ALMAC

Partnering to Advance Human Health

Case Study

Moving beyond the transactional

– Choosing a CDMO Strategic Partner

Cara Young of Almac Group discusses how CDMOs looking to differentiate themselves are moving past discrete offerings by extending into comprehensive services and fielding special teams to meet client needs.

Speciality Chemicals Magazine 37. 03 June 2017

Introduction

A contract development and manufacturing organisation (CDMO) has several key attributes that contribute to the success of its clients. Conventional wisdom holds that a CDMO should possess technical expertise, strong project management, and a history of on-time delivery. This remains true, but increasingly selective clients are also seeking more comprehensive capabilities and business flexibility from a single provider. Often clients need support from early phase development into launch and through post-commercialisation. They may also need support for specialised product development, such as designing paediatric dosage forms. Responding to these varied needs is a key differentiating factor. The following three examples showcase one CDMO's adaptability and the strategies it has provided to its clients from development to commercialisation.

Early phase development: API-in-capsule

For one client with an early phase project that was seeking to shorten its development timelines, the CDMO performed a preliminary evaluation to decide whether API-in-capsule was a suitable approach for clinical drug product. The evaluation was performed jointly by a multidisciplinary team of CMC experts from five separate departments.

The team began by scrutinising the client's data to identify possible challenges. In an ideal world, an API destined for automated encapsulation without excipients would have good aqueous solubility, high bulk density, good flow, and narrow particle size distribution. Most modern APIs lack these attributes, but these obstacles can often be overcome with skill and experience. In this case, the API presented poor flow properties, which were likely to cause problems during capsule filling. The CDMO's technical team adapted by customising filling parameters, such as tap frequency and pulse width to permit acceptable flow of the API; this was achieved in less than one day. As a result, an Xcelodose 600S (Capsugel) automated micro-filling system could be used to manufacture 15,000 capsules at two dosage strengths. The capsules were filled within three weeks (single shift, 40 hour working week). If the capsules had been manually filled, the campaign would have taken 500 hours.

Additionally the client benefited from:

- Small quantity of API needed to determine operating parameters
- Ability to fill a wide range of weights, including very low weights, accurately and quickly
- Existing API analytical methods could be used
- Elimination of content uniformity testing
- Leveraging drug substance stability data
- Dedicated API-contact parts instead of developing a cleaning verification method
- Ease of containment
- Mitigating risks associated with changes in API properties during chemical development

The success of this strategy for Phase I supplies led to the client returning for 140,000 more capsules for Phase II studies. This is beyond the intended use for the Xcelodose 600S; despite this, the team met the client's needs by substantially investing in operator training to ensure personnel were capable of efficiently diagnosing and resolving equipment issues.

In response to the client's request, the CDMO also offered capacity reservation, whereby the client could purchase blocks of manufacturing time in advance. This offered the client flexibility to run multiple small volume projects or multi-week campaigns with dedicated capacity guaranteed.

Late phase development: capital investment

For a second client, the CDMO installed and qualified a commercial equipment train that could meet the global demand for a low-dose novel peptide pharmaceutical product. This was achieved in less than thirteen months and within the projected budget.

At the time, the development project was in Phase III and used the CDMO's existing pilot scale technology. While anticipating commercial product approval, both partners recognised the knowledge-base built within the CDMO and agreed upon a strategic investment at the CDMO facility to prepare for scale-up and technology transfer into ongoing commercial supply.

The project presented technical and logistical challenges. First, the API was administered at an extremely low dose. Second, the client's forecasted commercial needs exceeded the capacity of the available equipment, requiring qualification of an entirely new equipment train. Third, the expanded facility needed to be ready for a commercial launch expected in 15 months.

A transfer team composed of development and commercialisation experts coordinated design, installation and qualification of three separate GMP suites: one designated for dispensing, another for fluid bed processing, and a third for encapsulation.

The accelerated equipment installation called for expansion of existing GMP space by over 1,500 sq. ft. in a well-utilised facility, without disturbing existing commercial operations. When it was completed, the new commercial suites incorporated: laminar flow booths with humidity control, Glatt GPCG PRO 120 fluid bed unit with a working capacity of up to 250kg, and IMA Adapta 100 encapsulation machine with throughput capacity of up to 100,000 capsules per hour.

The investment and installation of the new commercial suites demonstrated a commitment to building long term, strategic relationships. It allowed the CDMO to service a client's ongoing commercial needs while providing excess capacity to other clients seeking commercial scale fluid bed processing and/or high speed encapsulation technologies.

Post-commercialisation: paediatrics

A third client with a commercialised adult dosage form needed a corresponding paediatric dosage form with an easy-to-use packaging format. Joint client-CDMO teams worked together to identify a target product profile, and selected mini-tablets filled into stickpacks as the best presentation.

Mini-tablet development differs somewhat from standard tablet development. For example, surface-area-to-weight ratio of mini-tablets is significantly higher, which leads to higher ejection forces. Therefore, higher levels of lubricant are often needed.

Based on experience, the CDMO team carefully optimised several equipment features:

- Punch tip concavity
- Ejection scraper design
- Ejection cam position
- Punch and turret keyways

It also designed 37-tip punches, which allowed compression rates up to 550,000 mini-tablets per hour.

The team turned next to packaging. The process of filling stickpacks is more precise than most packaging operations because it controls the unit dose being administered. Stickpack filling systems therefore often use counting systems to precisely meter the number of mini-tablets delivered to each stickpack. In conjunction with a third party specialty vendor, the team identified, installed, and qualified a Merz SBL-50 machine that could operate at up to 80 cycles per minute.

Conclusion

It continues to be essential for CDMOs to maintain high levels of scientific, regulatory, and quality standards. Increasingly, CDMOs can best differentiate themselves by offering flexibility and adaptability to client business needs. From the examples above, it can be appreciated that CDMOs benefit from in-house engineering groups who have the ability to design, fabricate, and install equipment, and also work closely with third party vendors. Highly skilled operations teams can deliver manufacturing services beyond the routine. Project management groups that can step into expanded roles to drive capital investment projects can widen options available to a client. Finally, a creative business development team is key to understanding client needs and creating customised solutions.

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