STRENGTHENING CDMOS TO MEET INDUSTRY NEEDS FOR 2016 AND BEYOND

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Outsourcing companies pursuing an integrated services model aim to facilitate drug development and commercialization for drug sponsors by enabling them to work with a single partner for activities that often require multiple, specialized vendors.

With a single qualified partner, pharma companies can have simplified access to integrated analytical, development, manufacturing and packaging services, as well as a broad range of dose form manufacturing and similar services. Some contract development and manufacturing organizations (CDMOs) offer both API and drug product manufacture, while others offer formulation development and clinical supply manufacture to complement their commercial production operations. Regardless, the aim is to provide a seamless supply chain solution.

Along with integrated service offerings, CDMOs are increasingly motivated to offer an expanded array of enhanced drug-delivery technologies, giving their customers broader options for patient care. Delivery technologies can include various targeted and timed release/dissolution and formulation technologies.

This article discusses these industry trends and issues, focusing on the outsourcing model of consolidated companies offering development and manufacturing services, a broad range of delivery technologies, and why more drug sponsors are relying on full-service outsourcing partners to design and implement their programs. Included is an example of these trends: the consolidation of AAIPharma Services and Cambridge Major Laboratories, to form a full-service, global CDMO that supplies drug substance and drug product development, manufacturing, testing and packaging services.

CHANGE IS A CONSTANT

Looking at the state of the pharmaceutical-biotechnology industry in 2016, here are a few key trends:

+ The industry is facing issues such as continued demand to lower costs, improve productivity, build pipelines faster, streamline infrastructure, meet ever-more-rigorous regulatory requirements and shorten time to market.
+ Companies are increasingly relying on contract outsourcing partners to provide the services, expertise, infrastructure and technologies they need to compete successfully and get the necessary medicines to patients.
+ Just like their pharma and biotech partners, contract service providers are consolidating, forming alliances to strengthen their capabilities to satisfy current industry demands.
+ The global outsourcing industry has seen a rise in strategic alliances, acquisitions and joint ventures among contractors, intended to extend service offerings and meet demand.

According to Nice Insight's CDMO Outsourcing survey of over 500 outsourcing-facing pharmaceutical and biotechnology executives (2016), the percentage of respondents whose companies spend more than $50 million on outsourcing has remained fairly stable over the last three years (24% to 23%) 2013-2015.[1] The 2016 survey shows that 43% spend $51-100M annually on outsourcing. The percentage of respondents whose companies spend $10 million to $50 million on outsourcing decreased from 62% to 23%, and the percentage of participants whose companies spend less than $10 million also decreased (16% to 3%).[2]

In 2014 for example, Cambridge Major Laboratories, a full-service CDMO, combined with AAIPharma Services, to become a major global supplier of integrated chemistry, manufacturing and controls (CMC) services. With the merger complete, the whole has become greater than the sum of its parts. The combination offers proven expertise in API development, analytical chemistry, and finished dosage forms while significantly elevating their ability to support the market with expanded expertise and compliant infrastructure.

SOLID DOSE TECHNOLOGIES

Oral solid dose forms continue to play a major role in the contract manufacturing industry and this market is set for a new period of gradual expansion. Fixed-dose combinations, controlled-release dosage forms and other lifecycle management strategies will continue to have significance.[3]

Recently, AAIPharma Services–Cambridge Major Laboratories (AAI-CML) added additional capabilities and capacity for oral solid dose manufacturing, sterile manufacturing and packaging, as well as expanded development services. This expansion also included additional laboratory and headquarters space to support the increased demand for small and large molecule clinical and commercial products.

The new facilities and equipment complement the CDMO's dosage-form capabilities, which include minitabs, pediatric sprinkles, chewable products, sublingual tablets, orally disintegrating tablets, extrusion granules, and extrusion spheronization. Extrusion spheronization makes spheroids uniform with dense granules for controlled-release oral solid dosage forms with a minimum amount of excipients. AAI-CML also has the capability to manufacture highly potent API drugs, controlled substances and tough-to-manufacture moisture/oxygen-sensitive drugs.

PARENTERAL DRUG DELIVERY: MEETING ESCALATING CHALLENGES

According to Frost & Sullivan, sterile parenteral contract services make up about 82.8% of the total sterile outsourcing market. This includes small-volume parenterals (e.g., vials, ampoules, and syringes), which make up the majority of sterile CDMO services with 88.9% of market share, and large-volume parenterals (e.g., bags and bottles). The sterile parenteral manufacturing subsegment is expected to reach a market size of $6.5 billion by the end of 2016.[4] Outsourcing parenterals is anticipated to increase and continue to benefit established companies in this market.[5]

As individual companies and as partners, AAIPharma Services and Cambridge Major Laboratories have accomplished a significant amount of sterile parenteral fills in their aseptic manufacturing facilities processing small- and large-molecule parenteral products as well as lyophilized products, suspensions, emulsions, and terminally sterilized vials. The operational setup of the combined company allows for the seamless integration of services covering development, testing, and manufacturing from API to finished packaging.

PARENTALS OFFER CONSIDERABLE CHALLENGE

It's generally accepted that there are considerable challenges to success in the parenteral market, including quality concerns, stringent regulations and lack of funding. The aseptic processing of parenterals involves complexities such as protecting the sterility of a product as it moves through each phase of formulation, filtering, filling, and packaging.

THE PERCENTAGE OF RESPONDENTS WHOSE COMPANIES **SPEND $10 MILLION TO $50 MILLION** ON OUTSOURCING ALSO **INCREASED FROM 38 PERCENT TO 62 PERCENT.**

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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. Syed earned a BS in chemical engineering from New Jersey Institute of Technology in 2003 and an MBA from Cornell University in 2009.

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Companies specializing in the aseptic processing of parenterals are compelled to implement advanced controls, optimize internal processes and packaging materials and techniques to ensure drug quality and ultimately, patient safety.

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.

Stringent regulatory requirements must be followed, including maintaining compliance with US and international regulatory requirements, and 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 lead to cold chain and storage hurdles.

PROCESS CHALLENGES MET

CMOs capable of developing and testing lyophilization cycles on a lab scale can prove to be cost effective. Lyophilization can be an important process in maximizing the stability of a product and manufacturing processes around aseptic compounding equipment utilization have also become increasingly complex and resource intensive with specific environmental monitoring and controls.

The rapid expansion of biopharmaceutical products has resulted in a growing trend by companies in the space to commission the contract manufacturing of mostly parental biologic drug products. Sponsor expectations from a CDMO include broader analytical test methods for the release and stability of 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.

For example, 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.

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

Continuous investment in advanced technology, staff training, as well as constant monitoring of the market and industry environment are key behaviors every drug sponsor should look for. Similarly, proactively keeping up with new regulations pertaining to parenterals helps meet these challenges.

ON THE HORIZON

Looking ahead, pharmaceutical and biotech companies will likely continue the trend toward outsourcing solid-dose and parenteral development and manufacturing. At the same time, the complexity of active ingredients and production processes will grow. These changes will require strategic partnerships with highly competent, experienced CDMOs that have the expertise and thus the strength to meet new industry demands able to respond to current and future challenges through flexible operations and creative solutions to help their customers to handle increasingly complex supply chain relationships. It's obvious that it will continue to be critical for CDMOs to offer both individualized and integrated supply chain solutions to the marketplace if they are to be successful at helping their customers achieve the success they seek for their formulations and therapies. P

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