Electropolished							
Stainless Steel surface finish - pressure retaining plates	< 1.5 µm Ra, 240 (UK) Grit Sateen							
Stainless Steel surface finish - column frame	Bright polished							
Media Transfer Nozzle (-DM)	Manual actuation							
Media Transfer Nozzle (-DP)	Manual control with pneumatic actuation							
Terminations (sanitary clamp connections) i.d. (mm)	Column diameter (mm)							
	180	280	400	600	800	1000	1200	
	Mobile phase port	10	10	16	22	35	35	48
	Slurry inlet port	10	10	15	22	22	22	35
Waste outlet port	10	14	16	22	35	35	48	

Table 2. Technical data for Resolute columns 180 to 1200mm diameter

Design

The basis of design for Resolute columns is PD5500. Columns are CE marked in accordance with the European Pressure Equipment Directive 97/23/EC.

Materials of Construction and Chemical Resistance

Resolute columns are constructed from components and process wetted materials suitable for cGMP manufacturing of biopharmaceuticals.

Table 3 lists the major components of Resolute columns in contact with the process fluids (process wetted).

Table 4 lists the chemical resistance of Resolute columns. The information is compiled from several published sources, and includes test results for acrylic conducted by an independent laboratory.

Process Wetted Components	Material
Column tube	Acrylic (cast PMMA) Stainless Steel 316L (optional)
Distribution cell	Polypropylene
Nozzle body	PVDF / Acrylic ¹
Process terminations / Slurry nozzle tip	PEEK
Slurry inlet port (180 & 280mm columns) ²	PEEK
Slurry inlet port (400 to 1200mm columns) ²	Stainless Steel 316L
Bed Support	Polyethylene sinter Stainless Steel mesh (optional)
Seals	EPDM (Peroxide cured)
Seals	FEP encapsulated silicone
Wiper Blade	PTFE
External Components	Material
Stand, adjustable feet	Stainless Steel 316L
Castor	Stainless Steel 304L
Castor Tyre	Polyurethane

Table 3. Materials of construction : Resolute columns

Note: (1) PVDF / PVDF version available for increased chemical resistance
(2) Components not in mobile phase flow path

EPDM = ethylene propylene diene
FEP = fluoroethene propene

PEEK = polyetherether ketone
PVDF = polyvinylidene fluoride

Installation and Validation Documentation

Resolute columns come with a comprehensive operator's manual. The column validation support package contains comprehensive protocols and provides the required documentation and procedures to support FAT, IQ and OQ. To support validation efforts and efficient commissioning, the system documentation includes records of the pre-shipment test results.

Column Manual documentation includes:

- Operating Guide
- Materials and compatibility data
- Comprehensive parts list
- Sub-component manuals
- Spare parts recommendation
- Maintenance recommendations

Substance	Concentration	Column with acrylic tube	Column with stainless steel tube
Acetic Acid	25%	✓	✓
Ammonium sulphate	1M	✓	✓
Common process buffers	0.1M	✓	✓
Ethanol	20%	✓	✓
Ethanol	40%	✗	✓2
Ethylene glycol	50%	✓	✓
Formaldehyde	1M	✓	✓
Formic Acid	10%	✓	✓
Glycerol	100%	✓	✓
Hydrochloric acid	1M	✓1	✗
Hydrogen peroxide	40 volumes	✓	✓
Phosphoric acid	25%	✓	✓
Propan-2-ol	40%	●	✓2
Sodium chloride	2M	✓1	●
Sodium hydroxide	2M	✓	✓
TNBP (with 1% Tween)	0.30%	●	✓2
Trifluoroacetic acid	0.10%	✓	✓
Triton® X-100 surfactant	0.10%	✓	✓
Urea	8M	✓	✓

✓ Resistant ● Limited resistance ✗ Not recommended
 1 With polyethylene sinter 2 Specify PVDF / PVDF nozzle body
 A detailed list is available in operating manual

Table 4. Chemical Resistance : Resolute columns

Column Capacity and Ordering Information

An indication of Resolute column capacities in the range of 280 to 2000mm diameter with 100-300mm adjustable bed heights is presented in Table 5. Variable bed heights are also available in the ranges:200-400mm,300-500mm and 400-600mm, as well as fixed capacity columns from 180mm diameter. Columns may be specified with Acrylic or Stainless Steel tubes.

Description	Diam. (mm)	CSA (cm ²)	Adjustable Height (mm)	Adjustable Capacity Ltr.	Operating Pressure	
					psi	bar
Resolute 280 / 100-300	280	615	100 - 300	6.2 - 18.5	73	5
Resolute 400 / 100-300	400	1257	100 - 300	12.6 - 37.7	44	3
Resolute 600 / 100-300	600	2827	100 - 300	28.3 - 84.8	44	3
Resolute 800 / 100-300	800	5027	100 - 300	50.3 - 150	44	3
Resolute 1000 / 100-300	1000	7854	100 - 300	79 - 235	44	3
Resolute 1200 / 100-300	1200	11309	100 - 300	113 - 339	44	3
Resolute 1400 / 100-300	1400	15394	100 - 300	154 - 461	44	3
Resolute 1600 / 100-300	1600	20106	100 - 300	201 - 603	44	3
Resolute 1800 / 100-300	1800	25447	100 - 300	255 - 763	44	3
Resolute 2000 / 100-300	2000	31416	100 - 300	314 - 942	44	3

Table 5. Example of column capacities for Resolute columns with standard 200mm bed height adjustment range

For alternative column capacities and complete product ordering information please contact your local representative.

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016PP rev A Printed in England 0403