Syner•G

WHITE PAPER

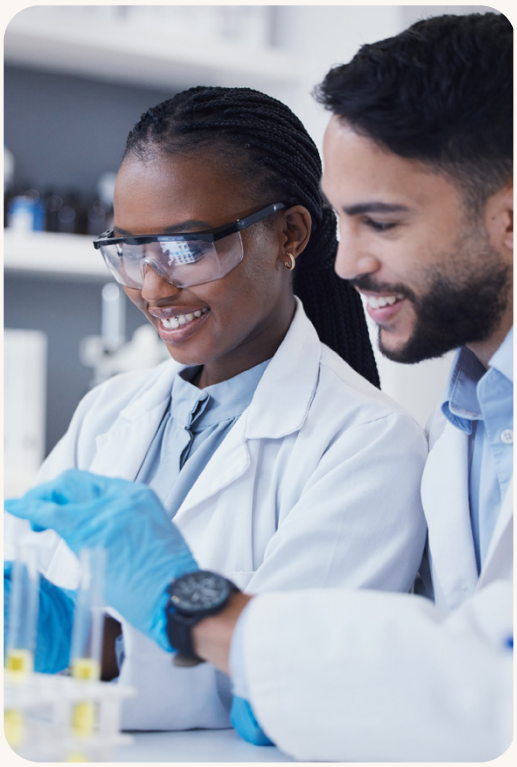
Navigating the Fast Lane: Strategies for Accelerated CMC Development

Balancing Acceleration with Safety and Quality while Building Long-Term Collaborations for Success

The "need for speed" that drove pharmaceutical developers during the pandemic is no longer a one-off phenomenon; it is increasingly becoming business as usual. This shift is reflected in the industry's demand for accelerated processes for chemistry, manufacturing, and controls (CMC) development. Given the risks implied by this market-driven acceleration, potential partnerships with contract development and manufacturing organizations (CDMOs) must be thoroughly vetted.

What does that mean for the development process?

It means abbreviating timelines for clinical studies without a correspondingly elevated level of risk around product safety. Recent technologies and approaches can shave as much as two months off the timeline from lead identification to establishing cell lines suitable for phase 1 production, which also speeds the path to Investigational New Drug Application (IND) filing and approval.[1]



Ensuring quality and safety in a rapid development environment

Choosing a CDMO early on involves clearly defining program goals, requirements, timelines, budgets, and target product profile expectations. Complete transparency from the start ensures a fully collaborative relationship, with robust communication policies that build trust and support the process.[2]

Nonclinical, product stability, or characterization data can slow IND filings. So, a rolling submission drives faster clinical start. Early interactions between developers and regulatory authorities proactively create strategies for joint review, including establishing risk mitigation options and clinical development plans, as well as clarity around – and access – to new FDA guidelines on Emergency Use Authorization that may waive some Current Good Manufacturing Practice (cGMP) requirements.[3]

Early Conditional Marketing Authorization (CMA) can be obtained through adherence to specific Committee for Medicinal Products for Human Use (CHMP) requirements. Those include positive benefit/risk, comprehensive unmet medical needs data, and clear benefits to the public of making the product available earlier. All this must outweigh the risks associated with requiring additional data, but technology can expedite the development process by providing critical process parameters (CPPs) that streamline the path to authorization.[4]

The ability to accelerate CMC is driven by newly streamlined cell line development workflows. These innovations have enabled the rapid generation of cell lines dedicated to vaccine production, with precise, automated, and integrated workflows that increase efficiency throughout the process.[5]

Small CMC organizations can assist pharmaceutical companies without their own facilities, especially in early-stage formulation development. However, late-phase clinical trials and commercial production, so pivotal to the delivery of new products, requires CMC partners that offer the full range of services that meet the complex and stringent requirements of late-stage development and commercialization.

Also,there are obvious advantages in performing all functions, including release testing, in a single facility, especially when streamlining and simplifying product development is top of mind.[6]

Upholding quality and safety standards have always been pharma's top priority. Now, an environment that emphasizes speed demands strict adherence to a comprehensive cross-disciplinary framework that states expectations and defines actions for each area; establishing vaccine platforms for drug substance, drug product, and analytics for immediate use; and full optimization of data, automation, and digital solutions.[7]

Pros and cons of accelerating development of vaccines

CDMOs with extensive experience and expertise in monoclonal antibody (mAb) development and manufacturing are better equipped to meet challenges presented by new modalities.[8]

AIDS, H1N1, and coronavirus have prompted expeditious development of therapies.[9] The vast and rapidly accrued warehouses of knowledge around infectious agents, pathologies, and immune responses have scaled up development and manufacturing. These rely on carefully crafted comparability studies and process qualification work. However, fewer lots produced overall means even fewer tested in clinical trials. Establishing specifications within compressed timeframes that sometimes rely on limited validation datais challenging.[10]

Now, the standard 10-to-12-month timeline for developing vaccines can be reduced to 5 to 6 months. Guaranteeing product quality and consistency requires comprehensive product, preclinical, and clinical trial data, and robust processes for pharmacovigilance and post product licensure.[11]

Reduced phase 1 timelines necessitate accepting a level of business risk. For example, using an unreleased cell bank in a cGMP facility may pose such a risk, but the probability of failure is low because of current control practices. Its impact on the facility would be evaluated, and potentially delay startup. However, all release testing would be concluded before product distribution, and patient safety ensured.[12]

Choosing a CDMO in the early stages of development

Evaluating a CDMO must include a comprehensive analysis of performance, including capabilities and expansion, flexibility, transparency, and talent retention.

A reputable CDMO's history includes successful and diverse projects involving multiple molecules and technologies. This includes obtaining regulatory approvals from multiple global authorities, thoughtful expansion of the organization's team, capabilities, and capacity. These attributes demonstrate commitment to ongoing and responsible growth and readiness to fulfill current and future clinical and commercial requirements.[13]

Expertise in a specific drug type, therapeutic area, and comparable products is highly relevant in assessing a CDMO. Making a common practice of screening various vaccine types, even for the same disease, indicates a culture that develops truly efficient and appropriate platforms.[14] Project management includes continuous and comprehensive reporting, smoothly coordinating teams of scientists and engineers, and robust support of GMP for global markets.[15]

Other considerations of CDMO performance include audit and compliance histories. CDMOs that pass that evaluation have demonstrated their experience, technical and regulatory knowledge, specialized skill sets, and expertise that enable streamlined development with minimal risk around compliance.[16]

Finally, it is imperative to work within transparent cost structures and estimates. Equally critical is establishing comprehensive agreements around intellectual property rights and confidentiality. These endeavors protect the interest of all parties and foster secure and mutually beneficial partnerships.

The importance of the right CDMO in late-stage development

Scalability is key to a CDMO's support of late-stage clinical and commercial requirements, particularly for therapies targeting highly specific patient populations. Experience in these areas indicates adaptability around market expectations and varying batch volumes during clinical and commercial phases.[17]

A proficient CDMO should also demonstrate expertise in managing analytical, quality, and validation aspects crucial for late-stage and commercial production. Proactive improvement in process design as projects advance into later stages is essential for ensuring high-quality, commercially viable products.[18]

Globalization introduces additional complexities, requiring CDMOs to navigate regulatory requirements and supply chain challenges in international markets. Partners well-versed in global operations are vital for successful expansion and adherence to diverse regulatory landscapes.[19]

Recognizing country specific requirements and working with those insights underscores the advantages of continuous engagement between developers and regulators, with international regulatory adherence CMC and good manufacturing practice (GMP) more crucial than ever. Early investment in CMC and GMP practitioners that prove themselves worthy is an investment in long-term success for vaccine developers.[20]

Expedited product development demands a delicate balance between leveraging regulatory flexibilities and implementing strategies to ensure product quality. A systematic approach is crucial, involving the identification and prioritization of phase-appropriate (CMC) concerns throughout the development process. In the early stages, regulatory scrutiny should emphasize issues confirming proof of concept, safety considerations, and strategies for comparability assessment and specification setting. Incorporating existing knowledge and new learnings becomes instrumental as development progresses.

Considerations must include bridging manufacturing processes, identifying critical unit operations for process validation, establishing assays for controlling critical quality attributes, and an openness to exploring alternative approaches along the way.[21]

Transformative partnership for pharmaceutical innovation

Given the risks implied by this market-driven step up in development and delivery, reliability, trustworthiness, deep wells of hands-on experience in CMC are imperatives. Syner-G stands at the forefront of CMC expertise with a commitment to guiding innovators through the intricacies of the CMC process, from start to finish. We are a dedicated partner in the development of small molecules, biologics, cell and gene therapy, and medical devices, with a suite of services that includes regulatory strategy, tactical activities, and technical and scientific writers.

What sets us apart is not only our deep knowledge and experience, but an efficient and transformative approach to the changing nature, practices, and expectations in the pharmaceutical industry. For clients, partnering with Syner-G is akin to flipping a switch. It not only enlightens every aspect of the process but provides nuanced guidance through a seamless integration of stated and agreed-upon goals, timelines, processes, and more. In an environment of intense global competition in which the "need for speed" is the new norm, partnership with proven CMC experts is only the latest "must" required by forward thinking and dynamic developers.

ABOUT

Syner-G

Since 2007, Boston based Syner-G has become a leader in supporting life science organizations across the development continuum from product design to commercialization. With more than 200 team members world-wide, and deep expertise in product development (CMC), regulatory strategy and submissions, and quality assurance, Syner-G offers a full complement of strategy, execution and program management, and submission support services. Syner-G integrates information and messaging around quality, safety, efficacy and competitive positioning, crafting the story behind the science. Syner-G offers comprehensive consultative outsourcing that supports the efficient movement of innovative discoveries through the pipeline to where they can make life enhancing and life-saving impact.

For more information please visit: synergbiopharma.com

REFERENCES

1. https://www.nature.com/articles/s41587-020-0512-5
2. https://www.linkedin.com/pulse/choosing-cdmo-right-capabilities-experience-expertise-meet/
3. https://www.nature.com/articles/s41587-020-0512-5
4. https://bioprocessintl.com/business/cmc-forums/cmc-strategies-for-expedited-program-development-regulatory-perspectives-session-1-of-a-cmc-strategy-forum/
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10386492/
6. https://www.bioprocessonline.com/doc/how-to-pick-the-right-cdmo-for-late-phase-clinical-trials-0001
7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10386492/
8. https://www.pharmasalmanac.com/articles/why-choosing-the-right-cdmo-partner-is-essential-in-todays-pharmaceutical-market
9. https://www.nature.com/articles/s41587-020-0512-5
10. https://bioprocessintl.com/business/cmc-forums/cmc-strategies-for-expedited-program-development-regulatory-perspectives-session-1-of-a-cmc-strategy-forum/
11. https://bioprocessintl.com/business/cmc-forums/cmc-strategies-for-expedited-program-development-regulatory-perspectives-session-1-of-a-cmc-strategy-forum/
12. https://www.nature.com/articles/s41587-020-0512-5
13. https://www.pharmasalmanac.com/articles/why-choosing-the-right-cdmo-partner-is-essential-in-todays-pharmaceutical-market
14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10386492/
15. https://www.linkedin.com/pulse/choosing-cdmo-right-capabilities-experience-expertise-meet/
16. https://www.pharmasalmanac.com/articles/why-choosing-the-right-cdmo-partner-is-essential-in-todays-pharmaceutical-market
17. https://www.linkedin.com/pulse/choosing-cdmo-right-capabilities-experience-expertise-meet/
18. 18 https://www.bioprocessonline.com/doc/how-to-pick-the-right-cdmo-for-late-phase-clinical-trials-0001
19. 19 https://www.linkedin.com/pulse/choosing-cdmo-right-capabilities-experience-expertise-meet/
20. 20 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10386492/
21. 21 https://bioprocessintl.com/business/cmc-forums/cmc-strategies-for-expedited-program-development-regulatory-perspectives-session-1-of-a-cmc-strategy-forum/