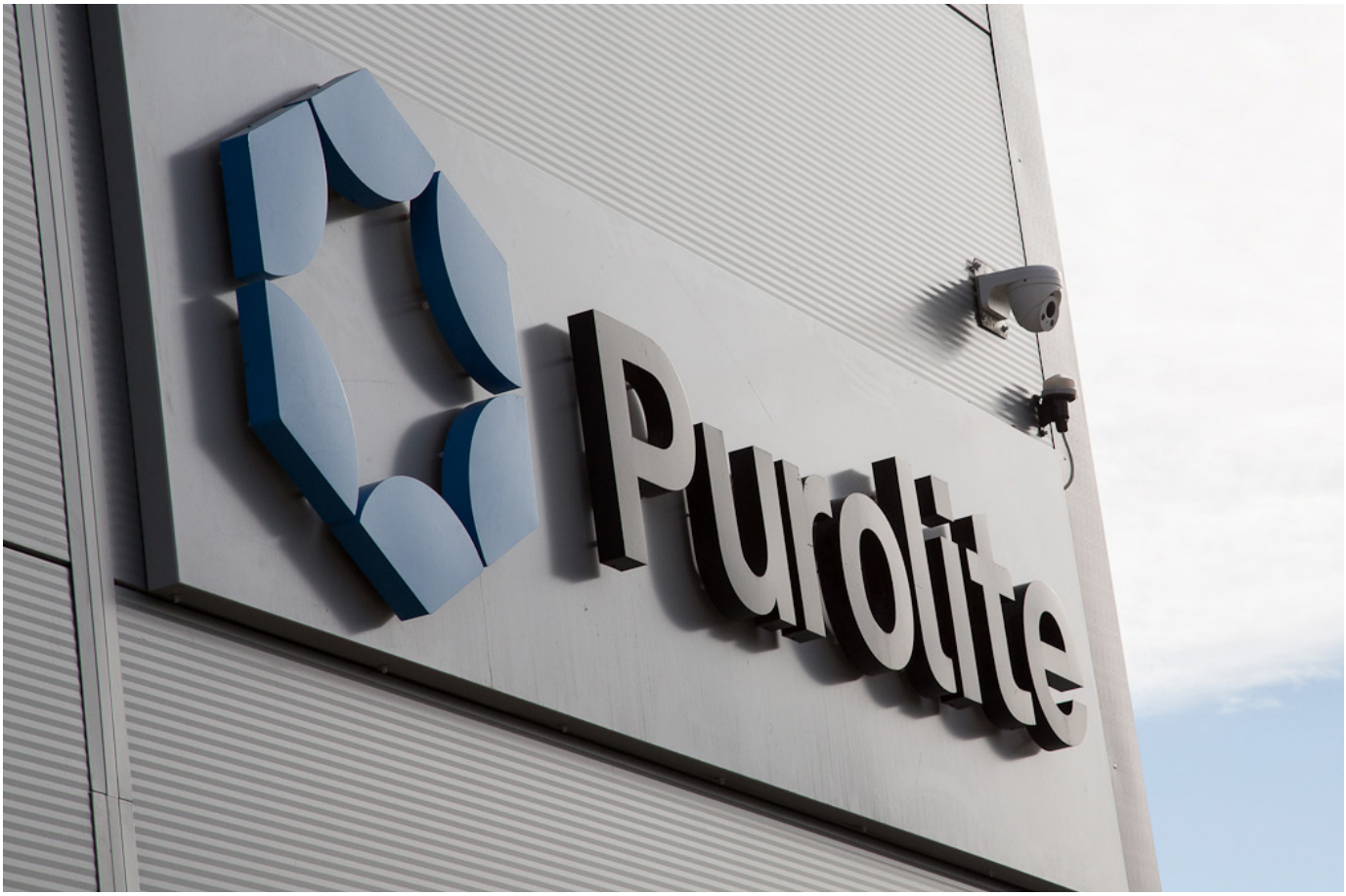
Praesto® Jetted (dT)18-DVB

Purolite®

Cross-linked styrene-divinylbenzene resin for purification of mRNA from *in-vitro* transcription



Why choose Purolite?

Since 1981, Purolite has grown into the world's premier resin-based separation, purification and extraction technology manufacturer and innovation leader, with manufacturing facilities, advanced research laboratories and over 1100 people employed world-wide.

Purolite focuses on any resin applications which involve end-user interactions with people, bringing innovative thinking and distinguished history of resin technology expertise to the global Life Sciences marketplace.

We provide APIs, enzyme carriers, immobilized enzymes and chromatographic resins of the highest quality, to support research and development and production-scale applications in global pharmaceutical, food and beverage, bioprocessing, cosmetics and fine chemical markets.

We bring innovative thinking and resin technology expertise to the global Life Sciences marketplace

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, and the highest product quality.

Security of supply

Ensuring reliable availability of our resins is vital to customers, and of paramount importance to Purolite. As a leading supplier of resin to the world's most regulated industries, we recognize that our resins are critical purification products.

As such, a real-world security of supply system is in place to support your process requirements for business continuity. Supply risk is managed end-to-end, with a global network of qualified suppliers. Long-term supply agreements with periodic audits ensure consistency and 'fit for purpose' performance. Purolite has manufacturing facilities at 4 strategic locations in the USA, Asia and Europe. Should Praesto production facilities in the UK be adversely affected to a level that would disrupt business operations, Purolite has designed manufacturing processes that facilitate rapid deployment at a different location. In this event, a rebuild plan would be implemented at our facility in Romania using an identical, modular design of the UK-based production facility.

Expanding manufacturing capabilities to meet global demand

Our state-of-the-art UK manufacturing facilities are capable of supplying one-third of global demand for all agarose-based bioprocessing resins. In addition to this, as of 2021 we have added a US-based facility to address the global demand for our pharmaceutical and life sciences products. This expansion will ensure security of supply with increased production and shorter product lead times. The new facility, located in King of Prussia near our global headquarters in Pennsylvania will feature two cleanrooms to manufacture active ingredients (APIs) and excipients and an agarose manufacturing facility equipped with our proprietary jetting technology for large-scale production of our Praesto agarose resins. We will also be offering enhanced warehousing options at our US site to allow for the secure storage of customer orders in an advantageous location.

This expansion will mean that Purolite is the only Protein A resin manufacturer to have two different manufacturing sites in two different continents.

Introduction

As a response to the COVID-19 pandemic caused by the SARS-CoV-2 virus, RNA vaccine technology has emerged to enable rapid development of critical vaccines. Traditional vaccine production methods hinder rapid development of vaccines due to requiring cell line production of viral proteins and time-consuming purification development. RNA vaccine technology utilizes lipid nanoparticle-encapsulated mRNA to deliver targeted genetic information to patient cells, allowing them to produce the viral protein, triggering an immune response.

Vaccine development typically commences with the synthesis of the mRNA (Figure 1). To start, mRNA production is facilitated by enzymatic in-vitro transcription (IVT), which uses a DNA template of the target, such as the CoV-2 spike protein. Following template linearization, the mRNA is synthesized from nucleotide triphosphates. Once transcription is complete, the starting template DNA is digested with enzymes while the produced mRNA is purified to take forward for formulation and filling.

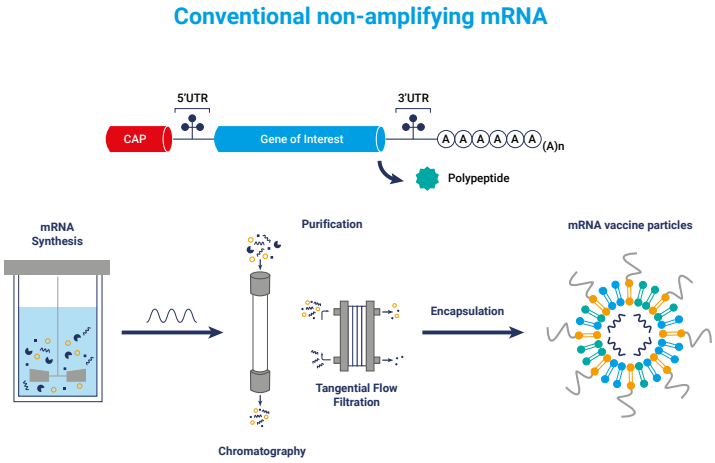


Figure 1. *Schematic representation of conventional non amplifying mRNA and the production of mRNA vaccine nanoparticles*

The generation of the mRNA is easier than attempting to produce and purify the spike protein itself in a laboratory for subsequent manufacturing at scale. However, mRNA synthesis and purification is not without its own challenges. As an emerging technology, a robust and compliant method of production has required rapid development and scale up.

Purolite has purpose designed the Praesto Jetted (dT)18-DVB affinity resin to address modern industry demand for a high performance, high productivity affinity resin for recovery of mRNA. By combining patented manufacturing technology with a rigid base matrix, one litre of Praesto Jetted (dt)18-DVB is capable of producing 12000 doses of mRNA vaccine from one purification cycle*.

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***Assumptions:**
- Based on available literature on dosing levels
- Column volume of 962 ml (7 x 25 cm column)
- Dose of 100 µg in 0.5 ml
- 60% yield from dT affinity step
- A further 20% reduction from subsequent purification steps, overall 40% yield

Praesto Jetted (dT)18-DVB

Praesto Jetted (dT)18-DVB Affinity Resin is the first generation of Purolite's Jetted divinylbenzene products specifically designed to purify mRNA from *in-vitro* transcription (IVT) manufacturing processes. The resin selectively purifies polyadenylated mRNA and offers flexibility in simple buffer systems and versatility in scaleup.

The 18-nucleotide length deoxythymidine ligand offers high selectivity and recovery of mRNA. Purolite's patented jetting technology gives a rigid bead with a uniform particle size distribution resulting in superior flow properties compared to batch emulsified alternatives.

- ✓ Bulk resins or pre-packed columns
- ✓ Our column packing experts can work with your scientists
- ✓ Validated, global supply

Typical Physical and Chemical Characteristics

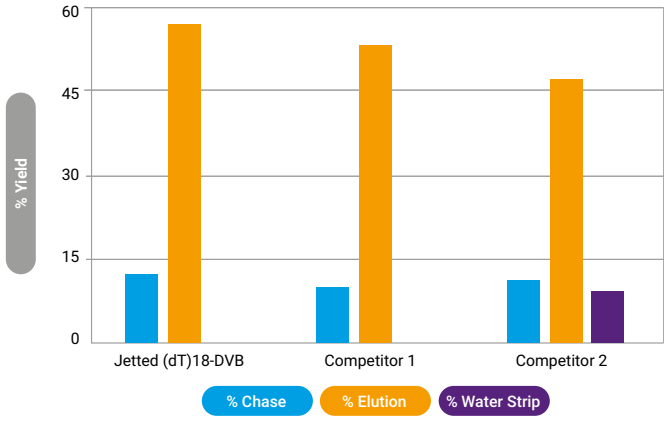
Polymer Structure	Jetted, crosslinked poly (styrene-divinylbenzene) beads
Functional Group	Poly (dT)18mer with proprietary linker
Particle Size (d50v) µm	50 µm
Dynamic Binding Capacity †	2 mg/ml PolyA
Binding Conditions	0.25M – 1M Salt, common buffers
Maximum Flow Capacity	Up to 400 cm/hr at 2 bar‡
Storage	20% Ethanol

† Determined at 10% breakthrough using 200 nt PolyA at 6 minutes residence time

‡ Data collected using AxiChrom 70, at 20 cm bed height, tested in 0.1M NaCl at 20°C

Process performance - customer evaluation

Praesto Jetted (dT)18-DVB was developed and tested through close collaborative efforts within the industry. The customer tested in laboratory-scale columns and quantified by a customer-specific assay. As demonstrated in Table 1, the customer evaluation resulted in yield and purity equivalent to current mRNA purification technologies.



Load Factor: 2.5 mg/mL of resin

Equilibration buffer = 0.25M NaCl, 10mM Tris, 20mM EDTA, pH7.2

Elution buffer = 10mM Tris, pH 7.2

Residence time = 10 minutes, 1 minute for Competitor 1

Figure 2: *Percentage yield of 4kb mRNA (with 100 nt PolyA tail) recovered from an in-vitro transcription process.*

	Fraction purity (%)		
Sample	Chase	Elution	Water Strip
Praesto Jetted (dT)18-DVB	24.2	80.9	N/A
Competitor 1	22.9	81.5	N/A
Competitor 2	25.4	79.2	89.6

Table 1: mRNA content in recovered fractions, as determined by HPLC

Pressure/flow characteristics

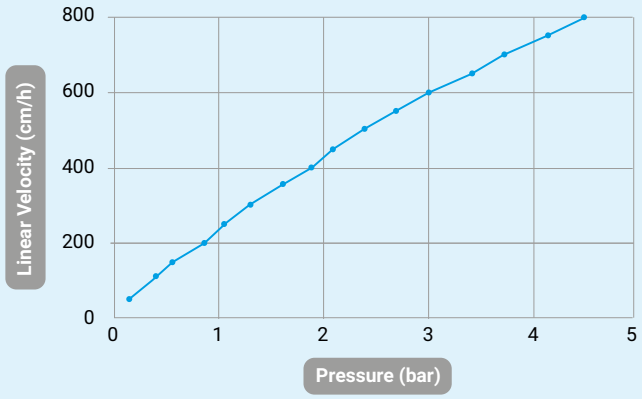


Figure 3: *Pressure/flow performance of Praesto (dT) 18-DVB packed into an AxiChrom70 at 20 cm bed height*

Excellent pressure flow properties

The rigid divinylbenzene base matrix provides excellent pressure flow properties of up to 400 cm/hr achievable with less than 2 bar pressure using 20 cm bed, 7 cm ID column, in 0.1M NaCl.

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Purolite, the leading manufacturer of quality ion exchange, catalyst, adsorbent and specialty high-performance resins, is the only company that focuses 100% of its resources on the development and production of resin technology.

We're ready to solve your process challenges. For further information on Purolite products and services, visit www.purolite.com or contact your nearest Technical Sales Office.

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