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Winning Formula: Keys to Success for Contract Drug Manufacturers

Over the last few years, pharmaceutical companies have increasingly outsourced "non-core" activities, in particular manufacturing. This enables them to cut costs and focus their energy, capital and management on research and marketing & sales, the two activities considered key for their value chain (see Figure 1).

This outsourcing drive has provided significant growth opportunities for contract manufacturing organizations (CMOs) around the globe. The volume of worldwide outsourcing has almost doubled since 2006. The growth of this market and the need for capital have attracted the interest of a number of private-equity players, which have made substantial investments in CMOs.

Yet contract manufacturing is a more complex market than it may at first appear. Companies are potentially exposed to a range of unpredictable factors, including changing government reimbursement policies or outright drug bans, such as the one that hit the analgesic Dextropropoxyphene in 2010. Positions can also be shaken by more predictable factors, such as branded drugs becoming generics and new product launches. Companies that succeed find ways to differentiate and protect their business

Figure 1

Value Chain of the Pharmaceutical Industry

	Research	Development	Manufacturing Packaging	Marketing	Distribution & Sales
Description	• Highly skilled researchers • Feed the research pipeline • Identification of new active principles	• Technical skills (formulation, trials, etc.) • Regulatory / administrative services	• Production capacities • Industrial expertise	• Differentiate and maximize drugs potential	• Logistics and coverage networks • Sales force
Type of players	• In-house research department	• Pharmaceutical companies • CMOs with in-house formulation expertise	• CMOs • In-house production capacities	• Pharmaceutical companies	• Pharmaceutical companies through in-house sales force

Winning Formula: Keys to Success for Contract Drug Manufacturers was written by **Arnaud Sergent** and **Serge Hovsepian**, partners, and **Nohmie Ben Rekassa**, a manager in L.E.K. Consulting's Paris office and **Ben Faircloth**, a partner in L.E.K. Consulting's London office. For more information, please contact lifesciences@lek.com.

by positioning themselves in sectors where underlying drivers are attractive and barriers to entry are high.

This *Executive Insights* focuses on the keys to success for CMOs. It details the differentiation strategies that have proven themselves in the marketplace and provides a roadmap for private equity groups and other financial investors.

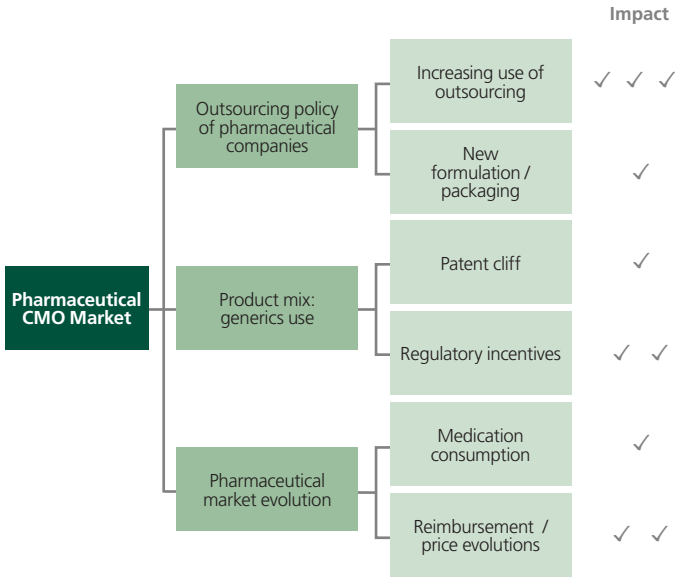
Opportunities and Risks in the Outsourced Manufacturing Market

Contract drug manufacturing is growing fast, driven by the expansion of the overall drug market and the increased trend among pharmaceutical companies to outsource (see Figure 2). The development of generic drugs has particularly benefited this market, as generic drug makers outsource as much as 80% of their production to CMOs. Branded pharmaceutical companies are also increasingly outsourcing their more mature molecules, although they typically continue to manufacture their newly launched drugs themselves for strategic reasons.

Although the overall outsourcing market is growing, CMOs are not all growing at the same rate. In fact, the contract drug market is highly segmented with each segment having different growth characteristics; as a consequence, each segment has to be analyzed separately. A segment is characterized by the typical size of the production run, the nature of the active pharmaceutical ingredients, the galenic form and the step of the product life-cycle. For each galenic form, for example, the drivers of demand and supply of production capacity can vary.

Figure 2

Outsourced Manufacturing Market Growth Drivers



CMOs can also be impacted by developments in a specific therapeutic area; they can be vulnerable to changes in the regulatory environment specific to a class or a product, or the launch of a new competitive product. One example of the potentially unpredictable nature of the market is to be found in France. Here, the state health insurance system, under pressure to reduce its deficit, decided in April 2010 to reduce reimbursements to consumers of dry cough syrup, from 35% to 15% of the retail price, and to end reimbursement for children below two years old. The drop in demand caused by this decision affected makers of all syrups, generated overcapacity in syrup production lines and negatively impacted the syrup contract manufacturing market segment as a whole.

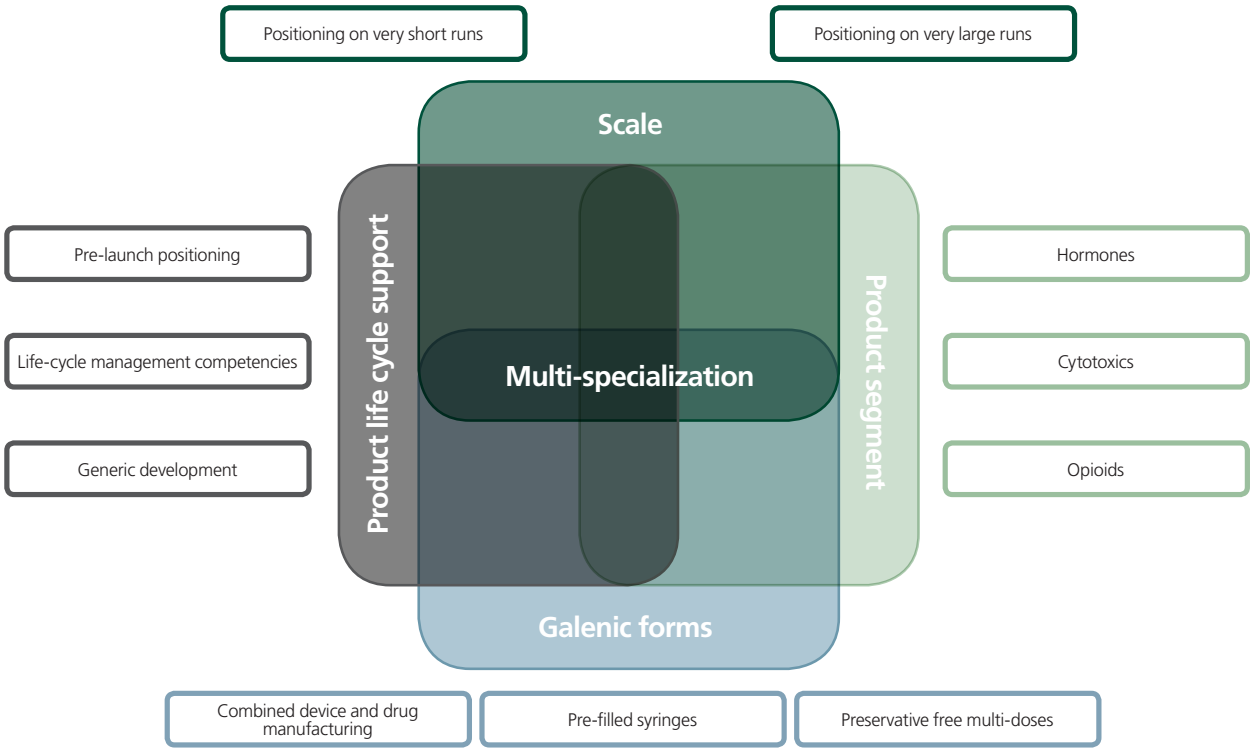
Strategies for a Hyper-Segmented Market

To help mitigate the impact of such potential risks, CMOs need to identify and position themselves in segments where growth prospects are strong and where they have, or can build, a differentiated position. They can do so in four different ways: in terms of scale, optimizing their manufacturing capability to support either very large or very small production runs; in terms of product segment, having the capability to manufacture products with complex or hard to handle active pharmaceutical ingredients (APIs); in terms of galenic form, offering a galenic form in which the market lacks capacity or capability; or finally by developing life-cycle management support competencies which they can offer to pharmaceutical companies directly, alongside manufacturing (see Figure 3).

• **Scale:** Size is a significant differentiating factor, as the biggest players achieve considerable economies of scale. However, small can also be beautiful: the ability to deliver very short production runs is also a differentiating factor, since it requires considerable

Figure 3

Specialization Strategies



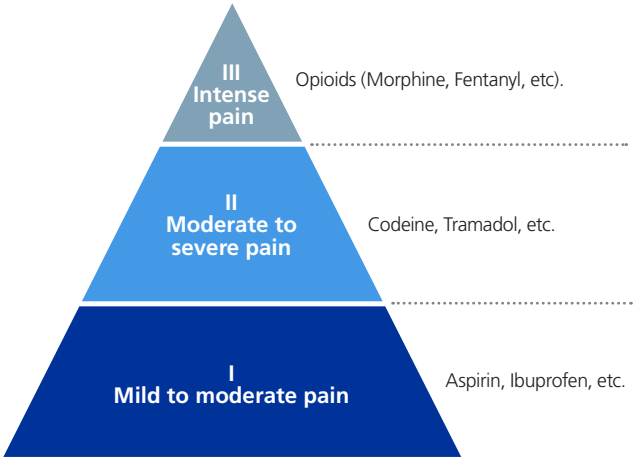
manufacturing flexibility. There is an increasing demand for large batch manufacturers to serve global blockbuster markets as well as for small production-run specialists to serve national niche markets. Building a global organization able to deliver large-scale contracts requires substantial financing and commitment, while being able to cater profitably for short runs also requires highly flexible, small-scale industrial capability. Those providers positioned solely to support mid-sized production runs for commoditized galenic forms, potentially face the biggest challenges.

• **Product segment:** Another successful strategy is for the CMO to focus on drugs with high underlying growth and whose active pharmaceutical ingredient is complex to source or handle. Examples include high potency drugs such as cytotoxic medicines used in chemotherapy and controlled substances such as opioids that are used to control and alleviate chronic pain (see Figure 4). The underlying diseases for high potency drugs have growing prevalence. The APIs used in these drugs often have specific licensing, authorization requirements and environmental or safety requirements and "clean room" manufacturing capabilities. Sourcing can also be complex. For example, in France, morphine has to be sourced through Francopia, a subsidiary of Sanofi, which has a license from the French Government to be the country's exclusive supplier. The requirement to establish a close relationship with Francopia is thus an additional barrier to entry for CMOs who want to manufacture opioids. In contrast, companies focusing on lower potency drugs are exposed to more competition and possible over-capacity in some galenic forms.

• **Galenic form:** Demand for sophisticated, specific galenic forms such as liquid stick packs, blow fill seal, multidose preservative-free drops, pre-filled syringes, aerosols and other forms combining the drug with the delivery system, is on the rise because they provide a range of benefits, including optimal drug efficiency, improved adherence by patients, safer use and limited side effects. These advanced galenic forms are often difficult to manufacture and not every CMO is able to produce them profitably. One example is preservative-free eye drops, mainly used to treat dry-eye

Figure 4

Pain Medicine APIs Classification



syndrome. These are seeing increased growth because they are safer for the cornea than multidose droppers containing preservatives and are cheaper than unidose packages. But they require an expensive, highly customized production line that acts as a barrier to entry for many CMOs and keeps demand ahead of supply. Companies focusing on the most common, traditional galenic forms, such as tablets, have to deal with overcapacity in the market, especially if they don't have a robust product segment strategy (see Figure 5).

• **Product life cycle support:** Some CMOs have built in-house development capacities which have allowed them to partner with generic drug companies in the development of generic formulations or with branded drug makers in the development of life-cycle management programs for existing drugs. These essentially translate into new formulations and / or galenic forms of existing products that have additional customer benefits, such as faster delivery or taste masking. Part of the development process includes "scaling up" from making prototypes to full industrial production. A CMO which has helped on the "scale-up" has an advantage when it comes to capturing the associated manufacturing contract, which will typically run for several years, thereby cementing the business relationship with the pharmaceutical sponsor.

Figure 5

Examples of Galenic Forms

Product Forms		Illustrations	Routes of Administration			
			Oral	Parenteral Injection	Transmucal	Topical
Liquid Forms	Sterile and non-sterile liquids Standard and unit doses		Liquid solutions or suspensions (drinks, syrups) Oral sprays	Pharmaceutical compounds for injection (intradermal, subcutaneous, intraosseous, intramuscular, intravenous, intraperitoneal)	Aerosols Inhalers Nebulizers Vaporizers Nasal spray	Ophthalmic, otic, transdermal liquids (drops) or lotions
Solid Forms	Granular or solid formulations, often packed in blisters		Powders Pills Tablets Capsules Gel-capsules Solid crystals Chewing gums		Powders for inhalation	Plasters
Semi-solid Forms	Pastes, ointments in tubes or containers		Oral pastes Jellies Liquid stick pack Sachets		Suppositories (rectal, vaginal) Ovules Hydrogels	Creams Pomades Gels Patches Films Balms Foams

CMOs seeking to pursue this route have two options: they can either position themselves at the tail end of sponsors' portfolios, specializing in reformulations of generics, or they can support branded drug launches, which often require investment in bespoke plant or material to support innovative manufacturing techniques and / or production scale-up (see Figure 6).

Multiple Specializations as the Path to Success

Successful CMOs choose one or more of these paths to differentiation. Yet they may still suffer from the risk factors noted above, even when they are active in an apparently sheltered and high-growth area of specialization. For example, even products that are manufactured in small batches with a complex API and an exclusive formulation can be subject to unexpected regulatory changes or lose share following the launch of a competitive product. Specialization strategies mitigate the risks, but cannot eliminate them altogether.

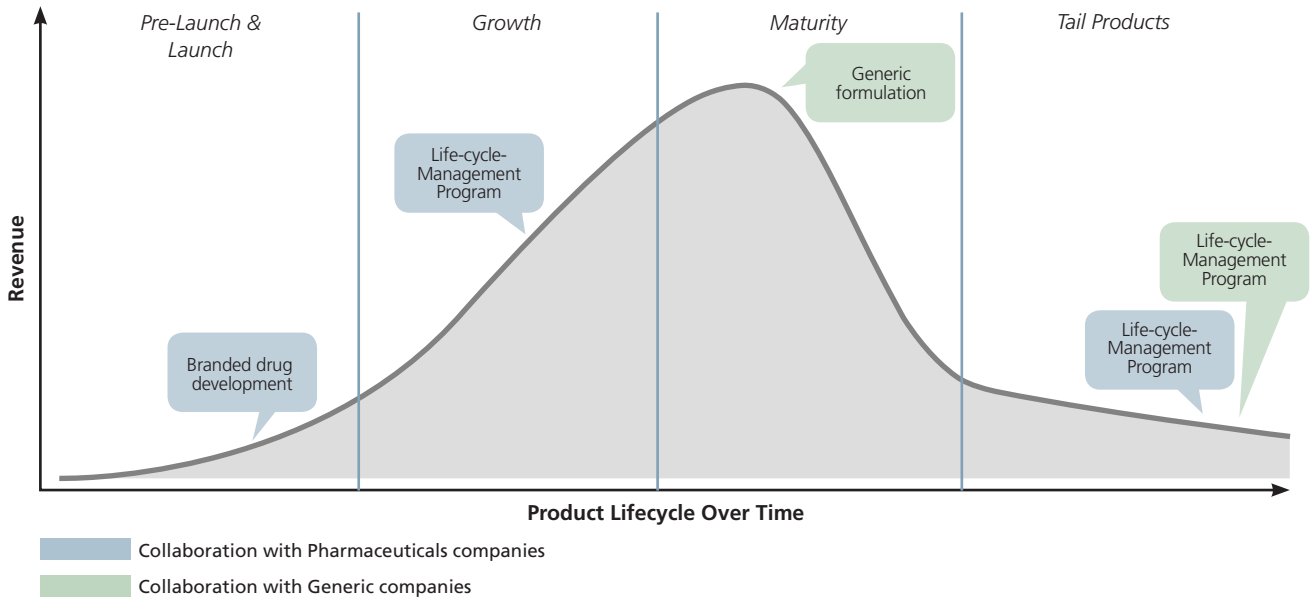
That's why successful CMOs are not just specialized in one market segment, but often have multiple specializations to insulate themselves against individual market risks.

Having only a limited share of sales dependent on the product "at risk" gives the CMO enough time to find other ways to fill its production lines. But developing multiple areas of specialization is no simple task. In order to successfully diversify risk, these areas of specialty have to be uncorrelated, which implies limited synergies across the different specializations, increased investment in capabilities and the identification of appropriate commercial opportunities.

Navigating this market is therefore complex. Yet the growth in the outsourced manufacturing market shows no sign of slowing, and the underlying drivers - a buoyant drug market, increased activity from generic players and more outsourcing - are all positive. There's every indication that market players will become more specialized and even multi-specialized in the years to come. For private equity players and other investors, this market growth offers potentially attractive returns, provided there is a clear understanding of where a CMO's competitive advantage lies. Where expertise is developed based on a careful read of the market, the rewards can be substantial.

Figure 6

Product Life Cycle Support Opportunities



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