# Fast-Flow peptide synthesis for scale-up

Fast-Flow peptide synthesis combines the benefits of continuous flow with the robustness of Fmoc/tBu solid-phase peptide synthesis.

Benefits of Fast-Flow synthesis using the PS-30 pilot scale peptide synthesizer over batch systems:



- Short synthesis times even at 30 mmol scale with Oxyma/DIC
- Reduced solvent consumption compared to batch SPPS
- Scale-up from lab scale with no further optimisation achieving identical crude purity
- Highest quality crude peptides only achievable using single-pass
- Real time in-process data including precise timing of aggregation events
- Fully automated synthesis including side chain(s)
- Fast loading and unloading of reagents and resin

In 2017 Vapourtec developed the Variable Bed Flow Reactor (VBFR), the key technology enabling Fast-Flow peptide synthesis. This VBFR maintains the swollen resin at a consistent packing density, minimising its volume, thereby eliminating channelling of reagents and solvents and maximising washing efficiency.

Vapourtec has now strengthened its position in peptide drug discovery by developing a new state-of-the-art continuous flow peptide synthesiser for scale-up applications: the PS-30 pilot synthesizer.

The PS-30 pilot synthesizer can make peptides of any sequence in the scale of 2 mmol to 30 mmol.

A GLP-1 peptide will take 18 hours to synthesise even at 30 mmol scale. The PS-30 pilot synthesizer is fully automated including, a solvent swap, side chain deprotection, such as the removal of Mtt groups with HFIP followed by coupling of side chains.

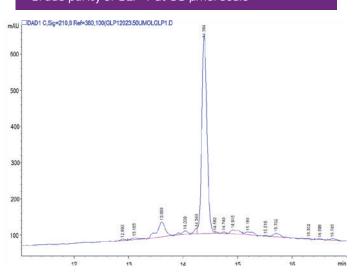
By utilising the R-Series platform and the PS-30 pilot synthesizer, users can synthesise peptides between  $50 \mu mol$  and 30 mmol yielding the same crude purity. Users can now optimise a process with just 200 mg of resin before running a 30 mmol synthesis, achieving similar purity.

Technical information per synthetic scale	50 µmol	2 mmol	30 mmol
AA usage	3 to 5 eq	3 to 5 eq	3 to 5 eq
Cycle time	10 min	17 min	28 min
Solvent usage for a GLP-1 synthesis	0.2 litres	5.2 litres	60 litres
Purity of a GLP-1 analogue	> 80 %	> 80 %	> 80 %
Compatible resins	PS, Tentagel, ChemMatrix		

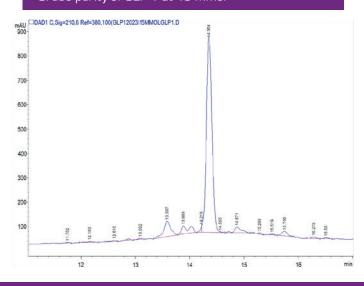




#### Crude purity of GLP-1 at 50 µmol scale



#### Crude purity of GLP-1 at 15 mmol



### Technical Specifications

Synthesis scale	2 mmol	30 mmol	
Resin loading	~ 9 g	~ 140 g	
Type of resin	Compatible with a wide variety of resins (i.e. PS, PEG, etc.)		
Cycle time per residue	~25 minutes		
Solvent usage per cycle	0.2 litres	2.0 litres	
GLP-1 synthesis time	~15 hours		
GLP-1 synthesis solvent usage	~5.2 litres	~60 litres	
Space required	2.8 m (w), 1.0 m (d), 1.6 m (h)		
Amino acid capacity	27 positions of 1 litre bottle		
DIC capacity	5 litres (1.6 M)		
DMF capacity	120 litres (3 x 40 litre refillable containers)		
Piperidine capacity	10 litres (neat)		
Formic acid capacity	1 litre (neat)		
Side chain addition	Automated solvent change and deprotection via HFIP		
DCM capacity	10 litres		
HFIP capacity	2 litres (solution)		
Minimum flowrate	10 ml/min		
Maximum flowrate	200 ml/min		
Maximum temperature	90 ℃		
Real time analysis	UV/Vis, automatic Fmoc AUC and resin volume change		
Waste management	Option to connect to centralised waste drain system		

Software features	
Sequence generator	Type ANY sequence of any length, up to 3 side chains
Coupling protocol	Five different tuneable coupling protocols
Deprotection protocol	Four different tuneable deprotection protocols
VBFR control	Adjustable packing density for different types of resins
Real time data	Flowrates, temperature, resin swelling and UV data
Real time analysis	Reactor volume and UV data are analysed after each cycle
Remote notifications	A SMTP protocol is built in the software to email users
User/Super User level	Two levels of access to safeguard protocols
Reagent monitoring	Reagent and solvent quantities are continuously monitored



## About Vapourtec

Vapourtec is the world's leading manufacturer of laboratory scale flow chemistry instruments. Founded in 2003, Vapourtec has been at the forefront of the flow chemistry industry ever since.

Headquartered near Cambridge, UK, Vapourtec design and manufacture the R-Series and E-Series flow chemistry systems together with an exciting range of innovative fast-flow peptide synthesisers. Vapourtec instruments have empowered chemists throughout the world to further scientific discovery.

Trusted by scientists, chemists, and fine chemical manufacturers around the world, the modular R-Series system has revolutionized the way many deliver the research, chemicals, and products we all rely on. With an installation base of more than 750 instruments, resulting in being cited in over 1,000 peer reviewed scientific publications, we continue to support our customers across the globe with the world-class products and services with which Vapourtec has become synonymous.









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