WHITEPAPER

Custom manufacturing in pharma – Why only the best survive

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The pharmaceuticals industry is undergoing dramatic change. The challenges: Empty product pipelines, pressure on prices, and emerging global markets. Only contract synthesis manufacturers who stand out due to particular skills or a wide range of services and are able to adapt rapidly to changed requirements will survive in this fiercely contested market.

The times when pharmaceuticals companies saw production as their core business are long gone. The logical consequence is that demand for „custom manufacturing" is gaining in impetus. Pharmaceuticals manufacturers are now considering quite specifically which parts of their production they can outsource to external service providers. More and more manufacturers are using their own resources to develop new active pharmaceutical ingredients (APIs), and above all for branding and marketing. Outsourcing is in. Following the big blockbuster era, contract development and manufacturing organizations (CMDOs) in the pharmaceuticals world are definitely on the up.

>> Full service across the whole value chain is becoming fashionable

What drives the market

According to the market research company IQ4I Research & Consultancy, amongst the key factors driving the market in pharmaceutical custom manufacturing are expiring patents on low-molecular drugs, the growing number of small molecules in clinical trials, a general trend towards outsourcing, investments by CDMOs, the increase in chronic and age-related diseases, the rapid growth in the oncology market, and new technological possibilities. But there are also obstacles putting a block on growth. These include contaminations, undesirable side-effects, the growing number of biologicals, and the very rigorous regulations. The market for biologicals is growing, although small molecules continue to be the primary driver in the global treatment market. According to research by IQ4I Research & Consultancy, in 2018 the FDA approved 59 drugs, of which only 17 were biologicals. With many small molecules, the patents are running out, smoothing the way for generics. Last year, 23 were licensed. The „imitators" are the most important driver for the market in custom manufacturing, which in 2018 posted its highest sales to date for API production and is set to enjoy further growth. Here, the expiry of patent protection plays into the hands of the providers. CDMOs with access to advanced technologies, such as continuous flow processes, low-temperature reactors and high containment plants, further increase the incentive to increasingly outsource production.

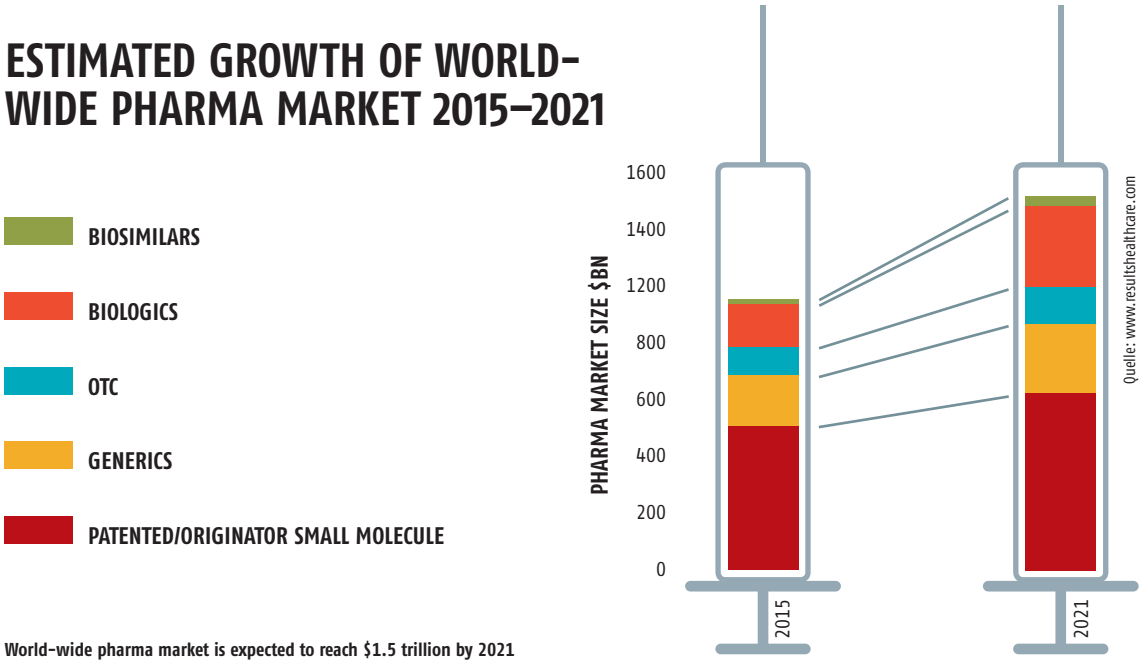
The market for finished dosage forms (FDFs) is also set to grow continuously to 2025, according to figures from the market research company. The causes for this are rising demand, increasing forms of dosing with controlled release, oral forms of administration for cancer treatment and the growth of generics in the area of injection agents.

Pharmaceuticals sector under pressure

According to the study „The pharmaceutical CMDO industry is consolidating" by auditors Ernst & Young (EY), the segment is growing at six to seven percent per annum, meaning that it is outperforming the pharmaceuticals business as a whole (up five to six percent). In 2016, sales by custom manufacturers worldwide were USD 62 billion.

In many countries, the healthcare sector is coming up against its limits. Governments

ESTIMATED GROWTH OF WORLD-WIDE PHARMA MARKET 2015–2021



World-wide pharma market is expected to reach $1.5 trillion by 2021

are passing on price pressure in full. „The financial pressure is so great that pharmaceuticals companies are outsourcing ever larger parts of the value chain, in order to be able to handle the risks involved in developing new drugs more efficiently and with greater agility," says Matthias Groh, a strategic consultant for Life Sciences at EY

Win-win situation for all

With the need to lower costs, the pharmaceuticals industry has rung in a paradigm shift from a vertically integrated business model to a supplier network. Custom manufacturers have become a key part of the pharmaceuticals market. They offer their customers a dynamic business model that extends beyond traditional production and increasingly covers the entire value chain.

For their part, pharmaceuticals companies benefit from not needing to invest a lot of money in building plants for new APIs. Outsourcing is the far safer option. After all, what happens with capacities that have already been built up if the drug fails in the third phase of its clinical trials? And that is a scenario which, in the past, all too often proved to be a reality. Even in the event of successful licensing, in the start-up phase it is difficult to estimate the production capacities required for patented drugs. The necessary flexibility can be realized at relatively low risk through outsourcing the investment-intensive production. That allows pharmaceuticals companies to concentrate their manpower on elements of the value chain that are more critical in competition.

One-stop shops making headway

Custom synthesis providers looking to perform at top level know the market and its requirements. They are either established experts in their field, with special synthesis expertise, or generalists who offer a wide range of services upstream and downstream of the actual production, through to „full service" – from market monitoring to consultancy, ideas for new products and their development, flexible and regulation-compliant production through to formulation and distribution. In other words, they master the entire global supply chain. But there will still continue to be providers whose „portfolio" consists of a single molecule. In a fiercely competitive environment, it is always an advantage to have a USP in your niche area. To sum up, custom manufacturers don't need to be able to do everything. But what they do needs to be good. To stand out in the international market from the many providers,

Bild: Lonza

Worker taking a sample.

however, many CDMOs have decided to offer the customer value-added in future through the full life cycle of pharmaceutical active ingredients.

Today, the pharmaceuticals industry accordingly expects customized all-round worry-free packages, enabling it to react more quickly to new trends, to implement product adjustments driven by the market or by instructions more quickly, and to shorten time to market.

The key phrase is customer service

Pharmaceuticals companies and CDMOs are increasingly acting as strategic partners. Here, price is certainly not (or no longer) the last word. Success will come only to those alliances which are based on good customer relations. Today, it is not enough simply to answer inquiries quickly and competently. Every custom manufacturer needs to measure up to major, international competition. In this environment, good customer service is something of a „secret weapon“. In fact, it is often the thing that tips the balance for long-term partnerships. According to experts, the pharmaceuticals industry is increasingly relying on „preferred suppliers“, because companies can then also save significantly more costs that way. But for that to work, „the chemistry needs to be right“ between client and provider. That well-known saying has lost nothing in translation when applied to the CDMO business.

Europe is holding many trump cards

Flat hierarchies generate a critical advantage for custom manufacturers, who are generally SMEs, compared to manufacturing pharmaceuticals companies, who for historical reasons are often trapped in rigid structures – and that advantage is great flexibility. Diverse, state-of-the-art synthesis possibilities and a high degree of automation enable many providers in Europe to achieve production that is best-prepared for all eventualities, in their multi-purpose plants. And when it comes to energy efficiency, too, the „old world“ may well have its nose in front.

Reliability and delivery on time go without saying, as with any other service. High plant safety and compliance with statutory regu-

lations, such as for explosion protection or GMP and FDA-compliant plants, are further arguments that European manufacturers are able to put on the scales. Often, strength of innovation is also a criterion that proves decisive in whether new customers can be acquired and retained.

The key to success is comprehensive solutions for complex, constantly changing requirements. Providers in the German-speaking region have done their homework. Thus they are able, for instance, to leverage their expertise for complex products based on multiple synthesis stages. Even where the stability of an active ingredient is dependent on the formulation and where that makes close collaboration with the client necessary, custom manufacturers based here can score through their proximity to the customer. The steady increase in energy prices also contributes to a modest degree too, in that the price difference compared to the competition – particularly from Asia – is falling all the time due to the higher transport costs.

North America has the biggest slice of the cake

In terms of market share in pharmaceutical custom manufacturing, North America has its nose in front. The USA accounts for the largest sales. Growth is being driven by the high investments in cardiovascular and cancer research, the growing demand for active ingredients for cancer and generics. Additionally, government reforms and the large number of FDA-compliant production plants are having a positive effect. That is the conclusion reached by IQ4I Research & Consultancy in their report „Pharmaceutical Contract Manufacturing Global Market - Forecast To 2025“. Last year, Europe succeeded in taking second spot. Here, Italy and Germany are dominant. Italy is the leading country for API manufacture, with three-quarters of sales being generated by exports. Germany leads the market for finished medicinal products. For the coming years, high single-figure growth rates are forecast for the Asia-Pacific region. The number of generics

Bild: Lonza

In USA Lonza is running a large scale production.

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Modern bioreactor technology is a must for contract manufacturers.

manufacturers is growing. In addition, there is a higher standard of living and life expectancy, along with rising population figures. China and India can offer the lowest costs of manufacture, due to the low wages of fully qualified employees. The focus in India is on the production of generics for the world market.

It is expected that the global market for pharmaceutical custom manufacturing will reach USD 95,904.9 million by 2025. The estimated capacity of the CDMOs is around 43% of the total production volume in the pharmaceuticals industry. In 2018, global production of low-molecular APIs was around 350 tons, according to estimates. More than half of this was manufactured by external providers.

The market share of the 15 biggest actors, according to research by the analysts at the market research company, was 10%-15%. The leading players in the global market include Aenova Holding (Germany), Cambrex Corporation (USA), Abbvie Contract Manufacturing (USA), Patheon (Thermo Fisher Scientific) (Netherlands), Albany Molecular Research (USA), Famar (Greece), Lonza Group (Switzerland), Glaxo Smith Kline (UK), Pfizer Centre One (USA), Wuxi STA Pharmaceutical (China), Almac (UK), and Recipharm (Sweden).

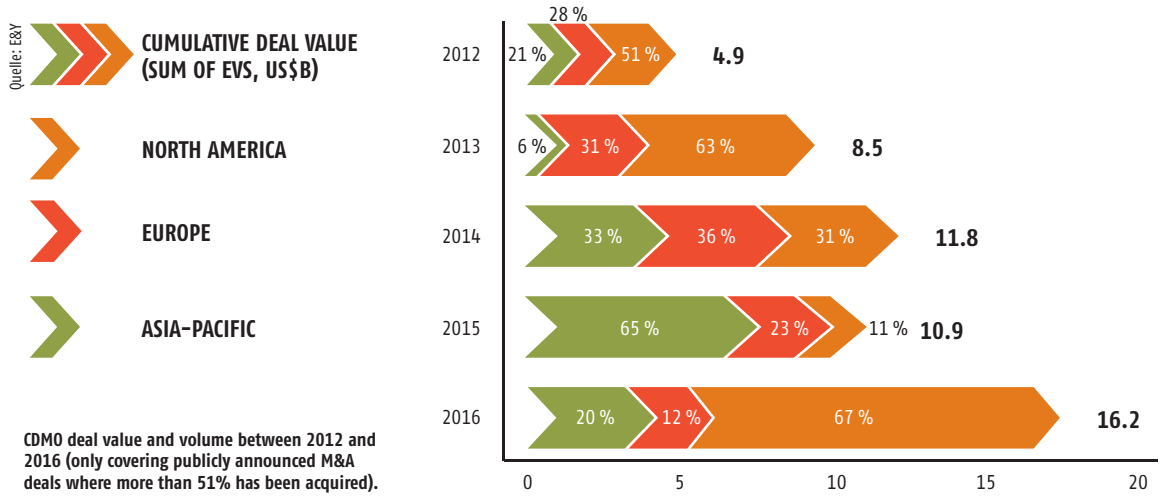
Consolidation is in full swing

For the pharmaceuticals industry, the CDMO market is simultaneously attractive on two counts: 1. As a business partner for outsourcing, 2. The companies can create a new pillar for themselves with subsidiaries operating freely in the market for custom synthesis.

According to EY, the forecasts are so tempting that even non-sector „tech giants“ such as Samsung can‘t resist. And the South Koreans have big plans: In Samsung Biologics, they are looking to develop the world‘s biggest biopharma production.

When it comes to mergers & acquisitions (M&A), as expected it is the „usual suspects“ who occupy the top slots. Heading the list of „top consolidators“ is Recipharm from Sweden, followed by ANRI and Patheon from the USA.

M&A VALUE AND VOLUME ARE GROWING



CDMO deal value and volume between 2012 and 2016 (only covering publicly announced M&A deals where more than 51% has been acquired).

So CDMOs are proving popular, and interest in M&A is growing, including with investors. The logical consequence is that the volume of transactions has grown from USD 4.9 billion in 2012 to USD 16.2 billion today. That corresponds to a 35 percent increase per annum.

The biggest deal to date was concluded in May 2017, When life science company Thermo Fisher Scientific acquired one of the world's leading companies, Patheon, for USD 7.2 billion.

In a heavily fragmented market with around 600 companies, consolidation and alliances are set to open up new, emerging markets and niche segments. Incidentally, company size makes little difference here.

Jörn Leewe, Partner at EY for Life Science Strategy, sees two key trends dominating future consolidation: Large CDMOs such as Patheon or Lonza are directing their M&A activities in a targeted way to close gaps in their value chain in order to satisfy every preference when it comes to outsourcing. This applies particularly for providers in Europe and North America.

Conclusion

There are many reasons arguing in favor of outsourcing, whether these are due to a lack of own capacities or focusing on more promising elements of the value chain from a profit perspective, such as development and/or marketing. But in every instance, one thing is sure – and probably also necessary: the pharmaceuticals industry can reduce its costs by doing so.

Custom manufacturers are enjoying a boom, and can even pride themselves on a higher rate of growth than the pharmaceuticals industry, which in the past has been blessed with growth other sectors can only dream of. These findings come from the auditors Ernst & Young. And they are arousing fresh interest, including from investors outside the sector. A wave of M&A is set to roll over the heavily fragmented market in CDMO, which will see fresh consolidation in the sector.

In order to remain competitive internationally, the service providers must either sharpen up their profile, or significantly expand their range of services along the value chain. Providers from Europe can defy competitors from low-wage countries with excellent synthesis know-how, modern multi-purpose plants, higher plant safety and good customer service.

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