Inside the Trenches: End-To-End CDMOs/CMOs

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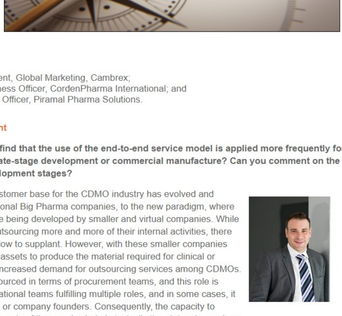


What does it take to implement an end-to-end-business model, meaning a single CDMO/CMO providing development and manufacturing services for both active pharmaceutical ingredients (APIs) and drug products?, from end-to-end CDMOs/CMOs.

An inside view

To gain a better understanding of the implementation of the end-to-end service model in terms of sponsor relationships, project management, and supplier metrics, *DCAT Value Chain Insights*, gained the input of some end-to-end providers for an "inside-the-trenches" view. Participating in the roundtable are:

- Matthew Moorcroft, PhD, Vice President, Global Marketing, Cambrex;
- Michael Quirmbach, PhD, Chief Business Officer, CordenPharma International; and
- Stuart Needleman, Chief Commercial Officer, Piramal Pharma Solutions.

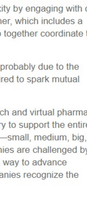
Early-stage versus late-stage development

Question: From your experience, do you find that the use of the end-to-end service model is applied more frequently for early-stage development as opposed to late-stage development or commercial manufacture? Can you comment on the use of the end-to-end model across development stages?

Matthew Moorcroft, PhD
Vice President,
Global Marketing
Cambrex

Moorcroft (Cambrex): The nature of the customer base for the CDMO industry has evolved and shifted away from being dominated by traditional Big Pharma companies, to the new paradigm, where the majority of new drugs in development are being developed by smaller and virtual companies. While Big Pharma companies were increasingly outsourcing more and more of their internal activities, there was always a captive component that was slow to supplant. However, with these smaller companies that often lack the necessary manufacturing assets to produce the material required for clinical or commercial supply, this dynamic has led to increased demand for outsourcing services among CDMOs. These smaller companies are often less resourced in terms of procurement teams, and this role is typically undertaken by the scientific or operational teams fulfilling multiple roles, and in some cases, it is even handled by the C-suite management or company founders. Consequently, the capacity to manage numerous suppliers across multiple parts of the supply chain is typically time-intensive and can lead to strains upon resources, and is one of the main drivers that the industry has benefited from in the birth of the 'full-service' CDMO.

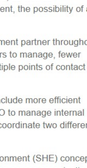
It is still in the early days of this approach, but there have been some attempts to quantify the true cost benefits within the industry, and some recent studies are extremely bullish about the advantages. While the data are still being generated, in its simplest sense, the industry is increasingly recognizing that it is beneficial to all customers, whether big or small, to deal with just one supplier for all of its products and services as opposed to many.



Michael Quirmbach, PhD
Chief Business Officer
CordenPharma International

Through the recent acquisitions of Halo Pharma in 2018 and Avista Pharma Solutions in 2019, Cambrex has added drug-product manufacturing and analytical services to its expertise in drug substances, and offering end-to-end services. As well as the additional services to develop and manufacture small-molecule therapeutics, these acquisitions have brought hundreds of new customers and capabilities to the company, which can benefit from a broader range of product lifecycle management than previously possible. Having integrated services can further improve delivery timelines for customers by efficiently transferring products to larger-scale assets and managing resources efficiently across the global network of facilities to accelerate development, manufacturing, and testing services. Additionally, early-stage customers provide a broad pipeline of clinical candidates, and the large-scale drug substance and drug-product facilities are well suited to receive those products as they progress to late-stage or commercial manufacturing.

Quirmbach (CordenPharma): We currently see the end-to-end service model being applied more frequently for early-stage development projects compared to late-stage and commercial manufacturing. In my view, the reason is simply that the full-service model has only recently experienced more interest, traction, and acceptance in the industry and buy-in from our customers, whom have started to think differently about outsourcing integrated development projects. In addition, more and more CDMOs are offering end-to-end services not available a few years ago by entering into the field or complementing their services with missing capabilities in either drug-substance or drug-product manufacturing. Customers tend to need to establish trust and first gain experience by outsourcing an early-stage project as a test before proceeding to any commercial project. However, we have also seen cases where a customer either re-launched or in-licensed a commercial product and were only looking for an integrated partner as part of their strategy to rebuild the supply chain, but these cases have been limited when comparing to the early-stage inquiries and ongoing projects our organization has received.



Stuart Needleman
Chief Commercial Officer
Piramal Pharma Solutions

Needleman (Piramal Pharma Solutions): Initially, the CDMO end-to-end service model was targeted to early-stage development because the goal was to help a client get to an investigational new drug application (IND). Numerous CDMOs, such as Aptuit, Almac, and Patheon, built branded integrated service offerings specifically to address the need for speed to IND. Over the last several years, the offering has changed, and now sponsor companies and suppliers are working across the entire development spectrum. This is a result of both the changing needs of the marketplace and the consolidation of CDMO service providers. Regardless of customer size, the Piramal Pharma Solutions (PPS) model of integrated services is based on a series of protocols specially designed to ensure success, encompassing software systems, technology transfer, project management and more.

Sponsor companies: large versus small

Question: From your experience, in terms of the types of sponsor companies interested in the end-to-end business service model, is it applied more for smaller pharma companies compared to larger companies?

Quirmbach (CordenPharma): Over the years, we have seen strong interest from Biotech and small-to-midsized Pharma companies toward the integrated supply concept in an effort to efficiently use their, compared to Big Pharma, fairly limited procurement, sourcing and CMC (chemistry, manufacturing and controls) resources.

Within smaller companies, the decision-making for outsourcing API and drug-product manufacturing very often resides within a small team of people, or sometimes even just with one person, who sees the benefit of reducing complexity by engaging with one company. Smaller companies with limited resources appreciate the streamlined interaction with one partner, which includes a global project team consisting of one primary key account manager and one global project manager, who together coordinate the program across the manufacturing infrastructure within the organization.

We have nevertheless started to see an interest from large pharma companies, albeit a gradual interest, probably due to the more siloed structures within these organizations, collaborations with which an extra effort might be required to spark mutual agreement among departments and the service provider.

Needleman (Piramal Pharma Solutions): The integrated service offering was typically targeted to biotech and virtual pharma companies since those organizations did not have the infrastructure, capabilities and resources necessary to support the entire drug-development and commercialization cycle. That is now changing as all types of pharma companies—small, medium, big, and virtual—see the value of developing strategic relationships with integrated CDMOs. Sponsor companies are challenged by limited budgets and have to work smarter to remain competitive, and outsourcing integrated services is a way to advance multiple candidates faster. At PPS (Piramal Pharma Solutions), we are seeing several Big Pharma companies recognize the value that end-to-end providers bring and embrace it.

Reasons for using an end-to-end service provider

Question: From your experience, what are some key reasons sponsor companies seek to use an end-to-end business service model compared to the traditional model having separate providers for API and drug-product development and manufacturing?

Moorcroft (Cambrex): From the beginning of the twentieth century until only very recently, the large proportion of small molecules in the clinical pipeline were being developed by the top pharmaceutical companies. Today, the data show that this trend has changed, and approximately 65% of the current pipeline are molecules being developed by small and virtual pharma companies, many backed by venture capital or private equity funding.

Historically, smaller companies would have sought to out-license their candidates sometime in the middle of the clinical trials (usually Phase II) and then the larger clinical studies were taken on by the larger, better resourced pharmaceutical companies. However, the recent increase in drugs that are being tested in smaller patient cohorts, such as oncology or orphan diseases, has allowed the development of these molecules to be taken on by these smaller innovator companies. The reduced patient/clinical burden of the sponsor company having to conduct lengthy and complex trials involving multiple indications, as well as coordinating hundreds, if not thousands of patients, has meant that with appropriate funding and investment, the possibility of a small company commercializing its own products is now an economically viable prospect.

For companies adopting this approach, using a fully integrated service provider to act as a development partner throughout the process is extremely attractive. From a resource point of view, it ultimately means less CDMO partners to manage, fewer supplier agreements to negotiate, fewer people involved in the decision-making process, and avoids multiple points of contact for each project.

Quirmbach (CordenPharma): In my opinion, key reasons for adopting a fully integrated supply model include more efficient interaction with the service provider, overall faster execution of a program, and responsibility of the CDMO to manage internal know-how transfer between the departments (API and drug product) rather than the customer having to coordinate two different external companies.

Other important advantages for consideration are the ability to utilize a harmonized safety, health & environment (SHE) concept, which is an important issue when handling highly potent compounds, as well as sound compliance policies across organizations. Finally, the streamlined contract negotiation process (ideally one contract) and overall lower costs (both internal and external) represent a strong financial benefit for the customer's successful program completion in accordance with its end goals.

This point is important to reiterate since the burden of any delays caused by the service provider's API site will fall on its internal team to manage within agreed timelines, instead of on the customer to sort out between separate companies operating with different procedures. Our experience has proven that the customer clearly gains more leverage with an integrated project, thereby creating, where technically feasible, a win-win situation for all involved.

Needleman (Piramal Pharma Solutions): There are a multitude of reasons, the baseline being the simplification of the supply base. Having a single point of contact (SPOC) is a huge advantage in both time management and project management. By working with a company like Piramal Pharma Solutions, a sponsor can see a candidate go from post-discovery to commercialization without the need to manage multiple suppliers or the cost and time delays associated with tech transfer between different service providers. Risk management is also an important consideration that can be addressed with the integrated model as is overall program speed. Collectively, these are the reasons why CDMOs are looking to acquire end-to-end capabilities and bundle them as an integrated, harmonized solution.

Project management

Question: From an implementation perspective, how does the end-to-end service model differ from the traditional service model as it relates to project management? Any key differences in terms of frequency or type of communication, cycle times, and the "hand-off" of drug substances for formulation development/drug product manufacturing or other issues?

Quirmbach (CordenPharma): Most importantly, the implementation of an efficient and successful end-to-end service model first requires a thorough understanding of the customer's consumption chain and ability to address the key points of each stakeholder in their ecosystem. Secondly, key account managers, together with assigned global project managers, are key facilitators in this model, where frequent and transparent communication (weekly/bi-weekly) are mandatory with the customer. Lastly, hand-off to other functions within the organization requires superior project management processes be in place, with involvement of both global and local project teams.

Needleman (Piramal Pharma Solutions): In the end-to-end service model, project management is the key to success. There is strong inherent value in establishing a single point of contact (SPOC) on the CDMO side who acts as the client advocate. The SPOC has the power to ensure that the delivery timelines are kept. Communication is always the key to successful collaborations, and this is no exception. With good communication, decisions are made more routinely and more effectively. Integrated offerings are only effective, however, if all of the services are harmonized. An integrated offering must not simply be different businesses linked together; it must be presented to the customer as a single business at the operational level. At Piramal Pharma Solutions, the commitment comes from the top down, with the establishment of a company philosophy and systems that create a single, customer-facing solution that facilitates easy customer interaction.

Supplier metrics

Question: From an implementation perspective, how does the end-to-end service model differ from the traditional service model as it relates to supplier metrics? Are there any unique metrics or key performance indicators (KPIs) at play?

Quirmbach (CordenPharma): The supplier metrics for a fully integrated service model are the same as the traditional model. Major key performance Indicators center around DIFOT (Delivered In Full On Time) and budget. Certainly, the effective implementation of global project management, in conjunction with the right set-up of cross-functional and cross-site teams on the part of the service provider, are also critical factors for a successful program.

Needleman (Piramal Pharma Solutions): The fact is, the only things that really matter are timeline delivery and execution. Schedule adherence is a key metric, which is real time versus on time in full (OTIF), and OTIF is after the fact. Sponsor companies expect accelerated timelines when working with one provider who manages all aspects, as they should. In theory, a premium could be charged for the services because the CDMO is adding value and making the work easier because there are less relationships to manage, but the challenge is to remain competitive.