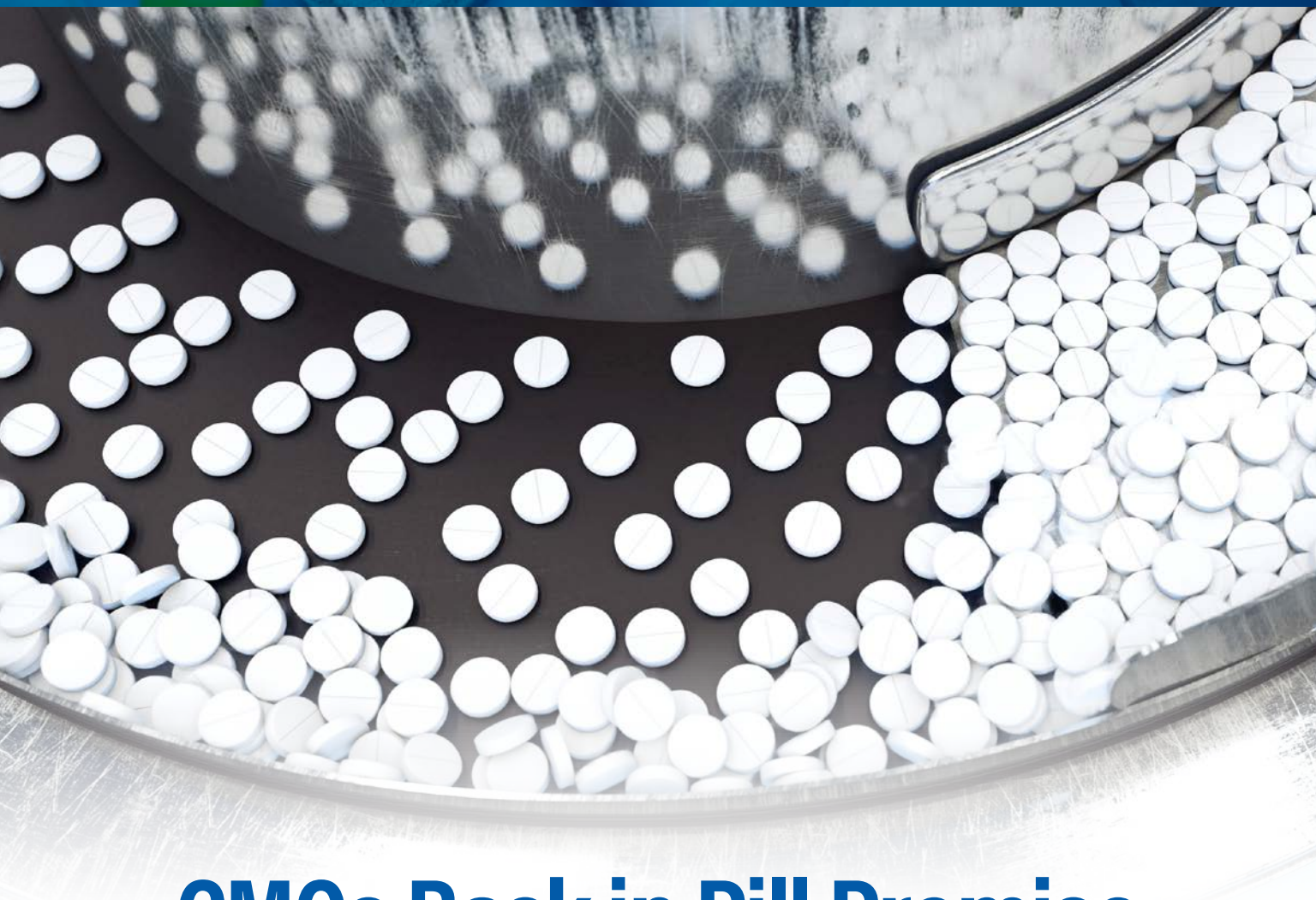

CMOs Bask in Pill Promise

OSD outsourcing expands as CMOs excel.

This is the second of a nine-part series of articles addressing pharmaceutical outsourcing industry trends.

SOMAN HARACHAND - CONTRIBUTING WRITER, CONTRACT PHARMA

A pill is always preferred to a prick. This simple premise, perhaps, explains why the oldest form of drug delivery are oral solids, which continue to dominate therapeutics pipelines despite the overarching influence of the all-new, all-powerful biologics.

As the most prescribed medications, oral solid dosages (OSDs) claim the lion's share of CMO and CDMO capacities the world over.

Contract manufacturing organizations (CMOs) say that the number of big pharma companies approaching them for OSD manufacturing and development services is increasing by the day.

"I see an increased trend in outsourcing [OSDs] recently, especially from Europe," says Dr. Krishna Prasad Chigurupati, chairman and managing director of Granules India, adding that he also notices an increased interest in in-licensing of OSDs too.

Granules is the global leader in the manufacturing of paracetamol, metformin, guaifenesin, and methocarbamol, as per the company website. With half-a-dozen facilities located in India and U.S., the Hyderabad, southern India-based integrated manufacturing company supplies active pharmaceutical ingredients (APIs), fixed dosage and pre-formulation intermediates (PFIs) to

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> —ABHIJIT BASAK, ERNST & YOUNG

over 70 countries around the world.

Further, Dr. Chigurupati adds that there seems to be a rising interest in outsourcing onco-OSDs, also.

DRIVING VALUE

CMOs anticipate an increase in demand in the coming days as well, as the sponsors have more OSD products in their pipelines.

A survey by Nice Insight reveals that solid dose manufacturing will be outsourced with the greatest frequency at 55 percent among the various pharmaceutical formulations.

Even though the market value percentage of solid dosages has been showing a downward trend owing to the shift towards high-value biologics, the propensity to outsource OSDs continues to grow albeit at a modest pace, aver analysts.

The global oral solid dosage contract manufacturing market size was valued at $34.3 billion in 2022 and is anticipated to exhibit a compound annual growth rate of 6.0% from 2023 to 2030, according to data provided by Research & Markets, a market research firm headquartered in Dublin, Ireland.

The increasing complexity of new drug molecules, R&D investments by large CMOs and contract development and manufacturing organizations (CDMOs), and rising demand for new therapies are driving the growth of the market.

Both large and small pharmaceutical companies weigh outsourcing OSD manufacturing as an important strategy, faced with rising cost pressures and a need to reduce time-to-market.

A growing number of innovators without in-house resources to take the molecules into the clinic are also looking for outsourcing partners that have a broad range of services that can take responsibility for development from the start.

In the meantime, CDMOs keep on investing in new equipment and facilities, provide dedicated project management support with personalized service, and offer real manufacturing flexibility.

While innovators are looking for solutions from the CDMOs in the new chemical entity (NCE) environment, the present trend on the generics outsourcing front is different.

In generics, it is all about adding value to what the CMOs are offering, aver experts. It is no longer acceptable to only serve as a "pair of hands" for the sponsoring companies. Today's CMOs must drive value using their technology, their development speed, and manufacturing capabilities. CMOs also must have quality people who are technically sound on par, at least, with the customer so that they can have one-to-one equal-level conversations and demonstrate trust, and drive value for the customer.

Excellence in manufacturing is key to business success, and CMOs, oftentimes, exceed sponsor expectations.

TECHNOLOGY IS CRITICAL

Evidently, specialized know-how gives an obvious edge to the CMO as it will drive outsourcing of OSD production.

To leverage the opportunity, flexible contract service providers address this challenge by developing newer processing technologies.

Granules India, for example, has pioneered the commercialization of pre-formulation intermediates and is currently one of the largest suppliers of PFIs in the world.

"We have developed an unimaginable scale in PFIs, especially with large batch sizes. This offers Granules economies of scale in manufacturing of OSDs," says Dr. Chigurupati.

Granules' experience over a decade producing millions of tons has given the company the capability of making PFIs which can run at very high speeds on compression machines. In addition, the scale allows Granules to operate high-capacity continuous coaters, both of which reduce the cost. It is not only the PFIs, but the company has also integrated the production of some of its major products right from the intermediate level. This also offers a one-stop solution for Granules' customers.

According to Granules, PFIs enable ease of operations for the manufacturer and offer cost and quality advantages on the supply chain, testing, technical and capital resources fronts at finished dosage manufacturers' sites.

Granules is a preferred PFI supplier to several global pharma companies. PFIs accounted for 22% of the company's total revenue in FY2021-22, shows its annual report.

Dr. Chigurupati affirms that technology will play a critical role in enhancing and optimizing capacities, capabilities, processes, and quality standards while ensuring cost efficiency for the business and customers.

DEMAND FOR DIFFERENTIATORS

In a similar way, the dose form is very important in today's environment where reimbursement is often based on clinical outcomes of therapeutics. Hence, patient acceptance of the treatment such as dose burden, swallowability, regimen com-

plexity, etc., as well as the treatment cost are significant.

Surveys indicate that timed-release technologies, either rapid or delayed, are found to be highly preferred. Among the multiple OSD delivery platforms, controlled release (CR) tablets are of the most interest. These product types are expected to be one of the top areas of growth for outsourced oral-dose manufacturing.

There is currently "a very high interest" in in-licensing Granule's CR and extended-release (ER) OSDs, according to Dr. Chigurupati.

Modified release reformulations can be a superior product when compared to the original drug in terms of efficacy, patient compliance, adverse reaction profile, etc. By reformulating a drug into a CR version, a company improves its efficacy, market success and extends patent protection.

"For an OSD contract services provider, development of a drug delivery platform technology is a key differentiator that gives a competitive edge to the firm in the marketplace, in terms of both positioning and price realization and more so in regulated markets," says Abhijit Basak, partner, life sciences strategy and transactions, Ernst & Young—Parthenon, Mumbai.

He adds that CDMOs, in fact, have moved away further from the controlled release or enteric-coated capsule delivery mechanisms to more complex dosage forms.

GO-TO (EMERGING) MARKETS

Reports indicating outsourcing behaviors say that pharma companies demonstrate a preference for considering CMOs/CDMOs from emerging markets such as China and India for OSD manufacturing. Outsourcing activity is quite substantial in the generics space in these markets compared to that for NCEs.

But many companies from Europe and North America are concerned that CMOs based in emerging markets may not have the same level of experience and expertise in IP protection and legal compliance as those in developed markets, which can increase the risk of IP infringement.

"However, it is important to note", say Aameena Taj and Rucha Kamdi, analysts from Grand View Research wing of Research & Markets, "that there are also CMOs based in emerging markets that have taken steps to address IP concerns and provide the necessary level of protection for their clients' products."

These CMOs and CDMOs are implementing IT controls, providing training to raise awareness about the importance of IP, conducting background checks on employees, and using confidentiality agreements with employees.

However, they caution drug firms to conduct thorough due diligence before selecting any CMO.

Moreover, IP issues correspond more strongly to primary manufacturing/API production than secondary manufacturing of OSDs, aver some experts.

Others maintain that whether it is manufacturing or development, there will be elements of innovation. Of course, the probability of infringement would occur more when the development aspect is involved.

However, leading CDMOs headquartered in India are of the view that concerns about IP are more of a myth, today, than a reality.

They say that the IP issues no longer figure high in the conversation with clients as used to be the case 5 or 10 years ago. Many CMOs and CDMOs have robust IT systems to put them on par with their counterparts in the EU or North America and safeguard the customer's IP data in every possible way.

SUPPLY SECURITY: THE WATCHWORD?

Disruptions in supply chain logistics and raw material capacity constraints that became acute during the pandemic continue to remain a source of concern for outsourcing firms.

The challenges could worsen in the coming days as the geopolitical tensions across the globe are feared to escalate further, many think.

Customers are now realizing that supply security is more important than price, points out a senior official from an Indian CMO. However, he appeared confident that the change is transitory and will smoothen out going forward.

Domain experts maintain that realignment mechanisms to mitigate the impact of current supply chain woes are slowly but steadily taking shape showing a tendency to get more regionalized than global.

"During the pandemic, associated and continued lockdowns in China, and the pharmaceuticals supply chain, which was consolidating over the last two decades, had created a supply crisis. While this pushed up prices of APIs and KSMs, it is also compelling global pharma firms into looking at regional supply hubs. This is an opportunity waiting to be explored," says Suresh Subramanian, partner, national life science leader, Ernst &Young, LLP.

Regional capabilities have become a must to de-risk the supply chain as the companies should not remain captive to one particular source. More companies, not just the generic industry but the innovators as well, will be re-routing to these regional hubs as part of de-risking their supply chain strategy and this will further facilitate growth in outsourcing.

Considering India's strengths in OSDs, Subramanian says it's likely the country will become a very important component in the global OSD outsourcing space as well as in the global supply chain de-risking play. **CP**

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