CMO Market Report

What's the way ahead for finished dose formulation providers?

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Pharmaceutical contract manufacturing used to be viewed as a one-off activity where a pharma company outsourced a drug for manufacturing predominantly because of capacity constraints or end-of-lifecycle considerations. However, in recent times, there has been a paradigm shift in the business model of contract manufacturers away from just a one-off manufacturing option to integrating themselves into the supply chain of pharma companies. They now cover the gamut from early stage activities including pre-formulation design, process optimization, and preclinical stage, to commercial manufacturing, fill-finish services, packaging and logistics, regulatory, analytical and marketing support. There are several challenges and complexities associated with the existing business model of CMOs globally, so market participants must adopt potential game-changing strategies, both to address unmet market needs as well as sustain themselves and grow in the highly competitive global pharma contract manufacturing market.

Challenges Based on the Existing CMO Business Model

- **Fragmented nature of the market combined with price pressure drive down CMO revenues**

The pharmaceutical contract manufacturing market remains highly fragmented, with many CMOs relying on one client for more than 50% of their revenues. This creates negotiating power for clients and supresses prices throughout the industry. Based on previous experience, cost, and size, nearly 60 to 80% of pharmaceutical companies consider going back to preferred suppliers. Furthermore, CMOs face immense price pressure because of tax incentives and lower inventories for low-volume products. Manufacturing costs are required to drop as much as 30% to generate tax savings. In September 2011, Patheon announced its plan to leave the semi-solids manufacturing market focus on sterile products and improve profitability. Similarly, in August 2011, Ben Venue Laboratories announced plans to exit the CMO market over the next few years to focus on its core generic business.

- **Lower unit volumes and new technologies will likely pose a threat to CMOs.**

Low-volume products such as niche drugs, orphan drugs, and generics, as well as emerging markets, present poor profit margins and lower inventories for CMOs, thereby resulting in price pressure and increased competition. The CMO business model is only able to address the basic requirements of global

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pharmaceutical companies in terms of unit cost, technology, IP protection, cost flexibility, and security of supply. This model does not cater to the restructuring costs (compensation arrangements and disposal of old facilities), financial impacts (tax implications, government subsidies, and exchange rate exposure), and commercial demands (local market approvals, portfolio, and brand). Hence, CMOs are expected to face additional competition from in-house manufacturing from even smaller companies with regard to novel technologies for finished dose formulations — disposable contact parts, continuous processing, automation, and pre-processed inputs such as SCF syringes — as such new technologies may change the in-out balance of CMOs.

Total Pharmaceutical Market: Forecast of Percent Combined Prescription Sales for the Mid-sized Pharmaceutical Companies by Molecule Type, Global, 2012–2017

Molecule Type	2012 (%)	2013 (%)	2014 (%)	2015 (%)	2016 (%)	2017 (%)
Small molecule	95	94	94	93	92	90
Therapeutic protein	5	6	6	7	8	10

- **Lack of Venture Capitalist (VC) funding for early-stage companies will result in less expenditure than precession levels**

Prior to the global recession in 2008, VC firms made significant investments in the pharma/biotech contract manufacturing industry; however, VC funding saw a steep decline during 2009 and 2010. Although the overall VC investment climate has improved as of 2012, a majority of VC firms prefer investing in companies with promising late-stage (Phase II and Phase III) drug candidates than in early-stage companies. Similarly, the U.S. and Asia seem to be more attractive targets for VC firms than Europe as Europe has been comparatively slow in regaining financial stability. In 2011, pharma R&D spending decreased for the first time in more than a decade in major markets such as the U.S. Less R&D spending will likely result in fewer drugs being developed and lead to fewer marketed and manufactured drugs. These outcomes would negatively affect the CMO industry in the future. Overall, VC investments in the pharma contract manufacturing market seem to be on a declining curve over the next five years as investors back away. However, expenditure for biotechnology R&D will grow because of increased interest from VC firms and greater funding availability.

Key Trends in Finished Dose Formulations

- **Big pharma will likely depend on small molecules; however, biologics are expected to spur growth**

Traditionally, the big pharma business model has been built on small molecule products that are affordable and relatively easy to manufacture. However, the patent cliff and the resulting commoditization of the small molecule market have forced big pharma companies to seek diversification into the large molecules/biologics space for therapeutic areas of high unmet need, such as oncology. Of the top 15 pharma companies, nearly 80% are expected to experience a net growth in their biologics portfolio. It is estimated that small molecules, which accounted for 87.0% of big pharma sales in 2012, will likely decline to 71.0% by 2017, while biologics will likely constitute 27.4% of big pharma sales in 2017, which is up by 8.5% from 2012. The big pharma shift to large molecules will likely be led by monoclonal antibodies (mAbs) and is projected to grow at a CAGR of 10.8% from 2012 to 2017.

- **Mid-sized Companies to Focus More on Small Molecules**

Ninety-five percent of the total sales of mid-sized pharma companies came from small molecules in 2012, and this percentage will likely remain relatively unchanged over the next couple of years. Interestingly, the strongest performing mid-sized pharmaceutical companies — Gilead, Celgene, and Actelion — are expected to derive their entire growth from small molecules. However, companies such as UCB, and Allergan plan to expand through the growth of their brands, Cimzia and eprattuzumab (mAb), and Botox (therapeutic protein), respectively.

- **Injectable Dose Formulations Likely to Spur CMO Growth**

Despite the current dominance of solid dose formulations, injectable dose formulations have experienced strong growth

Total Pharmaceutical Market: Forecast of Percent Combined Prescription Sales for the Top 50 Pharmaceutical Companies by Molecule Type, Global, 2012–2017

Molecule Type	2012 (%)	2013 (%)	2014 (%)	2015 (%)	2016 (%)	2017 (%)
Small molecule	87	84	80	78	75	71
Monoclonal antibody	6	7	9	10	12	14
Therapeutic protein	4	5	6	7	7	8
Vaccine	3	4	5	6	6	7

Unmet Market Need	Potential Game-changing Strategy
An integrated, end-to-end business model on a risk-sharing basis with clients	• Increased focus on preclinical development services such as formulation development, process support, process development, clinical trial manufacturing, analytical services, and regulatory support in addition to the core custom manufacturing services is necessary to integrate into the value chain at early life-cycle stages and to build long-term relationships with clients. • To attract more clients, certain CMOs will likely adopt a differentiation strategy that includes repositioning themselves among clients by promoting more services such as formulation improvements, alternate dose formulations, realtime order tracking, and logistics support. • Patheon and DPT Laboratories have been two such leading CMOs that have positioned themselves as development service providers capable of transitioning from offering clinical services to commercial manufacturing.
Installing new capabilities and anticipating capacity demand for careful weighing of benefits and risks	• Industry consolidation by means of acquisitions and strategic alliances to expand capabilities in new product and service segments as well as new geographies have made Aenova one of the fastest growing companies. • Aenova's foray into the liquid and semi-solid dose formulations segment by the recent acquisition of the Temmler Group in 2012 has resulted in a significant increase of market share and capacities to meet global demands.
Demand for next-generation biological therapies such as vaccines, anti-cancer therapies, gene therapies, specialized antibiotic treatments, and recombinant proteins	• Due to increased focus of big pharma companies on biologics to address unmet needs in therapeutic areas such as oncology, the injectable dose formulations segment, which is a low-volume, high-margin business, will likely be the growth driver for CMOs. • Key focus areas in sterile manufacturing of injectable dose formulations include vaccines, anti-cancer therapies, antibodies, gene therapies, specialized antibiotic treatments, and proteins. • Hence, investments and capacity expansions in injectable dose formulations manufacturing will help CMOs, particularly small and medium-sized ones, to grow and sustain their businesses in the market. • Cytotoxics and lyophilized products dispensed as injectable dose formulations are expected to be a significant source of revenue for CMOs; therefore, more CMOs will likely develop these capabilities.

during the past five years, with a CAGR of 18.7% from 2007 to 2012. The significant growth for injectable dose formulations is expected to continue during the next five years, driven by the following key factors:

- The highly sterile and aseptic conditions and skilled personnel required for manufacturing injectable dose formulations fuel demand for outsourcing as it appears to be a viable alternative to add additional manufacturing capacities for pharma and biotech companies.
- Cytotoxics are expected to be the key growth driver for the injectable dose formulations segment because of the robust demand for oncology and other high-potency drugs such as antibody conjugates, steroids, and IV fluids that require quick onset of action.
- Pharma and biotech companies prefer prefilled syringes (PFS) for existing and new products as PFS eliminate issues with overfilling of expensive drugs, thereby resulting in significant cost-saving benefits. This will likely be a major driver for outsourcing to CMOs.
- Other factors driving the growth of the injectable dose formulations segment include rapid onset of action, better therapeutic efficacy, and greater return on investments to manufacturers.

Thus several large CMOs are looking for investments and capacity additions for both primary and secondary manufacturing facilities. Consolidation in the form of strategic alliances between pharma/biotech companies and CMOs is expected to increase for expansion of manufacturing capacities for injectable dose formulations. The key participants in this segment include Baxter BioPharma Solutions, Vetter Pharma, and Catalent.

- **Shift Towards Emerging Markets as Favorable Outsourcing Destinations**

Even though the U.S. and western European countries are leaders in the pharmaceutical contract manufacturing market, there is a gradual shift in balance of control in terms of out-

sourcing manufacturing and research activities, particularly for solid dose formulations, from the developed markets to the emerging low-cost destinations such as India, China, Japan, and eastern Europe. As these emerging markets are highly price competitive and rapidly catching up with advancements in technology, they are expected to register robust double-digit growth rates in the long-term, resulting in pricing pressure in fragmented markets such as in Europe. However, issues with regard to quality, logistics and intellectual property (IP) protection restrict the outsourcing of manufacturing technically more challenging formulations — i.e., the injectable dose formulations — to the emerging markets.

- **Industry Consolidation To Improve Profitability**

The fragmented nature of the pharma CMO market will likely propel consolidation as a means to improve profitability. Many CMOs are struggling to reach profitability and some anticipate that nearly 30% of the current market participants are likely to exit the contract manufacturing business during the next 10 years, owing to intense price competition and poor profit margins, particularly in the liquid and semi-solid dose formulations. Consolidation in the form of acquisitions and strategic alliances to gain access to new, emerging markets and niche segments will likely emerge as a net win for both small and large CMOs. Large CMOs can expand their geographic presence, and small CMOs can leverage the technical expertise and resources of large CMOs.

Unmet Market Needs and Potential Game-changing Strategies

With outsourcing increasingly being looked upon as a strategic option rather than a mere cost-cutting tool, it is crucial that CMOs align their services and offerings to cater to the ever-changing dynamic needs of their global customers. Summarized below are a few key unmet market needs and potential game-changing strategies adopted by market participants to address them.

The global pharmaceutical finished dose formulations contract manufacturing market is largely governed by a number of structural parameters, including the performance of companies in terms of cost, capacity, R&D and technical expertise; the venture-capital industry; and establishment of mutual understanding between CMOs, sponsors, investors and policy-makers. While quality, timeliness and cost remain the top three factors influencing the decision of the choice of a CMO, differentiation strategies such as repositioning themselves among clients and capturing projects at early life-cycle stages — besides entrenching an integrated end-to-end business model — are likely to pave the way for sustainable growth in a market as highly fragmented and regulated as the pharma CMO market. ■