

## Improving the downstream processes of plasma proteins

In the middle of the last century, Cohn et. al developed a downstream process for human albumin using a plasma fractionation technique.<sup>[1]</sup>

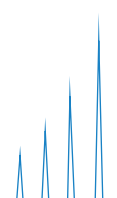
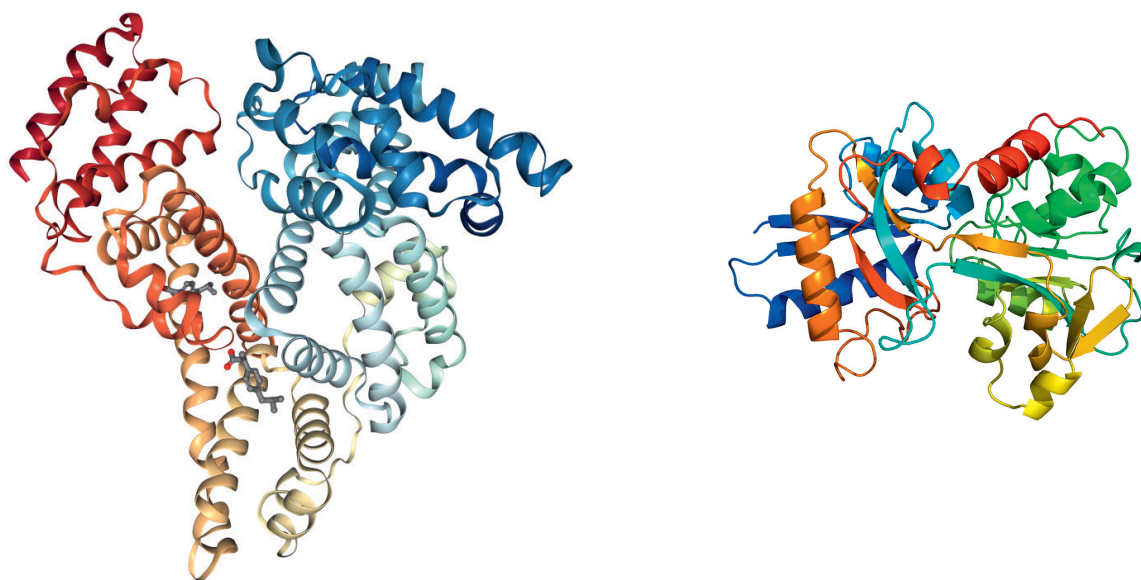
Today's requirements for purity and recovery are much greater. Also, the complexity of the proteins and the downstream processes has increased on the last decades. Therefore, new technologies are needed to address the new challenges for the downstream processing of plasma proteins.

IEX is widely used for the isolation of plasma proteins. The downstream process typically consists of capturing, intermediate purification and final polishing steps to achieve the final purity.

The currently common IEX resins suffer from limited flow rate which results in an extended processing time and reduced productivity.<sup>[2]</sup>

Consequently, high performance resins for the downstream processing of plasma proteins are needed to achieve the required rates and high purity. Compared to the commonly used IEX resins, BioPro IEX resins from YMC allow higher flow rates to increase the productivity by reducing the processing time.

Furthermore, by using the smaller particle sizes of YMC's BioPro IEX resins, the purity can also be optimised.



## Selectivity for plasma proteins

The increasing complexity of the plasma proteins requires new solutions to increase the purity and productivity of the downstream processes. YMC's BioPro IEX resins are available with a comparable selectivity in analytical particle sizes of 3  $\mu\text{m}$  and 5  $\mu\text{m}$  as well as in preparative particle sizes of 10  $\mu\text{m}$ , 20  $\mu\text{m}$ , 30  $\mu\text{m}$  and 75  $\mu\text{m}$ . The smaller the particle size, the better the resolution.

The example in figure 1 shows the separation of a plasma protein sample using a 5  $\mu\text{m}$  resin with a 50 mm bed length. This separation can be easily transferred to preparative grade particle sizes allowing a high purity isolation of the related compounds to be achieved. By using a longer bed length and optimising the eluent conditions the separation can be further improved.

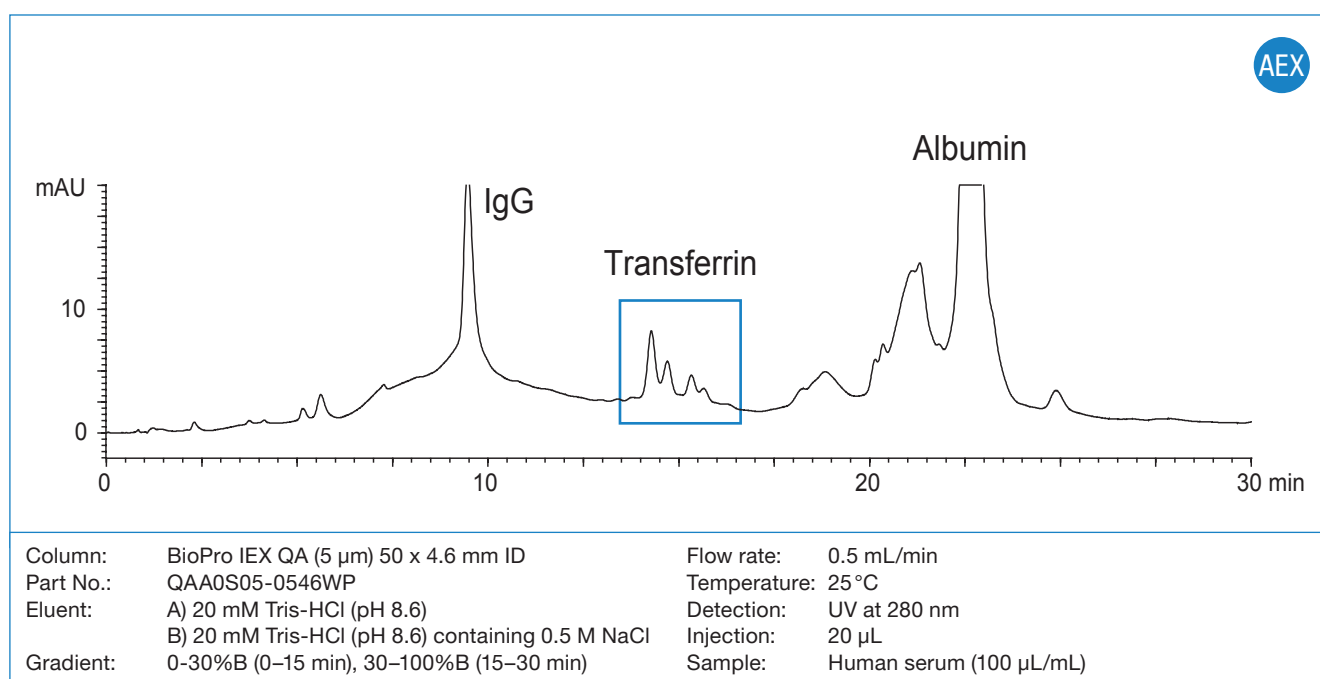
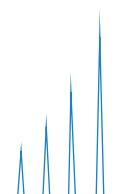


Fig. 1: Separation of proteins in human serum using a 5  $\mu\text{m}$  AEX resin

## Flexibility in process development

One of the advantages of YMC's BioPro IEX resins is its full scalability. This property provides an identical chromatographic behaviour across all particle sizes. This is beneficial, as separation and fractionation can be optimised on the analytical scale. Depending on

the required resolution the optimal bead size can be selected. Then, the process can be reliably transferred to the production scale. This enables highly flexible implementation of BioPro IEX resins, resulting in a perfectly tailored solution.



An illustrated example is shown below for two proteins: transferrin and trypsin inhibitor. This shows that the separation of the main peaks remains stable across the 4 different particle sizes. If the greatest resolution is needed e.g. in polishing steps, the smaller particle sizes are the optimum choice.

As can be seen, the smaller particles allow sufficient separation of trace impurities.

During a capturing process the 75  $\mu\text{m}$  material provides adequate separation. The two main peaks are well separated and resolved.

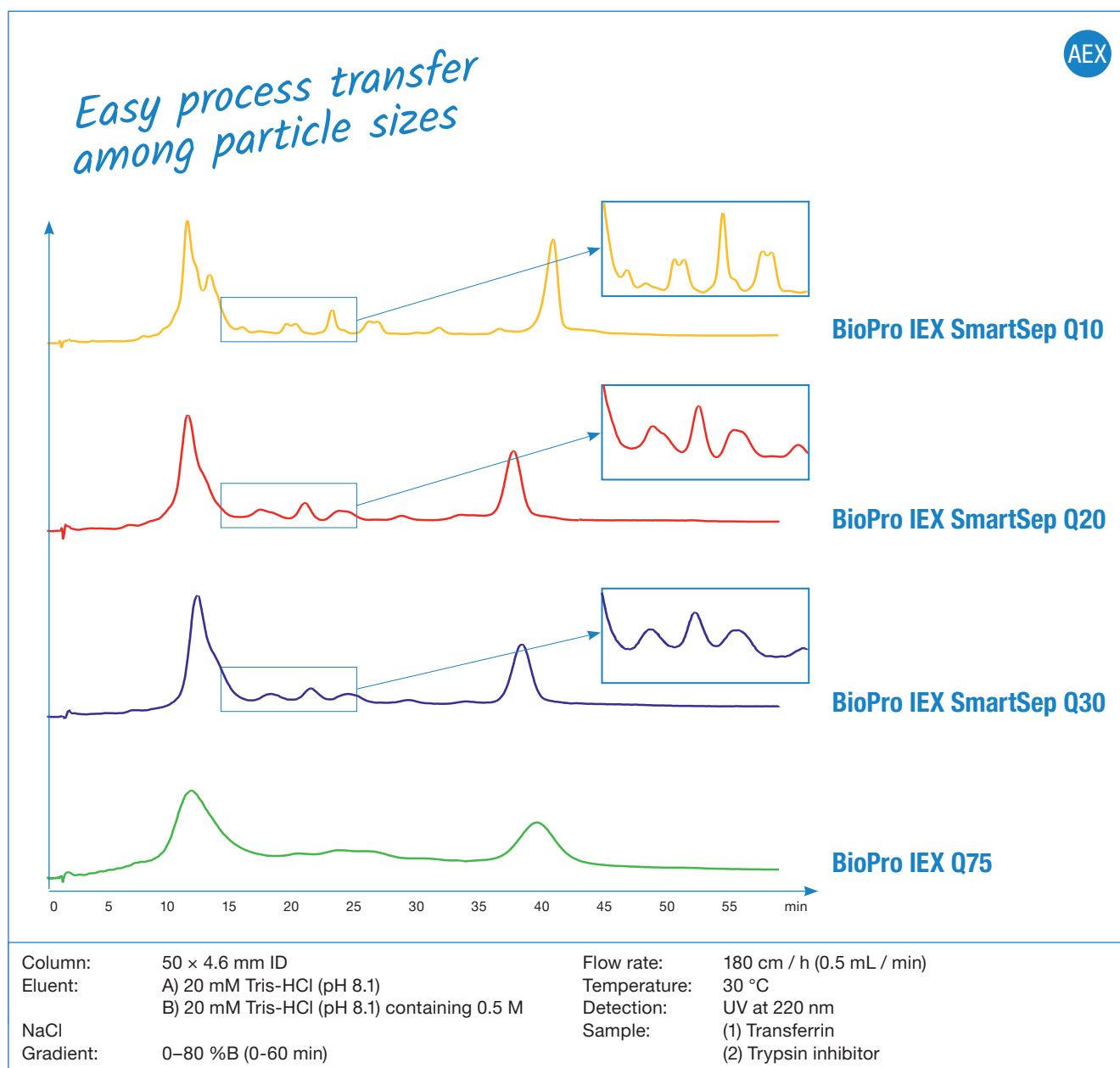
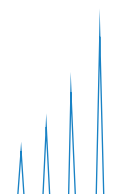


Fig. 2: Separation of transferrin and trypsin inhibitor using AEX resins with different particle sizes



## Increasing flow rates

As described by Raoufinia et al.<sup>[2]</sup>, low flow rates are a typical limitation for the use of conventional IEX resins. The pressure flow characteristic of a resin is the decisive parameter for the applicable flow rate range. Resins with improved pressure flow characteristics allow much greater flow rates. By increasing the flow rate, the productivity of nearly every process can be optimised.

For the initial capturing step, typically resins with larger particle sizes are used. Therefore, the pressure flow characteristics of YMC's BioPro IEX Q75 resin were compared with a commonly used AEX resin. The YMC resin is based on 75µm beads whereas the competitor's resin has a specified particle size of 90µm. By using smaller particle sizes, the resolution of processes can be improved resulting in an increased purity.

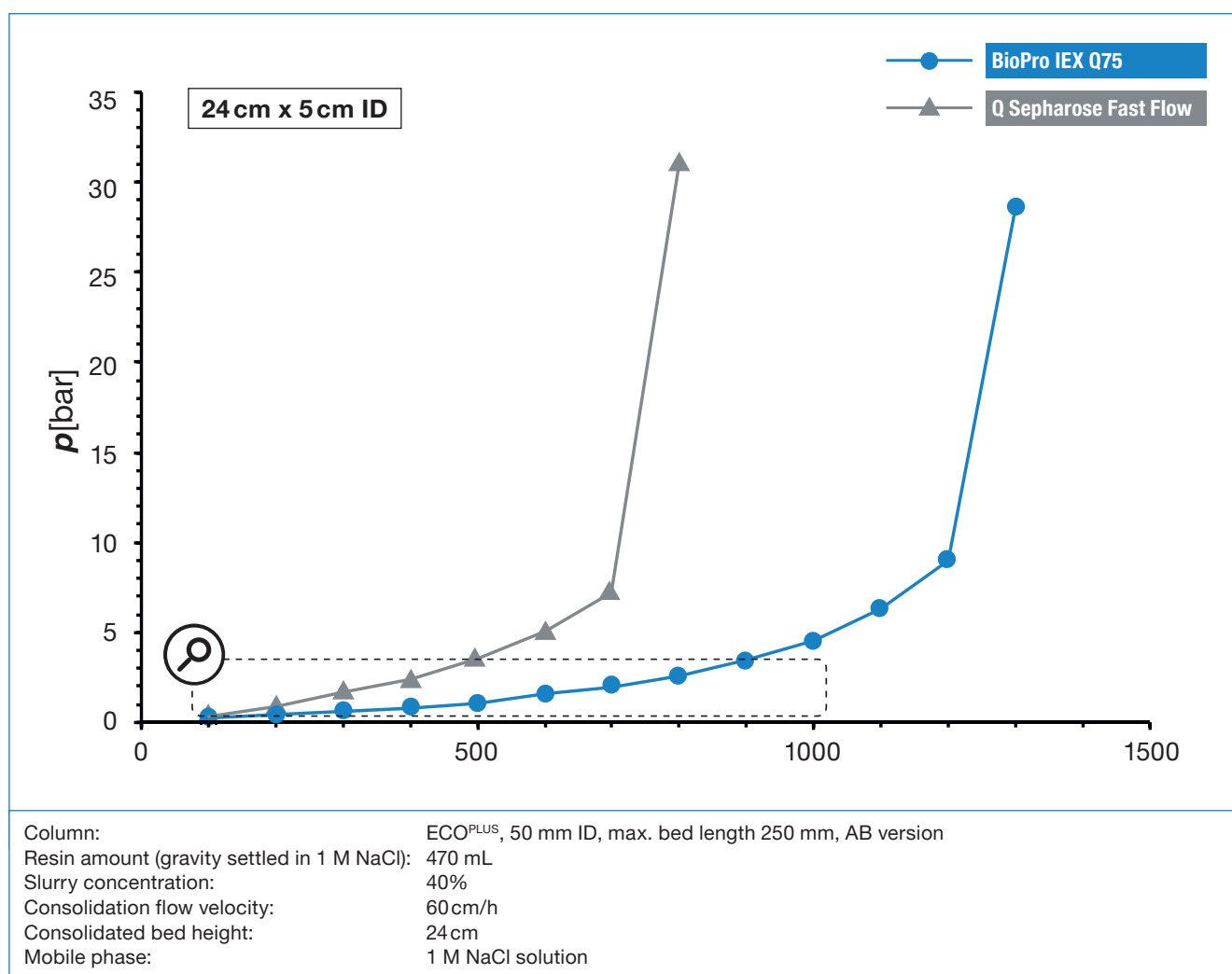
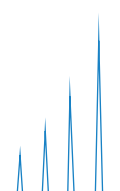


Fig. 3: Pressure flow curves for YMC's BioPro IEX Q75 and a competitor's resin



For the pressure range of up to 3 bar, the YMC resin can be used in a flow rate range of up to 800 cm/hr for the used bed length of 24 cm. Thereby, the productivity of a process can be doubled compared to the competitor's resin.

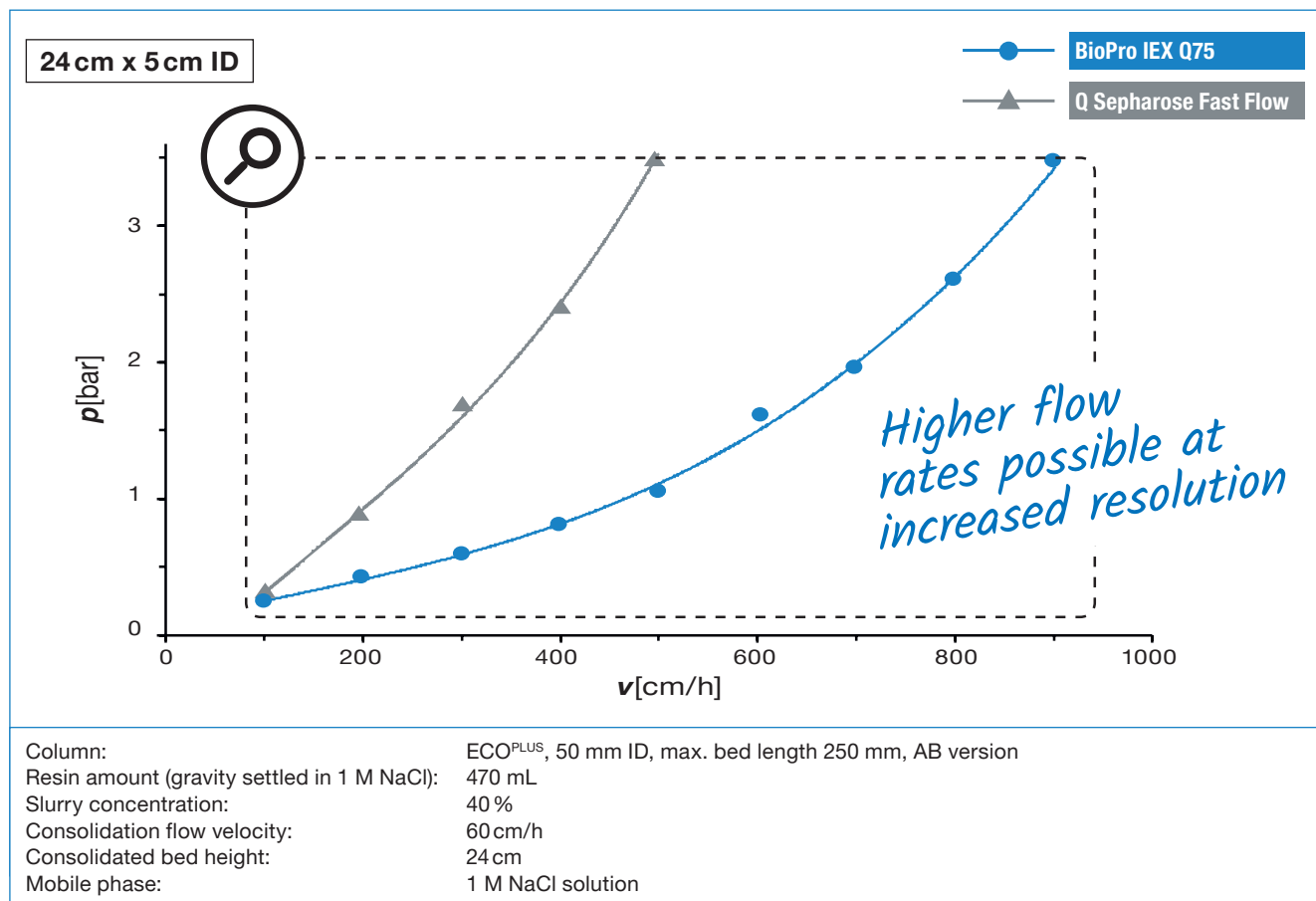


Fig. 4: Pressure flow curves for YMC's BioPro IEX Q75 and a competitor's resin for a pressure range up to 3.5 bar.

The pressure-flow curve of BioPro IEX Q75 suggests reversible compression behaviour over a wide range of linear flow velocity. Despite using smaller particles (75 µm) compared to the 90 µm particle size of the competitor's resin, BioPro IEX Q75 shows much better pressure flow characteristics.

## Conclusion

The IEX resins from YMC are perfectly suited for the use in downstream processes of plasma proteins. The resins combine a matching selectivity for plasma proteins with improved pressure flow characteristics to increase the productivity of virtually any downstream process.

- **Improved resolution**
- **Higher flow rates possible**
- **Increased productivity**

**Request a sample!**

[1] Cohn, E. J.; Strong, L. E.; Hughes, W. L. Preparation and Properties of Serum and Plasma Proteins. IV. A System for the Separation into Fractions of the Protein and Lipoprotein Components of Biological Tissues and Fluids. J. Am. Chem. Soc. 1946, 68(3), 459-475  
 [2] Raoufinia, R.; Mota, A.; Keyhanvar, N. J. Overview of Albumin and Its Purification Methods. Adv Pharm Bull. 2016, 6(4), 495-507

## Specifications

### BioPro IEX for Capture

BioPro IEX Series	BioPro IEX Q75	BioPro IEX S75
Ion exchange type	strong anion exchanger	strong cation exchanger
Charged group	$-R-N^+(CH_3)_3$	$-R-SO_3^-$
Matrix	Hydrophilic polymer beads	
Pore size	Porous	
pH Range	2–12	
Compression factor	1.05–1.15	
Particle size	75 $\mu$ m	
Pressure resistance	0.3 MPa	
Typical flow rate	200–1000 cm/hr Max. 2000 cm/hr	
Ion-exchange capacity	min. 0.10 meq/ml-resin	
Dynamic binding capacity	min. 160 mg/ml-resin (BSA)	min. 160 mg/ml-resin (lysozyme)

### BioPro IEX SmartSep for intermediate purification and polishing

BioPro IEX Series	BioPro IEX SmartSep Q10	BioPro IEX SmartSep Q20	BioPro IEX SmartSep Q30	BioPro IEX SmartSep S10	BioPro IEX SmartSep S20	BioPro IEX SmartSep S30
Ion exchange type	strong anion exchanger			strong cation exchanger		
Charged group	$-R-N^+(CH_3)_3$			$-R-SO_3^-$		
Matrix	Hydrophilic polymer beads					
Pore size	Porous					
pH Range	2–12					
Compression factor	1.05–1.15					
Particle size	10 $\mu$ m	20 $\mu$ m	30 $\mu$ m	10 $\mu$ m	20 $\mu$ m	30 $\mu$ m
Pressure resistance	Regular use: 3 MPa Max.: 4 MPa	Regular use: 2 MPa Max.: 3 MPa		Regular use: 3 MPa Max.: 4 MPa	Regular use: 2 MPa Max.: 3 MPa	
Typical flow rate	200–1000 cm/hr Max. 2000 cm/hr					
Ion-exchange capacity	min. 0.08 meq/ml-resin					
Dynamic binding capacity	min. 100 mg/ml-resin (BSA)			min. 100 mg/ml-resin (lysozyme)		


Regulatory support file available under non-disclosure agreement.  
Used in validated cGMP-manufacturing processes.

Customised material available on request.  
DMF registered with FDA.

## Select your screening kits and bulk samples for media selection and method development


YMC offers a number of ion exchange screening kits based on 1 mL or 5 mL columns and also bulk resin samples for testing. This provides a significant advantage and efficiency in resin screening and purification method development.

1 ml Type (26 x 7.0 mm ID)



- Resin screening
- Purification method development

5 ml Type (26 x 15.6 mm ID)



- Purification method development
- Loadability studies

*Please contact us to order your samples for testing.*

### Further sample options



**Robocolumn®**

Miniaturized prepacked columns (50 µL, 200 µm and 600 µL)  
High-throughput process development



**Bulk pack**

Chromatography resins for self-packing



**Minichrom™**

Prepacked columns with different dimensions and volumes



**Packed anal. Columns**

Prepacked PEEK columns  
50 x 4.6 mm ID  
100 x 4.6 mm ID

# Ordering Information



## Availability

- Large production capacity for YMC's IEX resins
- Lot sizes up to 400 L available
- Short delivery time even for large quantities
- Full compliance with GMP requirements

Regulatory support file available under non-disclosure agreement. Used in validated cGMP-manufacturing processes. Customised material available on request. DMF registered with FDA.

## Strong anion exchanger: BioPro IEX Q

Product	Particle Size	Code	Pack Sizes*					
			50 ml	250 ml	1 L	5 L	10 L	20 L
BioPro IEX SmartSep Q10	10 µm	QSA0S10	✓	✓	✓	✓	✓	✓
BioPro IEX SmartSep Q20	20 µm	QSA0S20	✓	✓	✓	✓	✓	✓
BioPro IEX SmartSep Q30	30 µm	QSA0S30	✓	✓	✓	✓	✓	✓
BioPro IEX Q75	75 µm	QAA0S75	✓	✓	✓	✓	✓	✓

\* Larger or customised pack sizes are available on request.

## Strong cation exchanger: BioPro IEX S

Product	Particle Size	Code	Pack Sizes*					
			50 ml	250 ml	1 L	5 L	10 L	20 L
BioPro IEX SmartSep S10	10 µm	SSA0S10	✓	✓	✓	✓	✓	✓
BioPro IEX SmartSep S20	20 µm	SSA0S20	✓	✓	✓	✓	✓	✓
BioPro IEX SmartSep S30	30 µm	SSA0S30	✓	✓	✓	✓	✓	✓
BioPro IEX S75	75 µm	SPA0S75	✓	✓	✓	✓	✓	✓

\* Larger or customised pack sizes are available on request.

## Preparative screening kits

Product name*	Particle Size	Pack size	Column volume	Product code
BioPro IEX Q75	75 µm	5 / pack	1 mL	BPQAA0S75-01PK
			5 mL	BPQAA0S75-05PK
BioPro IEX SmartSep Q30	30 µm	5 / pack	1 mL	BPQSA0S30-01PK
			5 mL	BPQSA0S30-05PK
BioPro IEX SmartSep Q20	20 µm	5 / pack	1 mL	BPQSA0S20-01PK
			5 mL	BPQSA0S20-05PK
BioPro IEX S75	75 µm	5 / pack	1 mL	BPSPA0S75-01PK
			5 mL	BPSPA0S75-05PK
BioPro IEX SmartSep S30	30 µm	5 / pack	1 mL	BPSSA0S30-01PK
			5 mL	BPSSA0S30-05PK
BioPro IEX SmartSep S20	20 µm	5 / pack	1 mL	BPSSA0S20-01PK
			5 mL	BPSSA0S20-05PK
IEX Selection Kit Q75/S75/Q30/S30	30 µm, 75 µm	4 / pack 1 per resin	1 mL	BPSIA0S99-01PK
			5 mL	BPSIA0S99-05PK

\* Other screening kits are available on request