The Importance of Clinical Trial Packaging and The Benefits in Outsourcing Your Small Molecule Packaging to a CDMO

Operating a clinical trial in what is a tightly regulated industry requires comprehensive, big picture thinking. Risks remain at all stages of the clinical supply chain, and they can make the difference between a successful study, or no study at all. Whilst businesses are continuing to navigate the COVID-19 pandemic, sponsors face challenges that require strategic planning and should avail of appropriate assistance, particularly in one area of clinical trial expertise – clinical packaging.

With so much focus on the emergence of biologics in recent years, it would be easy to surmise that the demise of small molecule drug development is imminent. That, however, is not the case. Undoubtedly, biologics and biosimilars are among the most advanced therapies available and have had a game changing impact across multiple therapeutic areas, from oncology to arthritis and to autoimmune diseases. Yet, while the biologics market growth is predicted to increase at a CAGR of 11.9% to USD 625.6 million by 2026,[1] a renaissance in small molecule drug development is challenging the industry narrative surrounding the long-term viability of investing in research and development (R&D) of small molecule drugs.

In fact, the pipeline for new drug manufacture continues to be dominated by solid oral dose formulations, with almost half (46%) of drugs in the development pipeline administered orally.[2] Furthermore, small molecules are recording the highest number of FDA approvals for decades and accounted for around 70% of New Molecule Entities (NME) approved for use by the FDA over the last five years.[3] There are also more small molecule phase I trials taking place than ever before, with in excess of 7,500 launched or entering development over the past five years.[4]

Growth in small molecule drug development is great news for patients, especially across oncology and orphan disease areas where investment is currently most concentrated.[5] However, it does raise the stakes for sponsors when it comes to achieving return on R&D investment. Increased competition, coupled with mounting study complexity, targeted patient populations and investor-driven need for speed makes optimising the processes that underpin successful clinical trials management, mission critical. One way to achieve this, while reducing risk and accelerating time to market, is to outsource vital components, such as clinical packaging strategy and implementation, to Contract Development and Manufacturing Organisations (CDMOs).

Key Challenges

Before weighing up the benefits of outsourcing clinical packaging strategy to a CDMO, awareness of the common packaging challenges sponsors of small molecule studies encounter is key. The first relates to the profile of clinical packaging. Packaging requirements and processes are typically unseen or overlooked and as such are not given the attention needed during a program's planning phase. The second relates to a lack of standardisation. Products, protocols, and patients differ with each study so unique packaging strategies must be crafted. Dosing formats for small molecule drugs are incredibly varied (covering tablets, capsules, inhalers, IV and injectors) and there is no one size fits all solution.

The third is change, or rather the impact of change – in study size, scope and clinical direction, as well as variable patient demand on packaging requirements. As such, to reduce risk of stockouts, sponsors must continuously monitor the broader supply chain to inform a responsive packaging operation. The fourth and final problem relates to institutional learning. For sponsors who manage clinical packaging activity in-house, vital product and/or program learning can easily become lost with personnel moves or changes in company strategy, which can jeopardise broader supply chain performance.

Early Engagement

Through early engagement with a CDMO partner, these challenges can be effectively managed, and programs kept on track. However, in order to weed out risk, it's imperative that sponsors engage CDMO partners at the earliest opportunity so that packaging strategy can be developed with the bigger picture in mind and processes streamlined. Engaging with a CDMO for clinical packaging support once the study and kit is already designed, planned, and submitted often necessitates expensive rework activity when initial plans fail to take into consideration factors such as use of shippers or blinding criteria.

Ensuring full kit design during the initial phase of planning is critical as this influences the materials, quantities, and tooling requirements. Lead times associated with the individual kit designs will impact duration and deliverables. The stability and dose form are also critical element as this can restrict the choice of packaging for the kit. Blinding should be explored at the earliest opportunity as it can impact packaging. Sponsors must be aware that timelines and study design can be impacted negatively if they do not know if the IMP and comparator drug are available and if blinding is even possible. From quoting to deciding on how many kits and if a comparator drug needs sourced; through to kit design; production and labelling; your CDMO should deliver right, first time bringing all elements together for distribution of final kits.

Selecting The Right Fit

The value of engaging early in a study's planning phase will be lost if the CDMO fails to offer the breadth and depth of expert services, technology and support sponsors need to develop cost-effective, patient-centric packaging operations that keep pace with the demands of modern small molecule trials. When choosing a CDMO partner, sponsors should look for a vendor that can provide an end-to-end packaging solution that includes design, sourcing materials, packaging, labelling and associated services – such as comparator sourcing, QP release, logistics and distribution. To deliver further value, these components should be project managed by supply chain experts and underpinned by integrated IRT technology.

Opting for an established CDMO partner with global infrastructure and expertise across sciences, pharma and clinical services will also ensure continuity as programs progress through the phases to commercialisation. A final consideration when selecting a CDMO partner should focus on the vendor's environmental management and sustainability credentials.

CDMOs are working around the clock with significant numbers of clients supporting domestic and global clinical trials 24/7. Unlike most sponsor businesses, CDMOs have the infrastructure in place to meet sponsor needs and study timelines and an understanding of the imperative to be able to react, adapt, move fast and to get drug from receipt to final packaging and onwards safely to patients. When you consider the regulatory requirements from the FDA, MHRA, EMA, it is vital that the right bottling lines, blistering lines and overall supply chain capabilities are in place to deliver for your clinical supplies. There is no packaging request that cannot be managed for small molecule, with a CDMO that has established manufacturing capabilities and decades of experience to help you get it right, first time.

Outsource to Optimise Operations

When it comes to primary packaging of solid dose, small molecule products, such as tablets and capsules, processes across trial phases must be as efficient and compliant as possible. A key benefit of partnering with an established CDMO is access to automation that can reduce primary packaging lead times and minimise waste. Access to engineering expertise for tailored tooling and packaging design capabilities is another prime advantage.

By working with a CDMO with holistic visibility over the entire clinical supply chain, primary packaging can play an active role in helping sponsors to reduce overages, plan for variable recruitment scenarios and create robust forecasting strategies that enable sponsors to contingency plan and de-risk clinical supplies. Optimised primary packaging processes and access to expert design and guidance will also minimise waste and negative impact on future stages of a study drug's lifecycle, including secondary packaging and distribution. Where secondary packaging is concerned, access to expert kit and patient pack design, enhanced label generation, fully automated labelling and production processes that reduce cycle time and promote compliance are key benefits of outsourcing to a CDMO with global resources at its disposal.

Flexible Study Design and Increasing RoI Potential

The small molecule market is anticipated to grow with a CAGR of 9.0% over the next seven years,[6] with small molecule drugs becoming increasingly complex and targeted; presenting both new challenges for sponsors to tackle and opportunities to exploit.

From entrepreneurial companies to big pharma, outsourcing clinical packaging strategy to capable CDMOs will help keep ambitious trial timelines on track, minimise waste and inefficiency and ensure continuous resupply to patients. It will also release sponsor personnel to focus their attention on core business activity, reduce operational costs, increase regulatory compliance and optimise processes to support expedited trial completion and return on investment.

In clinical packaging, elements which can change include study size, visit schedules, clinical site, patient demand and regulatory compliance. Scrutinising plans early in the process means that packaging alternatives can be modified as required. In one sponsor's case, early planning of the packaging design resulted in the switch from a visit kit to multiple weekly dosing in a compact wallet design. This not only made patients' lives easier but resulted in a reduction of overall clinical supply units from £300k to £108k, a time saving of an estimated six weeks and a cost savings of approximately £600k. To understand clinical packaging and ensure efficiency and compliance, it must be viewed as part of the bigger picture and undoubtedly, the benefit of outsourcing to a CDMO is a strategic business decision in order to mitigate risk and ensure supply to patients.

The Future of Small Molecules

Compounds over the coming years are possibly going to take a similar pattern to what we experienced in the past 10-15 years with antibiotics, where we saw changing trends on their perceived relevancy. What we are witnessing now is a renewed interest in antibiotics. Similarly, we are now seeing that small molecules have not gone and like antibiotics, they have just changed. As we look to the future, small molecules are being paired with biologics and gene therapies. Only time will tell, but these pairings are where we are likely to see small molecules thrive.

REFERENCES

1. https://www.globenewswire.com/news-release/2019/10/10/1928253/0/en/Biologics-Market-To-Reach-USD-625-6-Million-By-2026-Reports-And-Data.html#:~:text=Biologics%20market%20is%20growing%20at,and%2011.6%25%20CAGR%2C%20respectively.&text=On%20the%20basis%20of%20product,by%20vaccines%20and%20cellular%20biologics.
2. GlobalData: Drugs in preclinical, phase 0, phase I, phase II, phase III, pre-registration or IND/CTA filed as of 16 Apr 2020 (includes drugs exploring multiple routes of administration)
3. https://www.europeanpharmaceuticalreview.com/article/113231/trends-in-the-cdmo-industry-for-2020/
4. https://themedicinemaker.com/manufacture/small-molecules-sizable-market-opportunities
5. https://themedicinemaker.com/manufacture/small-molecules-sizable-market-opportunities
6. Europe Small Molecule Drug Delivery Market Forecast to 2027

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