Enabling a Sustainable and Mutually Beneficial CDMO Partnership

Use of Contract Development Manufacturing Organisations (CDMOs) is now the established norm in the pharmaceutical and medical technology supply chain.[1] The CDMO model has been shown to provide cost-effective, reliable and compliant solutions with speed to market for critical healthcare products.

This is achieved by leveraging the core competencies and experience of the contract giver (*e.g.* brand development, marketing etc), and contract acceptor (*e.g.* manufacturing excellence, quality operations, etc.) to allow for targeted focus on key operational pillars to drive overall programme success and synergies.[2] However, with many CDMO options available, all providing specialised expertise and solutions for diverse and complex activities, it can be difficult to know where to start with the selection process in a way that balances the fundamentals and aspirational goals.

Starting with the non-negotiables, companies must make sure that any partnership adheres to requirements laid out in current Good Manufacturing Practice regulations (cGMP)[3] by the US Food and Drug Administration and the European Medicines Agency (EMA).[4] The FDA sets out the minimum cGMP to assure that safety requirements are adhered to across the lifecycle of a drug and that it "Meets the quality and purity characteristics that it purports or is represented to possess."[5]

Beyond these critical requirements, there are several key considerations we recommend before engaging a potential CDMO.

Understand the Project Status and Objectives

Make sure you understand the exact capabilities that you require from a CDMO, including both the essentials and the nice-to-haves. This will vary, depending on what phase your project is at and the current timelines. Be clear about the known current risks that may impact on project timelines, such as raw material supply, testing queues if using external laboratories, regulatory approval, etc. Have mitigation actions for each of these risks been identified and assessed? Consider your forecast and strategy for when you expect to go to market. What funding is available and is this sufficient to accelerate the timeline if needed?

Research the CDMOs Identified

Next, do some basic research to differentiate between the selected CDMOs. Key factors to consider as part of your criteria for the selection of a CDMO include technical know-how and other key skill sets, quality and compliance, and approach to risk.

Technical Knowledge and Experience

Consider how long the CDMO has been in operation and if they have a proven track record in your niche technology. Review their case studies, success stories, and client reviews. Balance technical know-how with ability to deliver a quality product on time and within budget. That will mean weighing cost, speed, and quality in your decision-making. Sometimes speed incurs an additional upfront cost but can pay significant dividends in the long term with gaining market share. Ask whether the CDMO can support your forecast commercial ramp-up plans. Do they have the expertise in technology transfer and ability to scale-up? And can they offer an end-to-end finished product solution – from packaging to distribution to post-market surveillance?

Quality and Compliance

Regulatory compliance is a non-negotiable, so be sure the CDMO has a proven track record. Do they understand the FDA's definition of adulterated product *i.e.* "If it fails to conform to compendial standards of quality, strength or purity"[6] and the consequence of such a violation. Ask which regulatory authorities have audited them, when, what the outcome was and how robust their responses to regulatory findings were. Quality considerations are equally important. Make sure their quality management system (QMS) is suitable for you. Thoroughly critique the CAPA system, change control, deviation management, self-inspection programmes. Ask key questions about the CDMO's quality processes, including:

- Are internal issues identified and resolved in a sustainable and robust manner?
- How does the CDMO address issues that could impact product quality?
- From an infrastructure perspective, is the facility clean and well-maintained and does it meet all regulatory expectations? Is the facility equipped with the right technology and sufficient equipment capacity to handle your project needs? Is there an active contamination control strategy?

Align on Risk Attitude

Risk management is clearly defined in regulatory guidances, with ICH Q9 outlining that "effective and proactive quality risk management can enable better, more informed and timely decisions throughout the lifecycle".[7] Determine how well the CDMO can meet both regulatory and organisational requirements, including:

- Does the CDMO have a structured and documented approach to risk management?
- Does the CDMO develop defendable risk rationales and use their experience with other clients to determine how your project might be impacted?
- How does the CDMO adapt to change in a compliant way when things don't go as expected?

Organisational Expertise & Quality Management Maturity

The technical skillset of the manufacturing team is a priority; however, as part of the selection of the CDMO, it is important to review the skill set of the wider team, including quality assurance, quality control, supply chain, facilities, project management, regulatory and others.

- Does the CDMO have a strong quality culture in which those who have responsibility for oversight and control over manufacturing take ownership for quality, with patient safety at the centre?
- How does the CDMO's senior leadership demonstrate their commitment to quality and continuous improvement?
- Does the CDMO invest in training, mentorship programmes, professional

development and does it set high standards for excellence?
- Is there an active succession planning programme in place and are there retention measures to retain key skill sets?
- Does the CDMO drive a continuous improvement mindset and invest in electronic systems that provide real-time metrics and analytics?
- Do the values and core operating principles of the CDMO align with your company values and is there a symbiotic relationship between business and quality objectives? In simple terms, will the CDMO become an extension of your business?
- Are quality assurance personnel just problem finders or are they also solution providers?

Building and Maintaining the CDMO Relationship

Once you have selected a CDMO, be proactive and operate with a "one-entity" mind-set. That means being prepared to manage the unexpected and adopt contingency planning to deal with the "what ifs" of supply chain disruptions. You need to be clear and realistic with your project's goals, milestones and budget. In addition, develop targeted and customised scenario plans, such as best-case scenarios, assuming no project delays, as well as realistic planning, which assumes delays with regulatory approvals and possible repeat testing. In the same vein, identify risks early on and develop mitigation solutions, such as dual sourcing of critical components, targeted training programmes, regular audits, enhanced testing during the project phase and targeted updates on project status with the regulatory authorities.

Use standard templates for documentation consistency and have sufficient safety stocks in place. It's also crucial to develop a strong, transparent and honest communication plan, since a strong partnership is anchored in mutual trust and respect. Be clear what success looks like to you, for example, through agreed-on key performance indicators (KPIs) during product transfer and into commercialisation. And, crucially, ensure you not only have a Quality Technical Agreement, but maintain it as a living document.[8,9] Both parties need to be aligned on responsibilities, including "the who" and "the what" in the event of "the what if" scenarios happening.

The Right Model in an Evolving Landscape

The CDMO operating model is rapidly growing and adapting as agility and speed to market in a cost effective, sustainable and compliant manner become increasingly important. At the same time, companies must be assured that cGxP are met. In recent warning letters on the use of contract manufacturers, the FDA has made clear that contractors are regarded as extensions of the manufacturer and that it is the manufacturer's responsibility to ensure the quality of their drugs in keeping with current Good Manufacturing Practices (cGMP), regardless of agreements in place with contract facilities. "You are required to ensure that drugs you deliver into interstate commerce are not adulterated," the FDA stated, noting that, where products are considered "adulterated" under the FD&C act, both the Contract Giver and Contract acceptor should consider these words as an indication that a recall is warranted.[10,11]

The requirements of the European Medicines Agency (EMA) are similar to those of the FDA. They state that "a direct written contract should also be in place between the Manufacturing/Importers Authourisation (MIA) holder responsible

for Qualified Person (QP) certification of the product and sites involved in the various stages of manufacture, importation, testing and storage of a batch before it undergoes certification (hereafter: contract manufacturers)."[12]

With these considerations in mind, a partnership is best realised when the CDMO is seamlessly embedded as an extension to your existing business, rather than just being perceived as a third party. Such partnerships enable a win-win scenario with alignment on the technical non-negotiables whilst simultaneously ensuring shared operating values. To achieve this, the contract giver and contract acceptor must work collaboratively together as a single entity to achieve common goals – sharing a commitment to patient safety, quality, regulatory compliance, continuous improvement and underpinning that commitment through constant colla-boration and communication.

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