Praesto® Jetted A50

Purolite® is the first agarose resin provider to produce process-scale volumes of a uniform particle size bead.

Background

Purolite® Life Sciences has revolutionized the future of Protein A chromatography with Praesto® Jetted A50 by combining for the first time 'Jetting' technology - an innovative process that produces uniform size agarose beads with a very narrow particle size distribution - together with a new, high performance Protein A ligand, NGL-Impact™ A, from Repligen® Corporation.

This best in class Protein A agarose resin is a result of combining 70 years expertise between Purolite®'s jetted resin innovation, together with Repligen®'s ligand technology expertise. Praesto® Jetted A50 provides superior performance characteristics over traditional resins including:

Key Features

- Ultra-high capacity up to ~80* g/l, resulting in increased productivity from the same volume of resin
- Exceptional alkaline stability at 0.5 M NaOH, with the ability to use high concentrations (up to 1.0 M)
- Novel jetted base bead drives higher capacity due to increased surface area and improved mass transfer
- Up to 40% higher capacity than the current market-leading Protein A resin
- Supplied in OPUS® pre-packed columns

Praesto® Jetted A50 is the only bioprocess scale agarose resin available with a uniform particle size distribution. Designed to meet the future demands in mAb processing Praesto® Jetted A50 addresses the increased titres from today's bioreactors, and allows customers to increase productivity from the same manufacturing footprint.

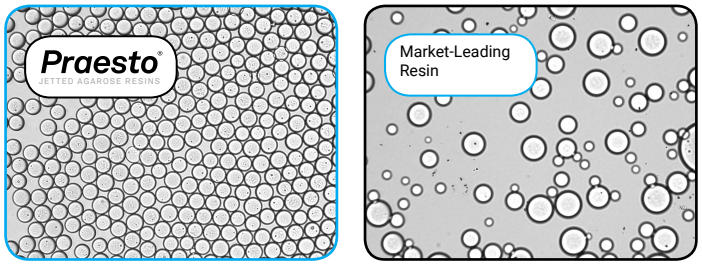


Figure 1: *Microscope image - Praesto® Jetted agarose resins*

In multiple successive trials, Praesto® Jetted A50 has consistently shown significantly improved performance over today's market leading Protein A resins, due to the unique benefits of an innovative new ligand coupled to a novel jetted base matrix.

The result is a new, best in class agarose based Protein A resin that delivers exceptional performance in terms of capacity, pressure flow and lifetime; whilst bioburden risks and cross-contamination in processes are managed more effectively due to the ability to use higher concentrations of sodium hydroxide.

For more than 30 years, Protein A affinity resins have been selected by biopharmaceutical developers for mAb purification. Today, Protein A affinity chromatography continues to be the preferred method for commercial purification of antibodies due to its very high selectivity and robust resin performance over repeated purification cycles.

*** based on in house testing as well as testing reported from independent companies DBC have in many cases been demonstrated >80mg/mL, a 40% increase over comparable resins.**

Addressing Biomanufacturing Challenges

1. Increasing productivity and process economic demands, from the same manufacturing footprint.

2. The ability to address the dramatic increase in upstream product titres, which drives the need for higher capacity resin. With an increase in over 40% compared to MabSelect Sure™ LX, *Praesto*® Jetted A50 provides up to ~80 g/l.

3. The need to control bioburden in processes. *Praesto*® Jetted A50 offers the user with the ability to use high concentrations (up to 1.0 M) sodium hydroxide. NaOH concentrations commonly used for CIP and sanitization of ion exchange and hydrophobic-interaction chromatography resins.

Protein A Ligand

The Protein A ligand used in the manufacture of *Praesto*® Jetted A50 is a modern, recombinant multimer called NGL-Impact™ A. Supplied by Repligen® corporation and developed in collaboration with Navigo GmbH™ to dial-in the features that are important in the Protein A marketplace – capacity, pH elution and caustic stability. NGL-Impact™ A is a 'best in class' ligand. Optimization of the ligand loading, together with the advanced jetted technology, results in a resin with very high capacity and excellent alkaline stability. The ligand is multipoint attached to the base bead, providing high capacity and low leakage.

Dynamic Binding Capacity

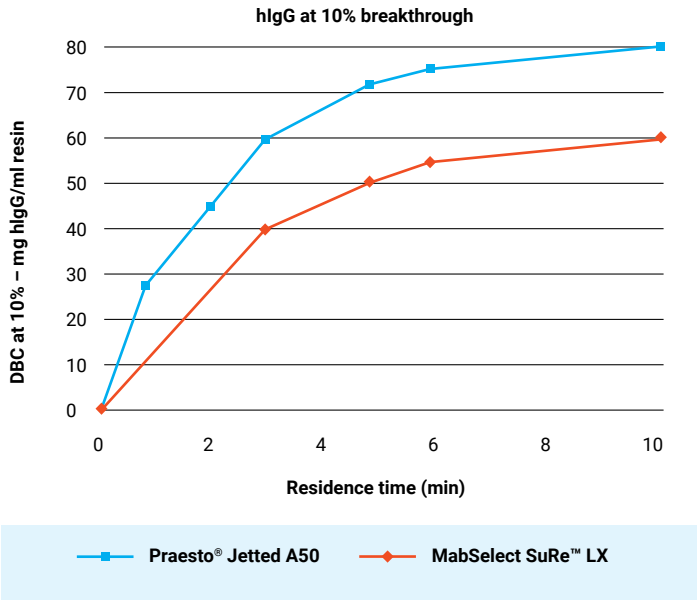


Figure 2: *DBC of Praesto® Jetted A50 compared to MabSelect Sure LX measured using hIgG at 10% BT*

0.5 M Sodium Hydroxide Stability

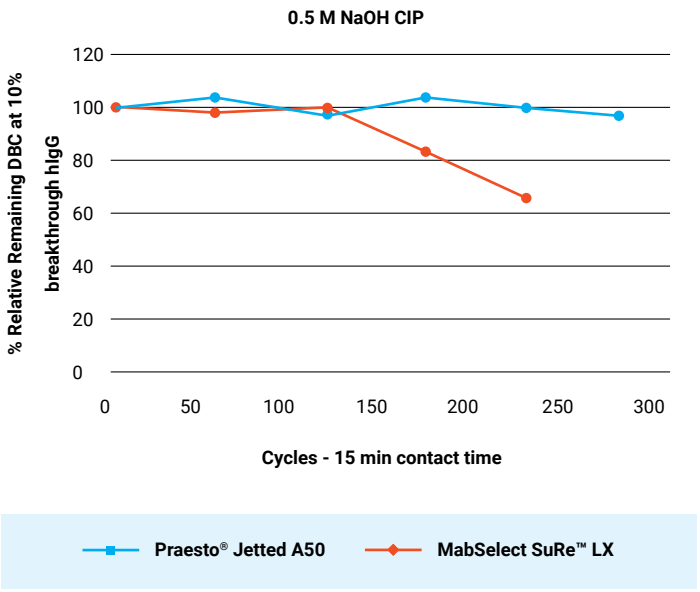


Figure 3: *Praesto® Jetted 50A compared to MabSelect SuRe™ LX, exposed to 0.5 M NaOH at ambient temperature in static mode. DBC was measured using hIgG at 10% BT and compared to the original dynamic binding capacity. Total exposure in hours was back calculated to 15 mins cycle time per CIP step.*

Jetting - Uniform Particle Size Beads

Jetting technology is a new patented method that produces agarose beads with a very narrow particle size distribution. Purolite® is the first agarose resin provider to produce process-scale volumes of a uniform particle size bead, for the purification of recombinant proteins and monoclonal antibodies.

Jetted resins provide superior performance characteristics over traditional resins, including improved pressure flow, resolution and packing reproducibility due to the bead uniformity.

Key Benefits of Jetted Resins:

- Scalable linear pressure/flow properties suitable for process scale
- No fines - resulting in lower pressure drop
- Higher resolution/selectivity for demanding separations
- Higher dynamic binding capacity as a result of surface area, porosity and ligand optimization
- Improved packing efficiency - reduces expensive column packing failures
- *Praesto*® Jetted A50 particle size = 95% between 35 and 90 µm (Uniformity coefficient <1.3). MabSelectSure™ LX - particle size = 95% between 45 and 120 µm (Uniformity coefficient 1.9)

Pressure Flow

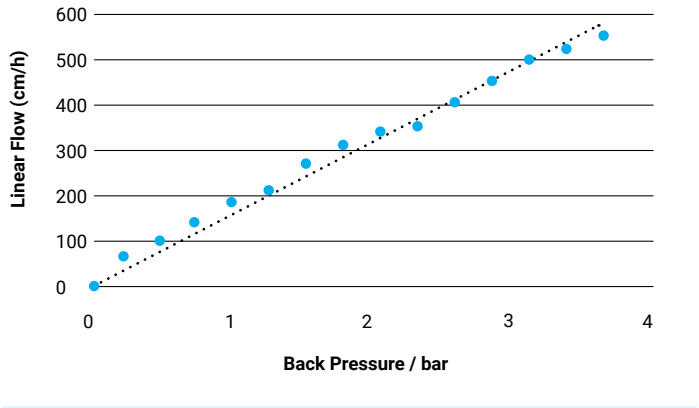


Figure 4: *Pressure flow performance of Praesto® Jetted A50 in a 2.6 cm ID column packed at a 20 cm bed height, column packed at 4 bar back pressure. The pressure flow properties at process scale would enable columns to be run at 300 cm/h at a 20 cm bed height.*

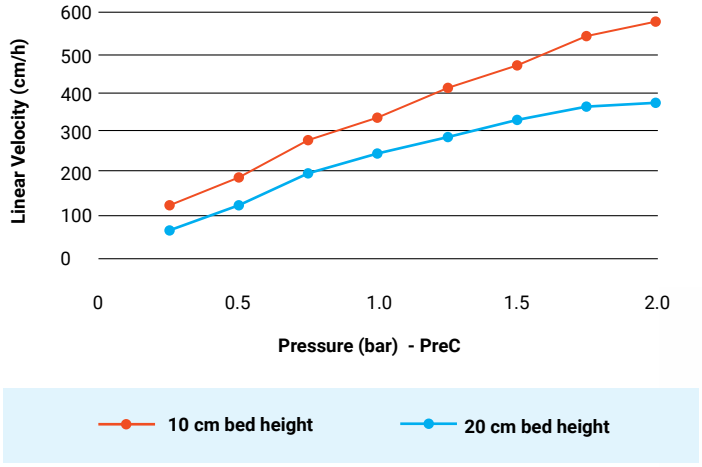


Figure 5: *Praesto® Jetted A50 - Pressure flow AxiChrom 200 (10 & 20 cm BH). Base matrix - 50 µm (CF 1.20)*

Thanks to Fujifilm Diosynth Biotechnology for the use of their demo equipment, used to produce this data

FUJIFILM Diosynth biotechnologies

Particle Size Distribution

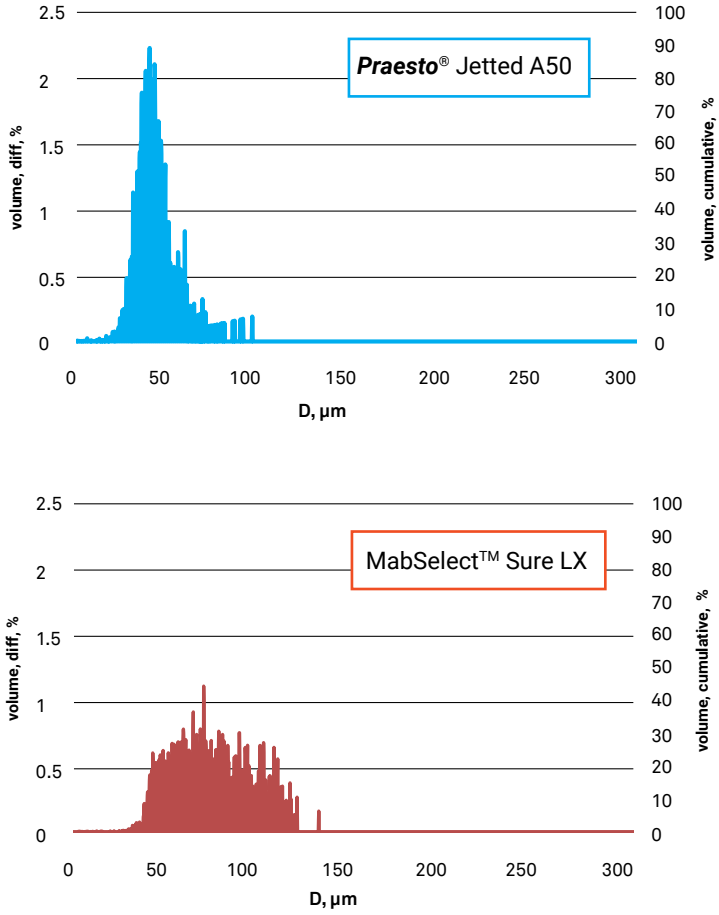


Figure 6: *Particle size distribution of Praesto® Jetted A50 compared to MabSelect™ Sure LX (traditional batch emulsified).*

Praesto® Jetted A50

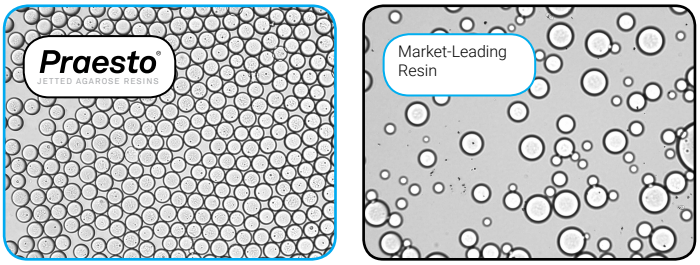
Purolite® Life Sciences' jetting technology has enabled the development of a 50 µm resin which, as a result of surface area, porosity and ligand optimization, displays exceptionally high binding capacities, even at short residence times. It is capable of being run at process-scale, which has not been possible with traditional batch wise emulsified agarose resins.

The improvements in the properties of the resin has been achieved by the jetting production method, which enables more control in gelling time. This in turn creates a more uniform internal bead structure, enabling a smaller particle size, whilst maintaining a desirable pore structure for protein capture without detriment to the pressure flow performance. The more uniform bead particles result in better packing in a column which reduces back pressure issues, which limit flow rates of smaller resin sizes, as well as expecting higher HETP, ease of packing and elutions with less tailing.

Environmental Benefits

Jetted uniform beads also have several important benefits to the environment over standard agarose resin beads. Jetting technology is a continuous manufacturing process that produces beads in a more efficient way, with very high yields, dramatically lowering leadtimes and improving the overall supply chain.

Since the beads are uniform in size, it removes the need for extensive sieving, thus generating considerably less waste. Another environmentally friendly advantage with this new technology, is that it eliminates the need for high levels of organic solvents compared to standard agarose resin beads, like toluene commonly used in traditional manufacturing and is a major advancement in 'green manufacturing'



Praesto® Jetted A50: Typical Physical & Chemical Characteristics	
Application	Affinity capture of Fc containing biomolecules
Polymer Structure	Highly cross linked agarose, uniform size beads
Appearance	Spherical, uniform size beads supplied in 20% ethanol slurry. On request 2% benzylalcohol
Ligand	Recombinant multimer - NGL-Impact™ A
Dynamic Binding Capacity	~ 50 g/l at 3 mins residence time and up to ~80 g/l at 10 mins residence time[1]
Average Particle Size[2]	50 µm
Particle Size Range	95% between 35-90 µm (Uniformity coefficient = <1.3)
Pressure/Flow Specifications	> 450 cm/h at 3 bar in a 2.6 x 20 cm column
pH Stability, Working Range	3 - 12
pH Stability, CIP (Short-term)	2 - 14
Recommended Storage	2 to 8°C, 20% ethanol

[1] DBC at 10% BT by frontal analysis with hIgG.

[2] $d_{50}v$ is the median particle size of the cumulative volume distribution.

Placing your Order

To place your order simply contact us via email or telephone using the information on the bottom of this page, and quote your order number from the table below. *Praesto*® Jetted A50 can be supplied both loose in the following pack sizes; 25ml, 100ml, 500ml, 1L+ on request.

It also can be supplied prepacked in OPUS® columns by Repligen®. Available in RoboColumns with 200 ul column volumes, and MiniChrom available in 1 and 5 ml CV.

For scale up/validation, pilot manufacturing and cGMP manufacturing operations we have an agreement with Repligen® to pack Praesto® resins in 0.5 cm diameter to 80c m diameter OPUS® columns with flexible bed heights.

If you would like to discuss how *Praesto*® Jetted A50 can benefit your purification process, we have dedicated experts on-hand across the globe to provide knowledgeable, same-day technical assistance.

***Praesto*® Jetted A50 Ordering Information**		
BULK RESIN	**PACK SIZE**	**ORDER NUMBER**
***Praesto*® Jetted A50**	25 ml	PR0550-166
***Praesto*® Jetted A50**	100 ml	PR0550-164
***Praesto*® Jetted A50**	500 ml	PR0550-165
***Praesto*® Jetted A50**	1 L	PR0550-310
PRE-PACKED COLUMNS	PACK SIZE	ORDER NUMBER
***Praesto*® Jetted A50 MiniChrom Column (8 x 20 mm)**	1 x 1 ml	PR0550-175
***Praesto*® Jetted A50 MiniChrom Column (8 x 100 mm)**	1 x 5 ml	PR0550-176
***Praesto*® Jetted A50 RoboColumn (5 x 10 mm)**	8 x 200 µl	PR0550-174
***Praesto*® Jetted A50 RoboColumn (5 x 10 mm)**	8 x 600 µl	PR0550-279
***Praesto*® Jetted A50 HT Column (Quantity of 5 columns)**	5 x 1 ml	PR0550-575
***Praesto*® Jetted A50 HT Column (Quantity of 5 columns)**	5 x 5 ml	PR0550-576

The *Praesto*® Range

The *Praesto*® range offers a selection of modern, high-flow Affinity and Ion Exchange agarose resins, delivering exceptional results from Protein A to high-resolution polishing steps. The range also includes a full selection of *Praesto*® Pure base matrices, and pre-activated resins in a variety of source chemistries.

All *Praesto*® products provide an advanced, high-flow, highly cross-linked agarose base matrix. The entire range benefits from excellent pressure/flow characteristics and stability for optimal recovery of active proteins.

Discover *Praesto*® at: **www.purolite.com/life-sciences**

Stability from a Robust Supply Chain

Regulatory Support

Purolite® Life Sciences provides customers with regulatory support documentation for *Praesto*® products, used in regulated environments. Comprehensive regulatory support files are available for each *Praesto*® resin, and are provided under a confidential disclosure agreement.

The purpose of this Regulatory Support File (RSF) is to provide assistance with:

- Process development of clinical and commercial purification processes
- Manufacturing validation
- Quality control tests
- Standard Operating Procedure (SOP) for cleaning in place (CIP) and sanitization
- Application for various regulatory licenses or compliance
- Plant and document audits

Quality

Purolite® maintains a global Quality Management System (QMS) which supports BSI requirements of ISO 9001. Compliance is monitored and maintained through a quality assurance and regulatory team, who conduct internal audits to ensure operations meet the guidelines and protocols for equipment and procedures. Our teams are given continuous training on quality processes to ensure batch-to-batch consistency.

Security of Supply

As a leading supplier of resin to the world's most regulated industries, we recognise that *Praesto*® resins are critical purification products. To confirm our commitment to the security of supply of these resins, Purolite® will bring on line in 2018 a full-scale manufacturing facility, in Wales UK. This will provide 100,000 L capacity per annum in batch sizes of 600 L. This is equal to 30% of today's global demand for agarose resins within the biologics market.

Business Continuity and Disaster Recovery

Ensuring reliable availability of *Praesto*® agarose resins is vital to customers and is of paramount importance to Purolite®. As such Purolite® has a real-world security-of-supply system in place to support your process requirements for business continuity.

All agarose related activities occur at our centralised facility in Llantrisant Wales, UK. This includes R&D, current manufacturing, customer applications, quality and regulatory affairs together with commercial operations.

Raw Materials

Our raw material suppliers are selected and qualified from leading manufacturers. With at least one alternative supplier, raw material stock is managed through a globally coordinated inventory system to ensure security of supply. Additionally, quality control protocol is in place.

Repligen®

Repligen® is a bioprocessing-focused life sciences company bringing over 35 years of expertise and innovation to our customers. Repligen® is a longtime market leader in Protein A, with two facilities that produce the majority of the global Protein A ligand demand to biopharmaceutical customers worldwide. Repligen® has comprehensive business continuity plans, with multiple Protein A ligand manufacturing sites both in Waltham, MA and Lund, Sweden.

The Repligen® and Purolite® Partnership

By consolidating over 70 years expertise between Purolite®'s jetted resin innovation, together with Repligen®'s ligand technology expertise. Purolite® Life Sciences has revolutionised the future of chromatography by combining 'Jetting' technology - an innovative process that produces uniform size agarose beads with a very narrow particle size distribution - together with a new, high performance Protein A ligand, NGL-Impact™ A, from Repligen® Corporation.

NGL-Impact™ A was developed as part of Repligen®'s collaboration with Navigo Proteins GmbH™. This new ligand has outstanding performance attributes when immobilized on jetted agarose bead technology, with ultra-high binding capacities and excellent alkaline stability. These attributes are important in providing improved monoclonal antibody capture to handle increased upstream product titres, and in allowing higher concentrations of sodium hydroxide (NaOH) for sanitization of resins. Purolite® Life Sciences's jetting technology is a new patented method that produces agarose beads with a uniform particle size distribution to drive higher capacity and increase pressure flow properties.

About Purolite® Life Sciences

Purolite® is a trusted supplier of resin to the world's most regulated industries with over 35 years' manufacturing and more than 25 years' regulatory experience. Through innovative R&D, Purolite® Life Sciences offers a range of bioprocess scale high flow agarose resins for the purification of monoclonal antibodies and recombinant proteins. With almost four decades of resin knowledge combined with our customer-focused approach and global manufacturing capacity, Purolite® Life Sciences is committed to:

- Enhancing the security of supply for agarose resins, enabling dual sourcing
- Regulatory and quality expertise
- Innovation – Jetted, uniform particle size agarose

100% focused
on resin technology.

One of the world's largest
agarose manufacturing facility.

De-risked long-term supply
through dual-sourcing.

25+ years of regulatory experience
from FDA inspected cGMP facility.

Over 35+ years of experience in solving advanced
R&D and purification challenges.

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Poland
Romania
Russia
Singapore
Slovak Republic
South Africa
Spain
Taiwan
Tunisia
Turkey
UK
Ukraine
USA
Uzbekistan

Purolite Life Sciences brings Purolite's innovative thinking and distinguished history of resin technology expertise to the global Life Sciences marketplace.

Over three decades, Purolite has grown into the world's premier resin technology manufacturer and innovation leader, with production plants and advanced research labs across the globe.

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