

# CHIMIA REPORT/COMPANY NEWS

Firmen stellen sich und ihre Produkte vor  
Companies present themselves and their products

Interested in a contribution? Please contact  
Swiss Chemical Society, info@scg.ch, +41 31 306 92 92

## PharmaBlock – Green, Intelligent, and Scalable Manufacturing of Peptides

PharmaBlock is a fully integrated CRDMO specializing in small molecules and emerging modalities, including peptides, oligonucleotides, and ADCs. It supports partners across discovery, development, and commercialization with rationally designed building blocks, intermediates, APIs, and DS/DP. Leveraging advanced technologies such as flow chemistry, micropacked bed hydrogenation, biocatalysis, and heterogeneous catalysis, PharmaBlock drives innovation in chemistry, improves efficiency and safety, and advances low-carbon manufacturing.

Peptides play a vital role in modern pharmaceutical development. Conventional solid-phase peptide synthesis (SPPS), while effective, generates high solvent consumption and waste, leading to significant environmental impact. In addition to its extensive catalog of natural and unnatural amino acids (UAAs), PharmaBlock has developed an integrated manufacturing platform to reduce Process Mass Intensity (PMI), improve scalability, and align peptide production with green chemistry principles.

### Liquid-Phase Peptide Synthesis (LPPS)

LPPS operates in a homogeneous solution without solid support, reducing solvent use and improving scalability. It enables easier purification and characterization of intermediates and is well suited for short, cyclic, and fragment-based peptide synthesis. As the primary platform for fragment condensation, LPPS allows efficient incorporation of UAAs and complex modifications with high purity. Well-characterized fragments are then assembled into full-length peptides, enhancing overall yield and product quality. Parallel fragment synthesis further shortens production time compared with conventional linear SPPS.

### Continuous Flow Liquid-Phase Peptide Synthesis (CF-LPPS)

CF-LPPS integrates the scalability and flexibility of LPPS with the precision and enhanced mass transfer of microreactors, improving efficiency, safety, and process control while reducing waste and environmental impact. It enables rapid high-throughput screening and seamless scale-up through parallel microreactors, ensuring consistent quality from laboratory to commercial production. With real-time monitoring and full automation, CF-LPPS delivers precise reagent control, reproducible synthesis, and integrated continuous workflows. Combined with AI-driven data analysis and digital modeling, it enables dynamic optimization, robust scalability, and intelligent, sustainable peptide manufacturing.

### Enzyme-Assisted Peptide Synthesis (EAPS)

Compared to fully SPPS, conventional hybrid processes can significantly reduce PMI in long-chain peptide production and improve quality control, but they mainly rely on chemical ligation methods. These require an additional cleavage and purification step, creating inefficiencies and limiting green chemistry progress.

EAPS offers a promising alternative. PharmaBlock has developed a peptide ligase library that enables precise assembly of unprotected peptides in water. Products can be recovered via centrifugation and filtration without secondary cleavage, greatly reducing PMI. Future immobilized enzyme systems could enable continuous production, representing a major improvement in sustainability, purification efficiency, and large-scale peptide manufacturing.

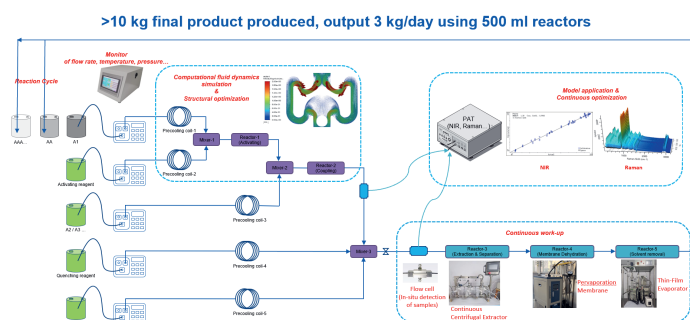
## Downstream Processing and Purification

Traditional peptide purification relies mainly on reversed-phase chromatography, which consumes large amounts of acetonitrile and generates disproportionately high waste relative to product yield. Advanced approaches such as multi-column counter-current solvent gradient purification (MCSGP) substantially improve sustainability by reducing PMI by ~70%, while also increasing yield by 20–30% and enhancing production efficiency by 20–25 fold.

In downstream post-treatment, replacing conventional column chromatography for concentration and salt exchange, which also relies heavily on organic solvent usage, with membrane-based technologies and electrochemical desalting systems further enables greener and more efficient processing.

## Case Study: Cyclic Peptide Manufacturing

The initial SPPS-based synthesis relied heavily on DMF and large-scale reversed-phase chromatography purification (up to ~500 g batches), making it economically and environmentally unsustainable for large scale. To address this, an LPPS route was developed, reducing DMF use by over 20-fold and replacing chromatography with crystallization of intermediates. Building on this, a CF-LPPS process was introduced, integrating continuous reactions, work-up, membrane separation, and process analytical technology (PAT). This enabled fully continuous linear peptide synthesis, followed by cyclization using micro-channel and a continuous stirred-tank reactor (CSTR). Overall, the evolution from SPPS to LPPS to CF-LPPS reduced DMF usage to less than 1/100 of the original process and eliminated chromatographic purification and lyophilization, significantly improving sustainability and process efficiency for cyclic peptide production.



## Conclusion

PharmaBlock has established an integrated manufacturing platform that combines SPPS, LPPS, CF-LPPS, and EAPS to lower PMI, enhance scalability, and align peptide production with green chemistry principles. This approach demonstrates how sustainability principles can be embedded into pharmaceutical manufacturing systems to minimize environmental impact while ensuring high product quality and scalable production.

## Contact

**PharmaBlock**

PharmaBlock Sciences (Switzerland), AG  
www.pharmablock.com  
saleseurope@pharmablock.com  
+41 44 725 11 00