



These days, many companies facing increasing pressure to reduce costs, risk and time-to-market, and maximise efficiencies, have converged on a similar strategy — to outsource non-core functions. This is why companies as small as start-up biotechs and as large as the pharmaceutical and biopharmaceutical majors outsource peptide production needs ever more increasingly. Whether these companies need research-grade materials or GMP-grade materials, they are realising cost-effectiveness and efficiency by outsourcing peptide production.

# Outsourcing

## PEPTIDE MANUFACTURING



**CAPTIONS FROM LEFT TO RIGHT:** SOPs at American Peptide Company's GMP manufacturing facility in Vista, California, US, are strictly followed and meticulously documented during the manufacturing process by the trained staff of highly qualified specialists. The facility is designed to accommodate large-scale manufacturing of pharmaceutical drug substances for clinical research. | Two technicians at work in the company's Vista, California, US, facility. | A technician monitors peptide solid-phase synthesis, an American Peptide Company specialty. | Shawn Shirzadi. | All peptides manufactured in the US must meet Federal Government's 'Guidance for Industry for the Submission of Chemistry Manufacturing, and Controls Information for Synthetic Peptide Substances'. The guidelines stipulate that lot-release specification (a set of tests and acceptance criteria that must be met before product is released) must be sufficient to ensure the identity, purity, strength and/or potency of the peptide and demonstrate lot-to-lot consistency.

### Why Outsource?

Outsourcing makes sense, allowing companies to benefit from a service-provider's experience and avoid making costly investments in equipment and training. Peptide manufacturing can be complicated, as tiny variations in processes, reagents and reaction conditions can produce large changes in the end-product's quality, stability and consistency, compromising the ability to meet regulatory standards. Maintaining consistent production protocol requires a level of skill and equipment that in-house manufacturers may lack.

Peptide manufacturing requires extremely specialised equipment and components and a highly skilled and knowledgeable personnel. Firms lacking in-house expertise and equipment or firms with limited capacity should consider outsourcing peptide manufacturing needs to a contract manufacturing organisation (CMO).

Specialised CMOs often offer a range of services from process development all the way through commercial scale-up and can be valuable partners in helping to speed a product to market.

### Reduce Costs and Risk

The initial high cost of procuring start-up equipment makes outsourcing an attractive alternative to in-house production. It eliminates the need to make expensive investments in equipment, which shifts what would otherwise be fixed costs to variable costs and reduces investor risk. This holds true particularly for companies with early-stage projects that face a dubious outcome.

In further evidence of the cost-effectiveness associated with outsourcing, CMOs purchase materials and consumables in bulk, so customers benefit from economies of scale.

Additionally, outsourcing saves companies time and money they would otherwise spend tracking down needed materials, then authenticating, analysing and validating them. These latter functions have become particularly burdensome since the requirement for supplier audits and regulatory documentation has increased with more scrutiny of the

supply-chain. Companies can improve the security of existing supply chains by turning to CMOs, which often have existing relationships with reliable and qualified suppliers.

### Expertise

Peptide production is complex and therefore CMOs that specialise in their manufacturing must have personnel experienced in all approaches — including solid-phase and solution-phase peptide synthesis, purification and lyophilisation — so they can choose the most cost-effective, efficient and reliable methodology for the customer's specific product. In addition, the experienced CMO personnel can offer custom modifications such as organic conjugations and peptide PEGylation, if the customer desires.

CMOs' expertise translates into higher efficiency and lower production times. It also allows companies to focus on their own core competencies, bringing innovative drugs to market faster.

### Regulatory Support

Regulatory demands are increasing for pharmaceutical manufacturers. As experts in peptide manufacturing, CMOs have staff specifically dedicated to keeping up-to-date on regulatory changes that pertain to peptide manufacturing, both domestically and internationally. Dedicated personnel ensure that manufacturing facilities remain compliant with current GMPs. CMOs also often maintain relationships with regulators and can better guide customers through the complex and often-changing regulatory landscape.

### Project Management

Because CMOs focus solely on peptide manufacturing, they assign project managers who can support customers from product development through the final implementation of full commercial production.

Project managers are the liaisons between the CMO and the customer. They work with CMOs' internal teams to provide

guidance and support to customers on a full range of services, including: process development; scale-up production; analytical and process validation; stability studies; Chemistry Manufacturing, and Controls (CMC); Drug Master Files (DMF); and regulatory support.

### How to Choose a CMO

While there are several benefits to the outsourcing of peptide production, these benefits are contingent upon finding the right outsourcing partner. Companies are at risk in handing off important manufacturing projects, since they are largely at the mercy of an outside contractor. Therefore, it is necessary for companies to perform in-depth research to reassure themselves of the suitability and reliability of a CMO partner before committing to a business agreement.

### Quality of Equipment, Facility and Production Capabilities

In partnering with a CMO, companies should ensure that the vendor has the appropriate manufacturing and analytical equipment for their projects and that the equipment is well-maintained.

The chosen CMO must have adequate capacity to handle the project and have enough capacity for downstream projections. The customer must ensure that the production process in use at the CMO's manufacturing facility will produce high-quality products with good yields. Inadequacies in the facility will create inevitable delays and may compromise a product's integrity. CMOs should be able to provide a customer with good analytical methods for the product. Each product should come with a Certificate of Analysis (COA) with required QC results.

### Quality Procedures

Companies must also consider a CMO's quality system. This includes process analytical technologies that monitor the disposition of materials as they move through the manufacturing process and systems that implement corrective actions and preventive actions (CAPAs). Companies should

also inquire about CMO's validation procedures and protocols, as well as the mechanism for recording changes in standard operating procedures (SOPs) and systems to capture and analyse data. They must know how the CMO chooses, audits and validates its suppliers and must inquire about the CMO's contingency plans for alternate suppliers in the event that a primary supplier faces shortages or has difficulty providing ingredients and/or consumables.

### Check for Regulatory History

Another critical point for consideration is whether or not a particular CMO contracts peptide synthesis, as the FDA will ultimately hold the company that is outsourcing the job responsible for regulatory compliance. Therefore, a CMO's ability to comply with FDA regulations is crucial for the company to operate within the market. CMOs that fail to comply with FDA and other regulatory mandates risk compromising their reputations and those of their customer companies. Therefore, it is imperative to be mindful of the CMO's regulatory history.

Much of this information is in the public domain. For example, a company would need to know whether the CMO being considered has received any FDA-483 Observation and Warning Letter citations in the recent past. Letters are issued by the FDA if it comes to light that inadequacies exist in the quality of equipment, supplies or procedures. Citations may also be issued if a CMO is not following approved procedures or is not sufficiently documenting its activity enough for the FDA to make a determination about its levels of compliance. Companies must make sure that the potential CMOs are conforming to USP, ICH and other domestic and international regulatory standards.

### Financial Stability/Resources

Potential customers must investigate the fiscal background of any potential outsourcing partner. A fiscally imperiled CMO may be slow in paying suppliers or may be understaffed, creating unnecessary delays in production. A financially

insecure CMO may be tempted to cut corners on quality and services, which potentially compromise the quality of the company's products. In that same vein, companies must also take time to investigate that the CMO's suppliers are capable of meeting financial obligations.

### Communication

The key to a successful relationship between the customer company and CMO is prompt communication. The CMO must be readily available to apprise the company of progress on single or multiple orders. It is imperative for companies to demand, as part of the outsourcing agreement, to establish a clear line of communication. It should be made known who at the CMO will act as the primary contact responsible for providing regular updates on developments and to quickly respond to any potential questions.

There is no room for obscurity in the drafting of the supply agreement. The language of the contract should deal explicitly with issues of intellectual property in order for both parties to understand the proprietary information and recognise ownership of any intellectual property that may be jointly developed.

### Transparency

Companies and CMOs should be prepared that not all production and orders will proceed smoothly. It is crucial to recognise this and have safeguards in place for the company to know that the CMO will proactively inform it of delays or other difficulties.

### Service

All things being equal, companies should contract with CMOs that provide the best service. This relationship between customer and CMO is truly a partnership and the company should feel that its service provider is as concerned and attentive to its project as it itself would be. To ensure a productive relationship, customer service is paramount to making that partnership work.

### Ask for References

Some aspects of the CMO's performance can be ascertained by the company through validation logs, site inspections, audits and searching the public record. However, some aspects of the relationship may be more difficult to ascertain and can be assessed only by talking to the CMO's customers.

Potential customer companies should ask to speak to a potential outsourcing partner's current and previous clients to determine intangibles like customer service, communication and transparency.

Companies stand to realise significant cost and time savings by outsourcing peptide production to experts who can deliver a high-quality product. Potential customers that choose their partners carefully and wisely are in the best position to realise these benefits, so it is crucial that companies make certain their potential manufacturing partner has a history of compliant quality production and attentive customer service.

**BIOGRAPHY** Shawn Shirzadi has been with American Peptide Company since 2002 and currently holds the position of VP of Quality. In this role, he is responsible for operation of the quality control and quality assurance group at the company's Vista, California, US, GMP peptide-manufacturing facility. Prior to this, he was Director of Quality Assurance at the company, with responsibility for establishing quality assurance systems and policies. Shawn is knowledgeable in GMP, GLPs, GCPs and FDA regulations, and control for pharmaceuticals, vaccines and clinical diagnostic products. He holds a BS in Industrial Microbiology from the University of Long Beach (California, US) and an MS in Industrial Microbiology also from the University of Long Beach. Shawn is a member of the American Society of Microbiology (ASM), the International Society for Pharmaceutical Engineering (ISPE) and the American Society of Quality Engineers (ASQE).

**American Peptide Company**  
+1 408 733 7604  
sales@americanpeptide.com  
www.americanpeptide.com