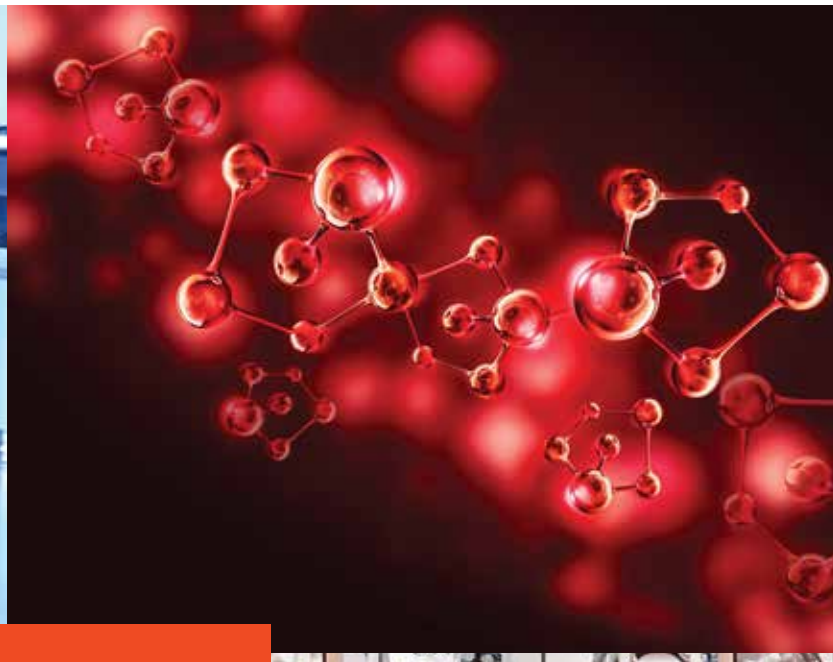
Piramal
Pharma Solutions



WHAT VALUE CAN AN INTEGRATED SOLUTION BRING TO YOUR OUTSOURCING STRATEGY?

ABSTRACT

Growing competition across the globe, clinical attrition, the complexity and costs of drug development and manufacturing, are all factors that impact today's pharmaceutical industry. As biologics continue to grow as a target area of research, pharmaceutical firms continue to develop creative strategies to advance their small molecule pipeline through clinical development. The growth in outsourcing is one strategy life science innovators are pursuing to address this evolving landscape; however, should a sponsor company seek the traditional route of utilizing multiple partners across the supply chain or does an integrated CDMO offer a more efficient and faster path to commercialization?

THE RISE OF INTEGRATED CDMOS

A key factor influencing the increase in CDMO services is sponsor companies that want to focus on core competencies internally while outsourcing non-core areas. The definitions of core and non-core continue to evolve as service providers develop more skills and capabilities in areas formerly kept in-house, such as synthetic and medicinal chemistry, discovery, and API manufacturing. A company with integrated offerings can provide a multitude of these services covering the entire drug life cycle, which offers significant advantages over the alternative of using multiple partners across the supply chain. These CDMOs are also often referred to as "one-stop shops" or "end-to-end solutions."

A CDMO that is "integrated" provides a fully connected supply chain, all the way from raw materials, development, and manufacture of the active drug substance to the final, formulated drug product. The right development and manufacturing partner can accelerate clinical development and drive value by standing out in the following areas:

Seamless tech transfer

The safe and efficient transfer of information about a drug product is essential, as a tech transfer determines if a service provider has the necessary resources available to meet the requirements for commercial development and manufacturing. The discussions necessary to ensure a successful tech transfer are better facilitated when colleagues are in the same company or even building, which is the case with an integrated CDMO.

More efficient management of resources and capacity

Integrated CDMOs have the ability to stagger capacity and availability of materials to ensure the timing of

each phase of development lines up with the sponsor's timeline. With multiple partners, there is a limited window of time you have to complete a phase of development. For example, if a sponsor's API is late or unexpectedly unavailable, this can have a domino effect on the entire project timeline. The window of opportunity to complete that phase could close, as the service provider likely has another scheduled campaign. In the same scenario with a "one-stop shop" CDMO, the drug product side of the business is constantly in contact with the API side to ensure they will be ready as soon as the API is available. As needs change, an integrated risk of generating an Out Of Specification (6). We have previously used a two factor (operator, cell bank) design for validation of a bioassay. In this paper we report the use of DoE in establishing the robustness of the bioassay "design space", with the centre point data being used for qualification and for determining the requirements to support validation of the bioassay using DoE.

CDMO can adjust its capacity and resources across the supply chain to re-align with the flow of the project.

Availability of documentation through a single source In terms of sharing information, many studies and pieces of documentation are needed during drug development, such as analytical methods, cleaning protocols, and regulatory filing information. Just as with a tech transfer, the exchange of this information in an integrated CDMO scenario is seamless compared to one where coordination among multiple companies is required.

Integrated program management team with a single point of contact (SPOC) for the client

A SPOC acts as a liaison between the project site and the customer. In the example of integrated programs at Piramal, an integrated CDMO with locations in the US, Europe, and Asia, the SPOC manages every program manager involved in the project in order to coordinate deliveries, etc. This provides the customer with one dedicated person who can provide a holistic view on the program and its status.

Each of these elements can have a critical impact on a product's time to market as well as the cost of development and manufacturing.

WALKING THE TALK: HOW TO EVALUATE AN INTEGRATED CDMO

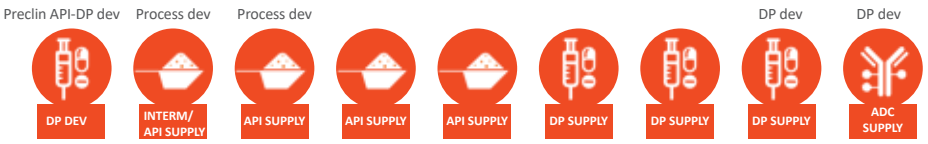
When the time comes to evaluate a partner, especially one where you will be putting "all of your eggs in one basket," it is important to consider several criteria to ensure you are working with a CDMO that does not just have the necessary qualities but also has a proven history of success. This requires reviewing several areas, including the CDMO's regulatory track record, the number of innovator products the partner has helped launch, the existing pipeline, and finally, the CDMO's experience in integrated programs.

For example, Piramal has a long and successful history, and has launched 34 products to support innovator clients, including blockbusters such as Velcade® and Ninlaro®. With 10 additional launches scheduled for this year, and a robust pipeline that includes 47 programs in phase III, Piramal has built a strong reputation as the 'partner-of-choice' for both large pharma and innovative biotechs. As a global leader in ADCs, Piramal has manufactured over 800 batches (including 400 GMP batches) for 130 different ADC candidates and over 50 different toxin/toxin-linker systems. With eleven facilities across North America, Europe, and Asia, Piramal has completed over 30 successful integrated projects that include discovery, drug substance, drug product, and clinical packaging.

Manufacturing and access to the necessary diagnostics. This is where QbD can serve as an extremely valuable approach. Pharmaceutical manufacturing is already complex, but when you add in the pressures of bringing a BTD to market, it can become even more challenging. Through this systematic approach to process development, manufacturers can have confidence that the safety and efficacy of their product will be maintained throughout production, regardless of the timeline it is on.

A GLOBAL LEADER IN INTEGRATED DEVELOPMENT = NO. OF INTEGRATED PROJECTS

- INTEGRATING GEOGRAPHIES
- INTEGRATING CAPABILITIES



PHASE	PROJECT #	TYPE OF PROJECT	AHMEDABAD PDS IN	AHMEDABAD IN	ENNORE IN	AURORA CA	DIGWAL IN	RIVERVIEW MI	LEXINGTON KY	MORPETH UK	PITHAMPUR IN	GRANGEMOUTH UK
PRECLIN-PH I	6	Route scouting – intermediate devpt-api supply (drug substance, multiple sites), synthetic chemistry	✓	✓	✓			✓				
PH I-III	4	Formulation development- Form supply (Drug Product, Multiple sites)		✓						✓		
PH I-III	5	API Dev- API supply- Formulation Dev.- Form Supply (Drug Substance, Drug Product, Multi sites)		✓	✓	✓			✓	✓		
PH I	5	Formulation development- Form Supply (Drug product, Multiple Sites)		✓							✓	
PH I-III	9	Process dev- Intermediate/API manufacture-DP manufacture, DMF filing/maintenance (DS, DP Multi sites)			✓	✓						
PH IV	4	Process dev- Intermediate/API manufacture-DP manufacture, DMF filing/ maintenance (DS, DP, Mult sites)			✓		✓				✓	
PH II	3	ADC Development- ADC Supply, import testing & packaging								✓		✓
PH IV	4	ADC Fill Finish							✓			✓

In the area of cancer, for example, where Piramal has established global leadership as a preferred integrated partner, the firm can provide end-to-end solutions by doing the ADC conjugation and the fill finish between its facilities in Europe and North America. Through the recent acquisition of the Ash Stevens high potency drug substance development and manufacturing facility in Michigan, Piramal expects to also supply the active ingredient for the ADC conjugation, thereby completing the integrated supply chain, minimizing client management time, and optimizing clinical development timelines.

A company's global presence is also a key factor as certain areas of the world, such as Asia, offer favorable advantages in terms of drug development. The growing middle class in this emerging market is reducing the disease divergence between the west and Asian territories, creating comparable disease incidence rates in these locations. This can increase the speed of patient recruitment for clinical trials, and, as a result, a drug's speed to market. The high level of regulatory quality oversight in these areas is also comparable to that of western countries, as audits in Asian territories are also conducted by the FDA and EMA. Possibly the most appealing benefit of Asian markets is the highly competitive costs. According to an evaluation by PricewaterhouseCoopers LLP, "Asian territories provide a significant cost advantage with manufacturing savings that can range from 50 to 80 percent of the cost that would be incurred if the manufacturing was performed in western territories."1

• **Knowledge** - striving for a deeper understanding of its domain and an aspiration to do things creatively

• **Action** - empowering to act decisively and to create value; consistency in thought, speech, and action

• **Care** - protecting the interests of its customers, community, employees, partners, and stakeholders while aspiring to be the best but to also be humble

• **Impact** - believing that every action by Piramal has an impact on the customer but has an even bigger impact on society and, most importantly, patients

Every project and every business relationship can encounter challenges during the drug development and manufacturing process. Rather than trying to predict whether they will occur, a sponsor evaluating potential partners should focus on how that service provider responds to any potential challenges and what its record is in doing so. An integrated CDMO brings a wide breadth of knowledge and experience from facing various levels of adversity across the supply chain. Finding one that also has a demonstrable track record and strong corporate values ultimately creates the optimal formula needed for industry success.

1. PricewaterhouseCoopers LLP, The changing dynamics of pharma outsourcing in Asia — http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=13213I

Piramal Pharma Solutions is a contract development and manufacturing organization (CDMO), offering end-to-end development and manufacturing solutions across the drug life cycle. We serve our clients through a globally integrated network of facilities in North America, Europe and Asia. This enables us to offer a comprehensive range of services including Drug Discovery Solutions, Process & Pharmaceutical Development services, Clinical Trial Supplies and Commercial supply of APIs and Finished dosage forms. We also offer specialized services like development and manufacture of Highly Potent APIs, Antibody Drug Conjugation and are well versed in technologies such as Bio-catalysis, Route Scouting etc. Our capability as an integrated service provider & experience with various technologies enables us to serve Innovator and Generic companies worldwide.

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