Pharma & Biotech 2017
Review of outsourced manufacturing
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Foreword

I am pleased to introduce you to our 2017 review of the outsourced manufacturing sector, where we share some of the trends observed in recent years and look to the future of the industry. In the last five years, the industry has enjoyed positive growth and there are certainly positive indications for the future. The team at Results Healthcare has been very busy serving a range of client needs, helping both buyers and sellers to achieve their strategic goals. We have grown and broadened the healthcare team in response to the firm’s clients’ demands.

2016 ended with uncertainties concerning the future of ‘Obamacare’ under the incoming US administration and debates on the outcome of the British referendum on membership of the European Union (EU) as well as the performance of the Chinese and broader Asian economies in 2017. Regulators including the Food and Drug Administration (FDA) have shown a tougher stance regarding pharmaceutical manufacturers, which has disproportionately affected Asian suppliers. In May 2016, the EU agreed new stricter rules on medical devices and in vitro diagnostic medical devices. Industry leaders need to maintain their awareness of these issues as the marketplace seems likely to continue to become ever more stringently regulated, providing opportunities as well as threats. The healthcare providers, entrepreneurs and their suppliers will need to navigate through relevant changes, however, we remain very positive for the short and long term.

Looking towards the future, there are strong indications of above GDP growth for the outsourced manufacturing sector, which we discuss in this report. This is driven by greater demand for manufactured product as well as an anticipated rise in outsourcing. This climate will continue to create opportunities for deals, M&A and consolidation in the sector.

Warm regards,

Kevin Bottomley
Healthcare Partner
Executive summary

This report is an update on the pharmaceutical outsourced manufacturing sector with the last Results' report published in 2013. By 2015, the global Pharmaceutical market reached $1.1 trillion and is expected to continue growing at approx. 5.5% per annum. Our analysis estimates that the total outsourced manufacturing market reached $71.5bn in 2015 and is growing at 6.6%¹. The sector’s faster growth above the pharmaceutical industry is helped by the anticipated transition to more outsourcing, as well as the good growth within particular subsectors. Small molecules dominate the pharmaceutical sector (approx. 83% by revenue) and are expected to continue doing so for some time; however, growing slower than biologics².

At the time of our last report, the outsourced sector in the West had endured some years of relatively low growth due to the pressure of low cost Eastern manufacturers, compounded by the relatively modest growth in demand for Contract Manufacturing Organisation (CMO) services. Since then, there has been a significant trend in repatriation of manufacturing from the East spurred by supply chain security concerns linked with increasing pressure from US and European regulators. In addition, there has been cost inflation in the East which has eroded the competitiveness and attractiveness of Asian suppliers.

Regardless of efforts to consolidate the sector, the landscape of the CMO industry remains fragmented. The major players in the sector only command a 2-4% market share each. This provides opportunities for investment with few significant incumbent majors. With increased competition, European and US CMOs are trying to differentiate in response to low cost competition; One-Stop-Shop is an example of this. Our analysis has found little evidence to support the promoted One-Stop-Shop model, despite the perceived benefits of the model such as simplifying supply arrangements. In the last decades, the cost base has been shaken by Asian competition which has grown to a level where a major proportion of "low value" generic products come from India and China. Recent FDA warnings will need to be addressed by some of these companies, as controls become more stringent.

Based on our analysis, biologics have received heavy investment for new facilities, motivated by anticipated growth and margins, whereas small molecules have been less favoured. Overall, pharmaceutical outsourced manufacturing is expected to increase in the coming years. Small molecule outsourced manufacture is expected to grow ahead of the respective pharmaceutical sector, which is helped by outsourcing. High potency active pharmaceutical ingredients (HPAPIs) have also been a sub-segment of attention for investment and differentiation, owing to the regulatory hurdles to operate in HPAPI environments and their foreseen applications in the growth market of oncology. Regarding drug product, acquisitions and investments have in a number of cases favoured sterile and aseptic fill, where shortages have been identified, as well as particular device segments.

Overall, the prospects for the sector remain strong, linked to the expected growth in healthcare. There is a strong case for investment in particular segments, subject to appropriate valuation and due diligence. This report highlights some of the trends that should be in the minds of CEOs, CFOs and investors.

¹ Invoice price basis from Outlook for Global Medicines through 2022, QuintilesIMS
² Results Healthcare analysis includes commercial and clinical manufacturing
³ A small molecule is a low molecular weight (< 900 dalton) organic compound that may help regulate a biological process, in contrast, biologics are larger and more complex compounds made by living organisms and their products (e.g., monoclonal antibodies that are commonly called mAbs)
Introduction

In general terms, outsourcing, consolidation and specialisation to One-Stop-Shop strategies are common words associated with mature manufacturing sectors. Despite continued innovation to help patients, the pharmaceutical manufacturing sector does not escape such labels. Many large pharmaceutical companies have divested significant manufacturing and logistics facilities. They do this as they strive to re-align strategic priorities, such as to accommodate drugs losing patents or a re-prioritisation of where they wish to add value (e.g. exiting a particular therapeutic area). The contract manufacturers have adapted and made use of opportunities provided to them by both small biotechs and large pharmaceutical companies, which has shaped the industry. This is not to belittle the impact of Asian competition with lower cost bases, which has driven businesses to re-think strategy.

This report is a timely update on the sector with the last Results report published in 2013, as there have been several significant mergers. In 2014, Royal DSM and JLL Partners announced the creation of DPx, a standalone company formed following the merger of Patheon with DSM Pharmaceutical Products. In the same year Catalent became a publicly traded company on the NYSE. In 2016, AMRI acquired Euticals to add to its API (active pharmaceutical ingredient) capacity. Through the period, companies have been built up through multiple acquisitions, such as the AeNova Group using private equity backing. At the end of 2016, Lonza agreed to buy Capsugel SA from KKR & Co. for $5.5 billion, which had acquired Capsugel from Pfizer for $2.4 billion in cash in 2011. In the same month, Lonza announced the divestment of its Peptides Business and Operations in Braine-l’Alleud, Belgium, to Polypeptide.

These mergers and the raft of other mergers completed since 2013 have helped consolidation in the sector. In addition to the headline grabbing mergers, there is an undercurrent of asset sales where CMOs are purchasing facilities from pharmaceutical companies. These assets can often be of high quality and may come with supply agreements with the vendor. Some CMOs have built significant concerns from multiple purchases of assets (e.g. Avara Pharmaceutical Services and CordenPharma).

However, despite consolidation being a repeated byword amongst CEOs, the process is slow and the sector remains fragmented. Big listed titans do exist, for example Catalent and Lonza as mentioned above, as well as pharmaceutical companies that also contract manufacture (e.g. Boehringer Ingelheim and Sanofi). Nonetheless, ownership remains largely private with significant family ownership, as well as private equity firms that have bought into the sector.

According to World Bank statistics, health expenditure represented 9.9% of GDP in 2014 and about a seventh of this is pharmaceutical sales. By 2015, the global Pharmaceutical market reached $1.1 trillion and is expected to continue growing at 5.5% per annum. There are fundamental drivers, such as population growth, ageing population and GDP growth. Pharmaceutical companies appear to have turned a corner away from a patent cliff feared some years ago; new launches with indications for hepatitis and oncology provided a boost in recent years. The overall pharmaceutical market growth supports contract manufacturing, if outsourcing trends continue.

The extent to which the growth trickles down depends on the level of outsourcing and the ability of contract manufacturers to capture value. Our analysis estimates that the total pharmaceutical outsourced manufacturing market reached $71.5bn in 2015 and is growing at 6.6% per annum. The extra expected growth above the pharmaceutical industry is helped by the anticipated transition to more outsourcing. Biologics are expected to be a significant area of growth; however, they are starting from a lower base and there is a greater bias against externalising biologics production. Small molecule commercial outsourced manufacture is expected to dominate the sector for many years to come, and deliver a growth of 6.4% annually.

This report provides a review of the trends in the outsourced manufacturing market by first reviewing the outlook for the pharmaceutical market that forms the customer group. Following this an overview of the CMO market and its participants is provided, before commencing on the review of the trends. Taking into account the trends and analysis, the report considers the case for investing in the sector. The report ends with a conclusion that captures the key findings of our analysis.

4 Catalent was created in April 2007 when The Blackstone Group acquired the Pharmaceutical Technologies and Services segment of Cardinal Health.
5 Inverse price basis from Outlook for Global Medicines through 2021, QuintilesIMS.
6 Results Healthcare analysis, includes commercial and clinical manufacturing.
Outlook for pharmaceuticals

I Growth from fundamentals including economic growth and a growing and ageing population, as well as new product launches.

I Partly offset by an increasingly concerted and coordinated downward pressure from payers on the price of pharmaceuticals, as well as the entry of biosimilars.

I Biologics and biosimilars are expected to have strong growth to 2021; however, small molecules account for most revenues.

In 2015, the total size of the worldwide pharmaceutical market was c. $1.1 trillion and it is estimated to increase to $1.5 trillion in 2021 (5.5% CAGR)\(^7\). Despite the attention on biologics and biosimilars, small molecules are still expected to dominate the market in 2021 (76% market share); however, the pace of market growth anticipated at 4% means that its market share is contracting in comparison to biologics and biosimilars.

The main constituent of the small molecule sector is patented and originator medicines, which represent around 54% of the total pharmaceutical market by revenue. It is anticipated to be the slowest growing segment at 3.4% CAGR to 2021. In comparison, helped by the opportunities of patent expiries, generics are expected to deliver a 6% growth in the period. It is important to consider that although generics are a relatively minor segment, 88% of dispensed drugs by volume are generics. The implications are that volumes are high, which feeds production capacity usage. As API and DP (drug product) supply chain utilisation and profitability is driven by volume of drugs sold and not market value, the outsourcing sector captures value from the rise in generics. Thus, due to the relatively higher volumes of generics sold, the market has a significant impact on the outsourced manufacturing sector. The supplier of API for generics may have multiple customers for the same product.

As already highlighted, the anticipated percentage growth rate of biologic and biosimilar markets far exceeds that of the more established small molecule markets. The biologics market is set to increase its total market share from 16.6% in 2015 to 22.2% in 2021. This is facilitated by an anticipated above sector growth of 10.9%. The biosimilars market, although growing very quickly, is expected to remain a minor part of the pharmaceutical market in 2021\(^8\). This is driven by the indicated difficulty of developing biosimilars, based on the progress to date. In comparison to generics, they generally require costly clinical trials to gain market approval, more time\(^9\) and the mastery of using living organisms to produce the API (such as mammalian cells). Nonetheless, companies, such as Samsung, have invested heavily to build capacity with expectations for biosimilars.

Oncology is the largest therapeutic area and generated 10.7% of all pharmaceutical market revenues in 2015. This is set to increase to 16.3% by 2022. The strong growth in this sector drives downstream trends in the CMO market such as an increased demand for cPAPis and injectable secondary manufacturing capacity. Anti-virals are the largest therapeutic area for the small molecule sector, followed by oncology. Strong growth of both areas is a significant driver of increased demand for small molecule API and DP contract manufacturing services.

Over 220 new drugs are expected to be introduced by 2021, which is a positive indication for the outsourced manufacturing sector\(^10\). Between the start of 2017 and the end of 2021, $147bn of pharmaceutical sales are at risk due to patent expiries\(^11\).

However, only $83bn of this is forecast to materialise. This difference in expected sales loss is because of weaker sales

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\(^{7}\) Invoice price basis from Outlook for Global Medicines through 2021, QuintilesIMS

\(^{8}\) Depending on different views, the biosimilars growth assumed is either ambitious or conservative. The subsector remains unproven in terms of revenues, but potential exists. In addition to several unsuccessful attempts to make biosimilars, new drugs and treatments are being developed, which may reduce the demand for copies of old drugs at least in countries where new treatments can be paid for.

\(^{9}\) Biosimilars are likely to take eight to ten years to develop and their development will likely cost between $100 and $200 million. For generic drugs, it is shorter (3 to 5 years costing $1 to $5 million). (Federal Trade Commission Report, June 2009). Costs and time lines could naturally reduce as regulators become comfortable through experience.

\(^{10}\) Outlook for Global Medicines through 2021, QuintilesIMS Institute

\(^{11}\) EvaluatePharma recent report World Preview 2016, Outlook to 2022
erosion of biologics after patent expiry, due to the difficulty in replicating these compounds. Another important factor to consider in the patented drug market is ‘churn’. As sales are lost from the market due to drugs going generic, new chemical entities (NCEs) enter the market and generate new sales. The overall effect on growth of the market may be small but this constant churn as new approved drugs enter the market and older products become generics, presents an opportunity to win new business and market share for outsourced manufacturers. Outsourced manufacturers can build a portfolio of generic APIs and they can provide each generic to multiple customers.

The outlook for the pharmaceutical sector looks positive; however, CMOs have the challenge to capture value from the product supply chains. Sizable pharmaceutical companies have their own manufacturing facilities. The decision to outsource depends on a number of factors, such as industry norms, technology, availability of internal capacity etc. Overall, the level of outsourcing is 24.6% at present and this is expected to grow (our forecasts assume it will rise to just over 26% by 2021). Thus, CMOs are expected to capture the market growth, as well as add growth through greater outsourcing. CMOs need to consider sub sector patterns, such as the rise in biologics and the need for more aseptic fill. In the coming section, the CMO market is reviewed for some of the key trends, which are often influenced by pharmaceutical companies’ activities.
CMO market

The market

- The total outsourced market is estimated at $71.5bn in 2015, growing to $105.0bn in 2021, of which 92% is currently dedicated to the small molecules commercial manufacturing supply.

- The sector has above GDP growth expectations at 6.6%, driven by the outsourcing trend and strong growth of the underlying pharma sector.

- Clinical manufacturing is important for locking-in clients, but is not a central source of revenues for most CMOs.

- Volume driven generics are expected to feed small molecule API demand.

The expected outsourced market growth is significantly above GDP growth expectations at 6.6% until 2021. This is driven by the strong growth of the overall pharmaceutical sector as well as an increase in the amount of manufacturing work that will be outsourced. The total outsourced market is estimated to have reached $71.5bn in 2015, growing to $105.0bn by 2021, which is mainly dedicated to small molecules and commercial manufacturing supply. The total potential commercial manufacturing market is $267.8bn assuming full outsourcing – at present it is estimated that about a quarter of commercial manufacturing is outsourced, so CMOs capture approx. $64.4bn of the commercial manufacturing market. In parallel to the pharmaceutical market most CMO revenues stem from the USA.

Figure 2: Breakdowns of the outsourced manufacturing market by sub-sector

$71.5bn
Outsourcing is increasing as a percentage of the whole manufacturing capacity because (i) facilities with products that become generic are non-core and are being divested and (ii) relatively more of new product manufacturing is outsourced. Using a third-party manufacturer can act as an additional site in a multiple site supply strategy, provide backup capacity and increased supply security. In addition, biologics capacity has been built up by CMOs to enable more production to be externalised.

The outsourced manufacturing market grows ahead of pharmaceuticals, helped by increased outsourcing and outperforming sub-sectors (e.g. biologics)

![Chart showing growth rates of different sectors](chart.png)

**Figure 3** Outsourced manufacturing sector vs. pharmaceutical market growth

Small molecule commercial manufacture forms the major part of CMO revenues (approx. $59.1bn; 91.8% of total outsourced market revenue in 2015). Even though it does not reach the expected growth of biologics and biosimilars, it does have a strong expected CAGR of 6.4%. The biologics CMO market is estimated at $5.3bn, it is starting from a lower base but is expected to grow at 8.3%. There is a greater bias for in-house production for biologics amongst the major companies, which has hindered outsourcing levels reaching those for small molecules. Nonetheless, outsourcing for biologics may improve in the future, as hurdles get resolved (e.g. the hesitance to move production owing to reproducibility concerns and regulation). Despite the capital-intensive nature of biologics, significant capacities have been built by CMOs in Asia – Fujifilm Diosynth and Samsung are two examples of investors in biologics capacity. WuXi AppTec has also announced a $1.20 million investment in an integrated biologics solution centre in Shanghai, China to open in 2017.

Major amounts of capital are required to enter the biologics market both for building capacity and acquiring a biologics company. Biologics need a technology base and manufacturing expertise which is completely different from small molecules; it takes a long time and much expense to acquire the necessary expertise and to build a good reputation based on a track record of completing successful customer projects. Pharmaceutical outsourced manufacturers have to work on customer projects starting from Phase 1 clinical trials because there is great customer reluctance to switch suppliers and cell lines once a product is in clinical trials. This means that customers with advanced projects are harder to win. Winning early stage projects could mean that significant revenues are a long way away: > 10 years.

In terms of commercial small molecule API, slightly more than half of revenues stem from contract manufacture of originators rather than from generics production. The balance of this may change in the future depending on patent expiries and the revenues from the contract manufacture of originator products. The notable benefit when manufacturing generics is the ability to supply multiple customers with the same API. Contract manufacturing arrangements do not normally allow this; however, multiple companies may produce the same API. Overall, greater growth is expected within the API small molecule segment for generics than for contract manufacture. Although clinical manufacture only represents a small proportion of CMO revenues, it is important for securing customers and building relationships that support commercial scale manufacturing. It is noteworthy to acknowledge that pre-clinical and clinical outsourcing is serviced by contract development and manufacturing organizations (CDMOs) and the commercial outsourcing market is supplied by CMOs – the distinction is difficult to apply as there is a high degree of overlap.

Less than half of revenues of outsourced commercial manufacturing are attributed to DP manufacture. Most of this comes from the Oral Solid Dosage (OSD) segment, which has approx. 48.5% market share. Overall, it is a mature segment and growing at a slower rate than other segments; however, it has a number of redeeming features. It is still expected to retain its lead in 2021. Oral medication has the benefit of being more convenient for patients relative to injections. There are innovations, such as coatings, where greater value can be captured. Large pharma companies have been consolidating production capacity with few new capex projects and as a result more OSD production is being outsourced.

The injectables sector is expected to grow at a strong CAGR of 10.5% until 2021, meaning this sector has the largest share of absolute growth. Manufacturing capacity shortages for sterile and aseptic fill have been driving investment into additional capacity. This is one of the fastest growing areas linked to the growth in biologics, oncology and generics. Nonetheless, the regulatory hurdles are more challenging and the investment required provides barriers to entry. In many cases the API is delivered from a customised dispenser which can include injection device and lance, and requires specific techniques and
Injectables, driven by pre-filled syringes, lead the absolute growth in DP

Figure 4 Breakdown of the drug product outsourced manufacturing sector - circle area indicates absolute sector growth until 2021

equipment for fill and finish. These present significant barriers to entry both for new competing products and CMO suppliers providing these highly-specialised drug and delivery device combinations. In terms of future growth, China is expected to be the main driver; however, the USA will remain the largest single market ahead of the EU.

The pre-fill syringe segment is expected to grow at 12.8% CAGR and will generate nearly 78% of sterile manufacturing revenue by 2021. The large share of market revenues is however not generated through increased manufacturing volume over ampoule or vial manufacturing but rather the largest unit cost of pre-filled syringes. Specialised delivery technologies such as pre-filled pen systems and auto-injectors are expected to see an even sharper rise. For liquids and semi-solids, which contribute 17% of drug product sector revenue, the growth shown in Figure 4 is driven by OTC and generic products.

The participants and mergers

- Diverse nature of players with many private/family owned businesses.
- Europe is the home to many of the leading CMOs.
- Higher valuations are achieved by companies offering more global, integrated and more technology intensive services.
- Merger activity has been strong since our last report. Divestments by pharmaceutical companies appear to be slowing.

Enterprises active in this sector come in all shapes and sizes. Many of them are rooted in fine chemicals, and may possibly have other areas of business that do not require the regulatory standards of pharmaceuticals. Some of the businesses have been built from buying multiple assets from pharma. The major players in the sector, which are in many cases listed, only command a 2-4% market share each. The sector is therefore very fragmented and thus there is room for consolidation. Geographically, Europe is home to most of the top 25 CMOs and even US CMOs have large European operations (e.g. Cambrex). Many of the companies are private or family owned, which explains to some extent the lack of consolidation discussed later in the report.
CMOs are trading at strong EV/EBITDA multiples thanks to substantial growth prospects in the sector

<table>
<thead>
<tr>
<th>CMOs</th>
<th>EV / LTM EBITDA</th>
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<tbody>
<tr>
<td>Patheon</td>
<td>17.1x</td>
</tr>
<tr>
<td>Recipharm</td>
<td>13.0x</td>
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<tr>
<td>Lonza</td>
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<tr>
<td>Catalent</td>
<td>12.6x</td>
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<tr>
<td>AMRI</td>
<td>12.4x</td>
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<tr>
<td>Consort Medical</td>
<td>12.3x</td>
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<tr>
<td>Cambrex</td>
<td>12.0x</td>
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<tr>
<td>Siegfried</td>
<td>11.2x</td>
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<tr>
<td>DSM</td>
<td>9.9x</td>
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<tr>
<td><strong>Median</strong></td>
<td><strong>12.5x</strong></td>
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<th>CROs</th>
<th>EV / LTM EBITDA</th>
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<tbody>
<tr>
<td>Quintiles</td>
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<tr>
<td>PRA Health</td>
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<tr>
<td>INC Research</td>
<td>13.7x</td>
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<tr>
<td>Charles River Labs</td>
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<tr>
<td>ICON</td>
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<tr>
<td>PAREXEL</td>
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<tr>
<td>Lab Corp of America</td>
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<tr>
<td>CMIC</td>
<td>8.3x</td>
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<tr>
<td>EPS</td>
<td>6.7x</td>
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<tr>
<td><strong>Median</strong></td>
<td><strong>12.5x</strong></td>
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Figure 5 Trading EV/EBITDA multiples of selected public companies, as of 13 January 2017

As can be seen in Figure 5, the EV/EBITDA multiples for most of the selected CMOs are between 9x to 13x. Companies which achieve premium valuations demonstrate a number of traits. Companies offering more services across the value chain and integrated services, allowing the formation of strategic partnerships, are more highly cherished by investors. Capabilities in specialized technologies, such as sterile fill, manufacturing of HPAPIs and large molecules/biologics, are more highly valued. Higher multiples are attracted by geographic reach and accreditation with various health agencies, such as the FDA and European Medicines Agency (EMA) – regulators are becoming increasingly demanding, so this is understandably a valued characteristic.

Merger activity has been strong and this is expected to continue. The total value of deals in the pharma outsourcing sector reached $5.5bn in 2014 and rose to over $12bn in 2015. Some of the main reasons for mergers are:

- To gain a more global footprint to meet client needs for global partners and large scale capabilities for greater cost efficiencies;
- To gain access to advanced technologies and provide more specialized services;
- To expand into other service areas and gain complementary capabilities in order to provide integrated services.

Divestments by pharma companies have helped CMOs increase capacities and some CMOs have been substantially built from acquiring divested facilities. There are currently a number of companies undertaking divestment processes but the rate of divestment appears to be slowing. Pharma companies have consolidated following recent mergers and divested non-core manufacturing sites. In addition, much of the consolidation in response to the recent patent cliff has subsided. Nonetheless, the assets are usually of high standard and have historically been run on a relatively high cost base. Acquiring CMOs need to transform these sites from being a cost centre to a profit centre.

Overall, the participants in the outsourced manufacturing market are diverse in size and scope of operation. They range from multibillion dollar pharmaceutical companies with side businesses in outsourcing to much smaller family/privately owned enterprises. The market still remains fragmented and consolidation has proven to be slow. Merger activity has been strong and this is expected to continue. Even though divestments from big pharmaceutical companies are slowing, there are still a number of opportunities to build businesses in this way.

As may be expected, not all of the mergers have run smoothly. Based on a Moody’s report, Aenova’s integration of Haupt has not achieved cost savings as quickly as planned. Within private companies, the cost structures, modes of operation, company culture and financial motivation of owners can be highly variable. This provides a challenge to M&A negotiations, due diligences and the subsequent effort to integrate entities.
Trends

One-Stop-Shop

- One-Stop-Shop is potentially a valuable differentiation strategy for CMOs.
- Although popular, the proof of concept for the strategy is limited and not all customers can benefit equally.
- One-Stop-Shop is partly a driver for M&A activity.

In 2016, Lonza announced that it is to build capabilities for drug product development services, as part of a One-Stop-Shop strategy for customers. The trend is evident across the sector, which theoretically should benefit both the customer and CMO. The notion is to offer a multitude of services to a customer, which should benefit from the convenience and efficiency of dealing with a single provider. The relationship should create the opportunity for the CMO to sell more products to the same customer, as well as develop lock-in models through increased switching costs.

By being able to produce API and DP, the customer can place one order for DP product and does not have to manage two supplier relationships with a separate API and DP supplier. The model extends to the bundling of CDMO services with CRO services to provide an integrated pre-clinical product supply and service package, the service package being normally the larger element. Examples include Aptuit’s “Indigo” offering and Almac’s (API & DP CDMO/CMO) collaboration with Covance (CRO). The objective of this bundled offering is to get products to “first in man” clinical trials as quickly as possible. The time benefit can be substantial: a typical drug makes $1 m/day profit during the period of sales under patent. Pharma companies try to ensure DP supply during clinical trials is not on the critical path, but this can result in having to make production commitments early, which can be trickier with multiple suppliers.

There is limited evidence of the success of the One-Stop-Shop strategy. It is positioned as a valuable service to start-up companies who have limited in-house resources. Smaller companies that do not have a procurement department may benefit from dealing with a smaller number of providers. Each provider is a new agreement or contract, a relationship to monitor performance on and if materials need to be transferred between providers it can be an unnecessary headache. However, small customers may not feel comfortable with large One-Stop-Shop providers, which may be perceived to prioritise larger customers. As with smaller companies, larger customers could also benefit from fewer relationships; strategic partnerships that have been seen in the industry can help to achieve this simplification. Nonetheless, larger companies may have different procurement teams looking at different areas of service needs. Thus, the relationship with one team may not travel to another team leading to the breakdown of the integrated model.

Adoption to the model is slowed by existing arrangements, particularly extended commitments. The time and cost for a pharma company to switch an existing launched drug from a multi-supplier supply chain to One-Stop-Shop are considerable; therefore, there would need to be a very large cost benefit to make the switch. For new products or projects, the attraction of One-Stop-Shop is greater. There is potential to get a product into a clinical trial more quickly if the CMO operates as an integrated team – faster to transfer product between API and DP plant internally rather than between two CMOs. It can be a better solution for challenging APIs, such as where API and DP manufacturing integration may be preferable.

What is clear is that One-Stop-Shop is being promoted as a differentiation strategy by the major players rather than there being a clear demand from customers. It is a marketing strategy that does not always reflect how big pharma sources CMO services (clinical supply, DP and API may be allocated to different sourcing agents within big pharma). Many companies
## Benefits of the One-Stop-Shop Model

<table>
<thead>
<tr>
<th>CMO with One-Stop-Shop</th>
<th>Customer</th>
<th>Investor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketing benefit/Differentiation strategy</td>
<td>Fewer supplier relationships</td>
<td>Ability to add value through investment</td>
</tr>
<tr>
<td>Cross selling/fewer relationships</td>
<td>Seamless transition between stages of development and production</td>
<td>Opportunities to combine enterprises to build One-Stop-Shop leaders</td>
</tr>
<tr>
<td>Ability to form strategic relationships that offer a range of services</td>
<td>May make outsourcing more attractive</td>
<td>Diversity of investment opportunities</td>
</tr>
<tr>
<td>Lock in customers through switching costs</td>
<td>May benefit product chemistry</td>
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*Table 1*

Continue to specialise in either API or DP, including some of the largest enterprises. For CMOs with a One-Stop-Shop model, and assuming sufficient scale, there are advantages. This has led to a number of mergers and expansions into new areas. As well as differentiation, the strategy can be seen as part of the consolidation trend in the industry, which is making companies target a minimum size. Overall, major CMOs who have competitive offerings in API and DP can increase profitability by reducing the competitive pressure they face through successful positioning of One-Stop-Shop.

### Consolidation and geographic reach

- The sector is fragmented and consolidating slowly.
- M&A activity has been strong in recent years, reaching $12bn in 2015.
- In comparison to CROs, the CMO sector is less consolidated and has few motivations to consolidate.
- Consolidation is helped by PE activity that is financing consolidation.

As highlighted previously in this report, the sector is characterised by fragmentation and slow paced consolidation. The sector has many private companies, as well as a long tail of small companies. Significant companies, including some listed enterprises, remain controlled by their founders or their families. Private control to some extent may explain the rate of consolidation, as owners may not wish to sell for personal reasons even when presented with lucrative offers. Our analysis indicates that the small molecule CMO market is consolidating at 10%-20% per annum, which is not as fast as may be warranted by the larger CMOs. The total value of M&A transactions in the

**Figure 6:** Consolidation of the CMO sector

Historically, consolidation in the CMO sector has been slow, leading to fragmentation with many small companies.

**Pharma outsourcing market**

~$71.5bn

**Consolidation**

10-20% of market per year

Total value of M&A transactions in Pharma outsourcing sector: $5.5bn (2014) to $12bn (2015)

**Consolidated market**
pharma outsourcing sector rose from $5.5bn (2014) to $12bn (2015). There is no strong drive from customers to consolidate. Nonetheless, CMOs can potentially benefit from synergies from being a larger player.

In comparison to the CRO industry, which shares a similar customer base, the CMO sector is far less consolidated. The top 7 CROs are estimated to capture over 50% of the market, whereas the top 10 CMOs are expected to have less than 30% of market share. The CRO market has consolidated, driven by the benefits of scale economies and drivers to outsource. Clinical trial companies, like Quintiles that have critical mass, are able to offer global clinical trials, solving the issues of coordinating multiple sites for pharmaceutical companies. Consolidation in the CMO sector has not been occurring at the same pace as the CRO sector, as companies are not under the same pressure to reach a critical mass.

Consolidation is happening through CMOs acquiring other CMOs (e.g. AMRI buying Euticals). Also, generics companies are merging, impacting consolidation amongst the generic API and DP supply base, because many generics companies also supply to other companies (e.g. Strides’ merger with Shasun). Strategic as well as financial investors are active in the sector, and PE companies are in some cases acting as consolidators.

The slow rate of consolidation is determined by several factors:

- **Consolidation is inhibited by the high exit barriers for traditional western CMOs and relatively low entry barriers for un-differentiated competitors from India/China**;
- **Consolidation is usually driven by market leaders. In recent times, several market leaders (Lonza, DSM, Dow Chemical, Rhodia, BASF) have either been in a weak position corporately (e.g. Lonza) or have regarded their CMO business as non-core**;
- **Many mid- and small-sized CMOs are family owned, these companies are less interested in growth via acquisition**.

Consolidation is now being driven by leading players and their private equity backers (e.g. DPx/Pathenon and ICIG). Involvement of PE firms in the sector means that M&A activity will likely remain strong going forward as they seek to grow acquired businesses through bolt-on acquisitions. Injection of fresh capital by PE firms will help drive growth of the sector.

**The rate at which consolidation is occurring at present is expected to support sustained or higher profitability for participants in the CMO market, especially when added to the current regulatory difficulties of several suppliers in India and China**.

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**Searching for niches of profitability**

- Biologics have attracted a large degree of investment for capacity building. The cost of capacity and needed know-how can hinder investment.
- The industry needs to take stock of the capacity it needs for the coming years. Lead times are significant to bring new capacity on-board.
- The more challenging HPAPI capacity has attracted investment, linked to the growth of the oncology therapeutic area.
- For DP, sterile and aseptic fill has similarly attracted investment.

Companies such as Bachem for peptide chemistry have used specialist knowledge in a particular segment to drive sales. Individual CMOs are continually looking for niches where they may have an advantageous position. The capital investment and regulatory approval process make it difficult to stay ahead of the curve for the demands of tomorrow. There have been a number of areas in the CMO Industry where capacity has been built up in anticipation of demand.

Biologics are one of the anticipated growth areas and capacity has been built up to respond to this. Historically, pharmaceutical companies often favour in-house production for biologics. There are a number of reasons for this, such as utilising internal capacity, difficulties of moving processes and security of supply. Nonetheless, outsourcing for biologics may improve in the future, as obstacles are overcome and pressures to outsource increase.

Another area has been HPAPI, which requires special manufacturing conditions to reflect the hazards of the substance group. The HPAPI manufacturing market is one of the strongest growing outsourcing sectors at a CAGR of 8.5%. Market penetration is the highest in the sector at over 34%, which will increase only modestly until 2021 as both CMOs and pharma are investing in manufacturing capacity. According to our analysis, approximately $2.5bn of new business is forecast to be generated between 2017 and 2021, meaning significant opportunity to gain market share for suppliers that have this capability. Growth in the sector is driven by strong growth of the biologics and oncologic markets, with 60% of oncology drugs being HPAPIs.

Beyond API capability, capabilities to handle HPAPIs during DP formulation and manufacture in dedicated suites are also in strong demand. The sector has seen significant investment in
additional capacity over the last 10 years to satisfy demand. At least 60 investments to add new facilities or extend existing capacity have been made since 2006, both for API and DP manufacturing. Some major investments in recent years include:

- New HPAPI facility in Shanghai by WuXi in 2014;
- Expansion of existing capacity at UK HPAPI facility by DPx/Pathen in 2014;
- Fareva announced a €25m investment in a recently acquired asset in La Vallée, France to add HPAPI capable facilities in 2015;
- Fermion announced in 2016 a €30m investment in its Hanko facility which will add additional HPAPI capacity;
- Alcami will open a new 500m² kilolab scale facility during Q1 2017.

Other areas identified include sterile and aseptic fill, where a number of acquisitions have included obtaining additional capacity. This is helped by the growth trend for biologics. A further DP area that has attracted interest is coatings and controlled release technologies.

Company strategies

- Most western companies see themselves as differentiated players.
- One-Stop-Shop is a popular strategy pursued by the large players.
- In the atmosphere of consolidation, size has been a goal for acquisitions.
- M&A is not a strategy followed by all, linked to the peculiarities of private and family ownership.

Some companies have focussed on buying assets (e.g. manufacturing facilities) rather than buying complete enterprises. Such assets often come with supply agreements; however, the acquirer needs to transform the business into a profit centre – manufacturing facilities within pharma companies are managed more like cost centres. Assuming they wish to continue the operation, they need to find new products to add to their pipeline to secure the future financial viability.

In response to increased low cost competition, western API companies have pursued differentiation strategies. There are few companies that would not claim to be differentiated in some way. Companies with a strong chemicals heritage, such as BASF and Evonik, have focussed on API. Some companies have diversified into nutrition and cosmetics. The profitability of such strategy has not been analysed, however, there are conflicts in mind-set that need to be resolved as pharmaceutical production is more regulated and producing cosmetics in a pharmaceutical setup may not be profitable.

The trend of consolidation has been motivated by a desire to build critical mass. With many small CMOs being in precarious financial positions, larger companies can be viewed more favourably by customers that wish to ensure that their supply is secure. Supporting this trend, PE activity has been transforming the sector through aiding consolidation and providing an instrument for restructuring. Aeonova is good example of this, which, back by BC Partners, has aggressively grown from $300m revenue in 2011 to over $800m through multiple acquisitions. Reflecting on the industries fragmentation, building companies with greater market shares is one of the ways to build a brand in an industry with many small players.

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Concluding remarks

Based on our analysis, the outsourced manufacturing sector is a fertile ground for investment, based on the growth prospects above expected GDP growth and the sub-sectors that can excel in the sector. Industry M&A trends over the last decade have transformed the outsourced manufacturing sector with some significant players emerging. Consolidation has not occurred at the pace envisioned by a number of industry leaders with the sector remaining fragmented, where opportunities exist for acquisitions.

The pharmaceutical sector is expected to come under more price pressure in response to the rising cost of healthcare and the need to balance budgets. In addition, the short-term growth boost from new medicines in hepatitis and cancer is expected to dwindle in the coming years. Outsourcing can be seen as a solution to reduce costs, so the sector could benefit from the trend. With the regulatory pressures of recent years, the choice of suppliers is more constrained, which places suppliers that meet regulatory requirements in a better negotiating position. Tougher enforcement of regulation has disproportionately impacted Asian companies, which has encouraged pharmaceutical companies to emphasise more the security of supply over potentially short-term cost savings.

The strategic direction of many leading CMOs is differentiation in an attempt to capture value. One-Stop-Shop is a strategy that has been used by some of the larger players to set themselves apart. Despite the plausibility of the strategy, the benefits to the client are not always clear. In the wave of announcements regarding investment in biologics, investors need to also consider the prospects for small molecules, which account for the majority of the market.

Not all sub-sectors are growing equally and new technologies are continually emerging. Investments in the sector need to take this into account. In addition, the routes to investing in the sector need to be congruent with the capabilities and strategy of the acquirer. The routes include buying complete enterprises, carve-outs and buying assets from the pharmaceutical industry, as well as organic growth.

Overall, the analysis indicates that the prospects for the sector are positive. The sector’s customers are expected to outsource more in the coming years. More importantly the growth is driven by factors affecting healthcare, such as economic growth and ageing population. To capture the expected growth and potentially perform better than the sector average, acquisitions need to factor in growth subsectors and the synergies with the acquirer. Small molecules should not be forgotten, as the outsourcing trends indicate potential for the outsourced manufacturing sector. As with any investment, due diligence and sector know-how remains key.