BOLSTERING CAPABILITIES FOR PARENTERAL DRUG DEVELOPMENT AND MANUFACTURING

→ **BY SYED T. HUSAIN** Chief Commercial Officer
AAIPharma Services–Cambridge Major Laboratories

Syed Husain serves as the commercial leader for AAIPharma Services–Cambridge Major Laboratories, leveraging in-depth experience in sales, business development, marketing, and operations for the custom development and manufacturing of small molecules, antibody drug conjugates (ADCs), peptides, biologics (mammalian- & microbial- based drug substances), and drug products. Previously Mr. Husain served as Head of Business Team at Lonza responsible for the API manufacturing business. From 2005 to 2013, he served in increasing Sales & Business Development roles of responsibility for APIs (chemical and biologic) and as Head of Sales & Business Development for the API manufacturing Business Unit. Syed earned a BS in chemical engineering from New Jersey Institute of Technology in 2003 and an MBA from Cornell University in 2009.

ABSTRACT

As the pharmaceutical and biotechnology markets undergo significant changes, companies are relying more heavily on CROs and CMOs to provide the needed services, expertise, and technologies to help them favorably compete in a challenging marketplace. Contract service providers, in turn, are strengthening their capabilities to satisfy current demands, in some cases by coming together. An example is the recent combining of AAIPharma and Cambridge Major Laboratories, forming a full-service global CDMO supplying drug substance and drug product development, manufacturing, testing, and packaging services. This coupling also supports drug sponsors facing the escalating challenges of developing and manufacturing parenteral drug products.

Contract development and manufacturing organizations (CDMOs) have been vigorously bolstering their capabilities to support the changing needs of pharmaceutical and biotechnology companies as the industry continues its transformation over the last few years. Pressures to reduce time and costs, expand product pipelines faster, and meet more stringent regulatory requirements are key drivers of the change. They are also triggering the continued growth of outsourcing, which is increasingly considered a strategic imperative. The greater demand for outsourced services is attributed in large part to the increase in outsourcing biopharmaceutical drugs, by both pharmaceutical and biopharmaceutical companies.

This article discusses industry trends and issues in the development and manufacturing of parenteral drugs and why more drug sponsors are relying on outsourcing partners to design and implement these increasingly complex programs.

TRENDS AND ISSUES IMPACTING PARENTERAL DEVELOPMENT AND MANUFACTURING

According to a 2015 Nice Insight survey of 2,300 pharmaceutical and biotechnology executives, the percentage of survey participants whose companies spend more than $50 million annually on outsourcing has remained fairly stable over the last three years. However, the percentage of companies that spend $10 million to $50 million on outsourcing has increased dramatically, from 38 percent to 62 percent, and the percentage of companies spending less than $10 million has decreased by slightly more than half.[1]

According to Frost & Sullivan, sterile parenteral contract services make up about 82.8% of the total sterile CMO market. This includes small-volume parenterals (vials, ampoules, and syringes), which make up the majority of sterile CDMO services with 88.9% of market share, and large-volume parenterals (bags and bottles). The sterile parenteral manufacturing subsegment is expected to reach a market size of $6.5 billion by the end of 2016.[2]

As the industry continues to outsource more of its development and manufacturing to contract research organizations (CROs) and CMO/CDMOs, pharma and biopharma companies are undergoing a wave of mergers and collaborations to build their internal strength. Just like their pharma and biotech partners, industry contractors, too, are forming alliances to strengthen their resources in response to new industry demands.

As an example of the trend of contract companies coming together, in 2014 Cambridge Major Laboratories, a full-service global CDMO providing active pharmaceutical ingredient (API) development and manufacturing, combined with AAIPharma, a global provider of pharmaceutical analytical testing, drug product development, and drug product manufacturing and packaging services, to become a major global supplier of integrated chemistry, manufacturing, and controls (CMC) services with centers of excellence in solid-state chemistry and formulation development services. The combination of these two highly respected, market-leading firms with proven expertise in API development, analytical chemistry, and finished dosage forms significantly boosted their ability to support market demand with expanded expertise and infrastructure. Recently, Atossa Genetics, the breast health company, signed manufacturing and quality agreements with the new organization, AAIPharma Services–Cambridge Major Laboratories, for the clinical supply manufacturing of an API in Atossa's leading drug candidate for breast hyperplasia.

One area where this alliance has brought considerable combined scientific and technical expertise is the development of clinical and commercial finished dose manufacture of parenteral drug products. Over the last four years, AAIPharma and Cambridge Major Laboratories have produced a significant amount of parenteral fills in its sterile manufacturing facility for small- and large-molecule parenteral products for liquids, lyophilized products, suspensions, emulsions, and terminally sterilized vials. The operational setup via the combined company allows for the seamless integration of services covering development, testing, and manufacturing from API to finished packaging through a single, dependable, flexible, and high quality vendor.

PARENTERAL MANUFACTURING REQUIREMENTS

PARENTERAL DRUG DELIVERY: MEETING ESCALATING CHALLENGES

Parenteral drug delivery is the second largest segment of the pharmaceutical market following solid oral dose delivery, and accounts for nearly 30 percent of the market share. Valued at $27 billion, the parenteral delivery market is expected to reach $51 billion by 2015.[2] Outsourcing parenterals is anticipated to increase and continue to benefit established companies in this market.[3]

Considerable challenges are prevalent in the market, including quality concerns, stringent regulations, and lack of funding. Aseptic processing of parenterals involves challenges such as protecting the sterility of a product as it moves through each phase of formulation, filtering, filling, and packaging. Companies specializing in the aseptic processing of parenterals must use advanced controls and optimal processes and packaging materials to ensure patient safety.

→ **COMPANY PROFILE**

About AAIPharma Services–Cambridge Major Laboratories

AAIPharma Services–Cambridge Major Laboratories (AAI-CML) is a world-class, full-service supplier of pharmaceutical product development, manufacturing, and packaging services. Our capabilities include API development and manufacturing, solid-state chemistry, formulation development, analytical development and testing services, clinical and commercial finished dosage form manufacturing (solid dose and parenteral), packaging, and stability services. We serve as a reliable, trusted partner, working to achieve our clients' goals by providing comprehensive services, from early phase studies to full-scale commercial production of APIs and finished dosage forms.

+ Market-leading CDMO with proven expertise in API development, analytical chemistry, finished dosage forms
+ Integrated CMC services with centers of excellence in solid-state chemistry and formulation development services
+ Support for all phases of pharmaceutical development, from critical preformulation studies to commercial production and product lifecycle management
+ Supported more than 500 IND filings and 50 NDAs and New Animal Drug Applications (NADAs) over the past 30 years
+ Formulation development, including early phase programs and generic drug development for human and veterinary applications
+ Biopharmaceutical analytical method development, method validation, and testing solutions with full complement of advanced analytical technologies, stand-alone or comprehensive support
+ Conduct more than 200 stability studies a year, with full ICH and custom storage conditions

Parenteral drug delivery is the second largest segment of the pharmaceutical market following solid oral dose delivery, and accounts for nearly 30 percent of the market share.

Many pharmaceutical companies do not have the resources necessary to manage the increasing complexity of producing and filling parenteral substances. To achieve optimal results, the development and manufacturing processes for parenterals require the high level of expertise and experience, as well as the specially designed infrastructure and sophisticated instruments and technologies, of a contractor that specializes in this area.[2]

Stringent regulatory requirements must be followed, including maintaining compliance with US and international regulatory requirements, including current good manufacturing practices (cGMP) to protect product safety, identification, strength, purity, and quality (SISPQ).

The parenteral drug pipeline has continued to shift from small molecules to complex biologics such as monoclonal antibodies (mAbs) and antibody drug conjugates (ADCs). A significant percentage of new items in the product pipeline are biologics. The expansion of biological therapies provides additional challenges for parenteral drug delivery specialists seeking to develop ways of improving standard injections and patient safety of these products. Biologics and biotech drugs are typically not stable in solutions, which can require cold chain and storage hurdles. Lyophilization can be an important process in maximizing the stability of a product. CMOs capable of developing and testing lyophilization cycles on a lab scale can prove to be cost-effective. Development and manufacturing processes around aseptic compounding equipment utilization have also become increasingly complex and resource-intensive with specific environmental monitoring and controls.

PARENTERAL MARKET

$27B
CURRENT VALUE

$51B
2015 EXPECTED VALUE

OUTSOURCING EXPERTISE NEEDED

The rapid expansion of biopharmaceutical products has resulted in a growing trend toward contract manufacturing of parenteral drug products. Outsourcing manufacturing affords biopharmaceutical drug sponsors a cost-effective, efficient way to gain the needed technical expertise, operational efficiency, and regulatory support needed to produce these products.

Sponsor expectations from a CDMO include broader analytical test methods for release, and stability of the increasingly complex drug products. The demand for analytic single-use systems has increased due to the need for multiple test methods to assess drug purity and stability.

The fill-finish process of aseptically prepared drug products requires sophisticated equipment in a highly controlled cGMP environment. These elements are vital to ensure product quality and patient safety. Single-use fill-finish assemblies must meet stringent requirements to ensure flow-path sterility and integrity as well as operational safety, and provide fill-volume accuracy. These solutions can also improve operational flexibility, and reduce capital investment in facilities and equipment.

Accuracy on the filling line is a significant technical challenge. Parenteral drug sponsors expect advanced filling lines that improve quality and save costs, such as fully automatic equipment to optimize yield. They are also interested in the ability to rapidly identify and characterize particles. In addition, there is a high demand for flexible equipment and processes, such as stainless steel and disposable systems, options in pumping and filtration systems, and the ability to handle new materials and injectable systems. These capabilities need to be paired with processes and equipment to contain drugs where limited toxicity data exists or potency/toxicity is high.

Continuous investment in advanced technology and staff training, as well as constant monitoring of the market and industry environment and keeping up with new regulations pertaining to parenterals, helps meet these challenges.

LOOKING FORWARD

Looking ahead, pharmaceutical and biotech companies will likely continue the trend toward outsourcing parenteral development and manufacturing. At the same time, complexity of active ingredients and production processes will grow. These industry changes will require strategic partnerships with highly competent, experienced CDMOs that have expertise and experience in this field and can respond to current and future challenges through flexible and creative supply chain solutions for their customers. P

REFERENCES

1. Walker N. Outsourcing Increasing to CROs and CMOs Known for Quality and Cost-Effectiveness. Life Science Leader. July 2015. Accessed at: http://www.niceinsight.com/articles.aspx?post=2492

2. Prefilled Syringes & Parenteral Contract Manufacturing: Improving for Flexibility & Customization. Drug Development & Delivery. May 2013. Accessed at: http://www.drug-dev.com/Main/Back-Issues/SPECIAL-REPORT-Prefilled-Syringes-Parenteral-Contr-565.aspx

3. Advanced Oral and Parenteral Drug Delivery Technologies. May 20, 2013. Accessed at: http://www.espicom.com/advanced-oral-parenteral-drug-delivery-technologies.html