

## Peptide Synthesis for the 21st Century



**GAPPeptides™**

### GAP Peptide Synthesis

#### *The Call for Green Chemistry*

While significant advances have been made in synthetic peptide manufacturing, the industry still is facing challenges that call for pushing the development envelope. Ever evolving applications, growing consumer needs and pricing pressures intensify the demand for competitive advantages that enable domestic manufacturers to compete with offshore providers for market share at home.

Attaining these advantages and winning new business requires, in part, innovation in production technology. For peptide synthesis, goals may include increasing efficiency of raw material inputs, optimizing asset utilization, avoiding hazardous reagents and reactions, using inexpensive, available raw materials and increasing throughput to produce more product in less time and in smaller reaction vessels. And, manufacturers must do this with an eye on achieving and or exceeding quality and regulatory standards.

The call for innovation in synthetic peptide production demands reliable and robust advanced technologies that embrace the principles for synthetic efficiency and of green chemistry, both of which have a positive impact on regulatory compliance, price pressure and the environment. In this 2nd article of our series, GAP Peptides shares more brief insights from recent research on an efficient, cost-effective innovative approach to peptide synthesis.

### Greener Solvent, Less Waste

GAP-PS (Group Assisted Purification Peptide Synthesis) delivers benefits that can significantly improve the environmental impact of peptide manufacturing. Solvent choice is critical for environmental impact; it is the bulk of the mass to be handled and disposed. GAP-PS utilizes 2-MeTHF, CMPE, and water for synthesis solvents instead of DMF and Ethyl Ether. Benefits of using 2-MeTHF include its syn-

thesis from renewable sources. This benefit, among others, has been recognized by recent peptide industry guidance that lists 2-MeTHF and CPME as green, alternative solvents for peptide synthesis.



*Dr. Cole Seifert, Chief Scientific Officer, co-founded GAP Peptides LLC with fellow inventor, Dr. Guigen Li, from their laboratory research at Texas Tech University. The highly efficient and scalable GAP-PS process achieves solubility control over the growing peptide by the attachment of an intelligently designed small-molecule GAP protecting group to a substrate of interest.*

During workup, GAP-PS uses a solution-phase liquid extraction process to wash the 2-MeTHF/peptide layer with aqueous solution that removes byproducts and impurities. GAP-PS replaces DMF with water as the solvent for byproduct removal, thus eliminating environmentally harmful solvent and drastically reducing overall solvent use. In a comparative case study with SPPS, GAP-PS reduced estimated solvent consumption during synthesis by > 80%. GAP-PS also reduced total combined raw material and solvent consumption by > 50%. In short, GAP-PS offers a manufacturing option that is environmentally sensitive and requires less raw material and solvent.

## Increasing Efficiency, Increasing Value

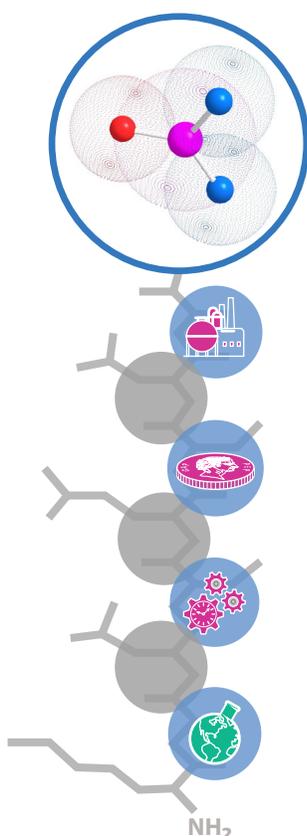
The measurable advantages found in GAP-PS are evidence that the solution-phase process provides greater efficiency in several areas when compared to SPPS. The novel process runs in homogenous solution rather than a resin suspension, which results in increased reactivity and efficiency, and less energy and wastes. Increases in output and throughput of the peptide synthesis process provides more product from a smaller working footprint than legacy methods. In addition to the solvent savings, the GAP-PS anchor molecule has a high loading > 3 mmol / g. Depending on the SPPS resin used for comparison, this allows GAP-PS to have a smaller footprint than SPPS washing and filtration steps. The increase in reactor utilization, combined with rapid phase separation, serves to increase pro-

duction throughput and reduce cost and environmental overhead. These are just a few examples of the drivers leading to the synthetic efficiency of GAP-PS.

## Answering the Call

Recently, several U.S. drug manufacturers announced expanded capacity in response to the pandemic crisis. But most of the capacity and best pricing is found offshore. Nevertheless, CMOs, CDMOs and Big Pharma continue to seek flexible, break-through technologies that enable more efficient, cost-effective and greener synthesis approaches for competitive manufacturing options. GAP Peptide Synthesis offers a platform approach to achieve scalable production of high-quality synthetic peptides at the lowest cost, and the least amount of waste in a low hazard environment.

## GAP Peptide Synthesis: 4 Advantages Over Solid-Phase Synthesis



### **GAP Anchor Molecule**

*Enables liquid phase synthesis and Group Assisted Purification*

### **Scalable**

Homogenous GAP-PS chemistry does not require specialized reactors or equipment.

### **Economical**

GAP-PS reduces material costs by 50%, while improving peptide yield over SPPS.

### **Efficient**

GAP-PS increases reaction efficiency and delivers high crude purity.

### **Green**

GAP-PS uses green chemistry, reduces solvent waste by 80%, and enables recycling.

To learn more about GAP Peptides' research and collaborative approach to licensing GAPPS technology, visit our website at [www.GAPPeptides.com](http://www.GAPPeptides.com) or email Dr. Cole Seifert at [cseifert@gappeptides.com](mailto:cseifert@gappeptides.com)