



Article

Oct 1 2007 (Vol. 27, No. 17)

CMOs Focused on Meeting Needs and Time Lines Firms Ramp-Up Capacity and Offer More Tools and Services with a Collaborative Approach

William Downey

Investments in new technologies, service offerings, and capacity are just a sample of activities undertaken by contract manufacturing organizations (CMOs) to meet the ever-increasing demands from pharmaceutical and biotechnology industry clients. In HighTech Business Decisions' recent report, Biopharmaceutical Contract Manufacturing 2007: Quality, Capacities and Emerging Technologies, 41 manufacturing directors identified meeting project time-lines as their top concern with their CMO, followed by flexibility with regard to resource and capacity management, cost control, project oversight, and quality.

Current time lines for a new project can vary between six and 24 months, according to the CMOs surveyed. A typical new project reportedly requires 15 months. The wide variation in deadline results from differences in scope, amount of process development already completed by the client, and the efficiency of the technology transfer process.

For projects with a generic or well-defined process, schedules can be reduced by six months. For those that require additional process development, however, deadlines are often pushed back three to six months.

Meeting project deadlines will likely continue to be a top concern even as various issues are addressed as two-thirds of the biomanufacturing directors surveyed would like to further shorten time lines over the next three to five years.

Major Challenges in Meeting Delivery Schedules

Understanding the level of services required for a new project is important for a CMO to realistically project the time required to complete the task. Often this data is not available when a collaboration is formed. "In general it is necessary to make some assumptions when dealing with very early-phase projects, and it is not uncommon for those assumptions to prove to be unreliable," explains Roger Lias, Ph.D., vp, sales and business development, for **Cytovance Biologics** (www.cytovance.com).

The largest challenge CMOs face is incomplete process development. "The major challenge that we have faced in the past has been with incomplete process development or a lack of process understanding on the part of the client before transfer to Xenova Biomanufacturing," says Jim Mills, Ph.D., leader of upstream process and technical business development for the company. "This has meant that further process development work has been needed following transfer of the client's process into our process development laboratories before it has been ready for GMP manufacturing."

Adding Process Development Services

The fact that incomplete process development is a CMO's biggest issue mirrors biomanufacturing directors' plans to outsource more process development activities to their CMOs. As might be expected, the smaller biopharmaceutical companies with fewer staff, less resources, and less manufacturing expertise typically need extra process development, manufacturing, and technical services.

For example, when **Alseres Pharmaceuticals** (www.alseres.com) contracted **QSV Biologics** (www.qsvbiologics.com) it wasn't just for QSV's cGMP manufacturing but also its process development capabilities. The deal was related to Cethrin®, a recombinant protein-based drug designed to promote nerve repair after acute spinal cord injury in preparation to enter Phase IIb/III trials.

QSV has significantly increased its staff over the past two years to meet the increasing demands of its customers for process development services.

“We currently have two independent process development groups each managed by a project manager,” states Richard Hetrick, director of business development for QSV. “Each process development team consists of a lead scientist with six to seven senior development scientists providing expertise in both upstream and downstream process development. A third project manager and process development group is scheduled to come online by December.”

Another example of a CMO offering additional services is the transaction between **CMC Biopharmaceuticals** (www.cmcbio.com) and **Morphotek** (www.morphotek.com) earlier this year. CMC was signed on for the development, GMP manufacture, and regulatory documentation support of Morphotek’s therapeutic antibody, which targets advanced melanoma and other cancers.

The main solution to keeping deadlines is for CMOs and their clients to work closely together. Commenting on how CMC tackles business, Diana Morgan, Ph.D., CBO, says, “At the beginning of a project, CMC staff will often visit the client in order to learn the process. It is also extremely helpful to have the client on site during the early stages of technical transfer as they can bring particular expertise of their cell line, which complements CMC staff’s expertise in the cGMP manufacturing process.

“To ensure this shared responsibility continues throughout the project, CMC Biopharmaceuticals puts together a steering committee for each project, consisting of representatives with a range of skills from both the client and CMC. This group, led by one of CMC’s experienced project directors, is ideally qualified to discuss any difficulties as they arrive, ensuring that the right decisions are made quickly, thus keeping the project on track.”

Consultative Approach

Eden Biodesign (www.edenbiodesign.com) takes a consultative approach with their clients in meeting their needs. “We grew out of a consultancy business,” points out Derek Ellison, Ph.D., business development director and cofounder. “While we didn’t believe there was a shortage of CMOs, we did believe there was a gap in the market for a CMO that was more of a development partner that could guide and advise clients in addition to making and releasing product batches.”

Eden Biodesign’s clients from its consultancy days successfully transitioned into the company’s lab-based services like process and analytical development and finally to cGMP manufacture, according to Dr. Ellison. “UCB, Silence Therapeutics, and Cancer Research UK are all examples of clients that began with our consultancy services before moving to contract development and manufacturing services.”

At **PacificGMP** (www.pacificgmp.com), Gary N. Pierce, general counsel and CBO, says that the company views itself as a development partner in the researcher’s effort to bring a new candidate to the public. “For instance, on a number of occasions we’ve had extended contact advising potential clients who are new to the single-use systems, even prior to their contracting with us. We think that gives valuable assistance to these researchers and, in the event the project comes to us, a head start on making the project a success.”

Menarini Biotech (www.menarini.com), which recently employed **Goodwin Biotechnology** (www.goodwinbio.com) to manufacture the mAb Abagovomab™, agrees that a good relationship between itself and the CMO is important. “Open and honest communication is key to a successful project,” states Andrew Slade, Ph.D., managing director at Menarini Biotech. “You need to have a system to break communication logjams. With Goodwin, we had a system with knowledgeable managers in place that allowed issues to be resolved quickly.”

For example, Dr. Slade points out, “people need to be proactive in discussing and anticipating problems. Many times the processes being transferred are not robust or sometimes information from the client is not complete. Both the client and CMO must be able to discuss the issues openly and freely.”

Furthermore, setting the stage for communication between the CMO and client must start at the very beginning of the client’s project, even before engaging the CMO. As Dr. Mills at Xenova explains, a biotechnology company should “ensure that research and discovery are carried out in a thorough way, bearing in mind that the work done at the client company is setting the basis upon which GMP operations must be built. For example, fully document all stages of research when creating premaster seed cell lines or laboratory processes including reagents and methodology.”

Proper communication also leads to better understanding of the client's individual needs and the ability to highlight issues immediately that may place the original project time lines in jeopardy.

"What helps is to build in an assessment period at the beginning of the project evaluation that takes a realistic look at the specific needs of a project and to talk that through with customers so that aggressive but realistic targets can be set," advises Simon Edwards, head of sales and business development, **Lonza Custom Manufacturing** (www.lonza.com). "Initial milestones that will really indicate the potential success early on are then identified. This is also important so that if there are technical hurdles to be overcome, they are flagged early and can be dealt with together with the customer."

Good communication requires a commitment on everyone's part, which in turn requires a commitment of time and resources from both parties. "While there is a place for e-mails, people talking to people is important," notes Tom Lytle, COO at **Neogenix Oncology** (www.neogenixoncology.com). "We have weekly teleconference meetings with Goodwin. Prior to each teleconference call we have a preconference call with our department heads to go over the agenda. We decide who will cover each agenda item. It is important that we are kept updated on schedules and budgets. In addition to the weekly teleconferences, we schedule face-to-face meetings every six to eight weeks."

In fact, Friedrich Nachtmann, Ph.D., head of biotech cooperations, at **Sandoz** (www.sandoz.com) even recommend that clients have "dedicated project managers and process experts on site during tech transfer and GMP manufacture."

Investing in Technologies

In addition to offering process development services, many CMOs are investing in new processes and technologies as well as ramping up capacity to meet industry needs. **Avecia Biologics'** (www.avecia.com) pAVEway™ technology for the manufacture of therapeutic proteins is an example.

"Our newly launched pAVEway technology platform is attracting interest at the preclinical stage, as some clients value a process that is largely defined at an early stage without the need for considerable rework as the project progresses," comments Kevin Cox, president and managing director of Avecia. pAVEway is expected to provide the client with improved expression levels, increased flexibility, and lower costs.

Similarly, **BioInvent** (www.bioinvent.com) strengthened its large-scale cGMP disposable manufacturing approach for mAbs through the acquisition of a Wave System 1000 (**Wave Biotech, LLC**, now part of GE Healthcare; www.wavebiotech.com).

"After a one year thorough evaluation of the smaller Wave 20/50, BioInvent decided to invest in the largest Wave System 200/1000 line," says Dan Andersson, senior business development director.

Pointing to another advantage with using disposables and meeting time lines, Andersson notes, "It took us only nine months from specification and ordering to starting up regular cGMP manufacturing." This is less than 50% of needed installation time for stainless steel tanks, he adds. "One key factor behind this rapid time line is the minimum need of qualification and cleaning validation."

Goodwin Biotechnology "increased its capacity to 500 L stir tanks, tripled process development capacity, and added upstream development," explains Stephanie C. Finnegan, CEO. In addition to the capacity expansions and greater resources devoted to process development in meeting its clients' needs, Finnegan explains that Goodwin has also "solidified a partner for molecular biology, developed proprietary purification techniques, and hired talented individuals with Phase III/commercial experience."

In addition to building a process development lab in India, the company plans to offer manufacturing services for commercial production in both the U.S. and India. "This has required significant capital investment provided by our parent company," Finnegan concludes.

Boehringer Ingelheim (www.boehringer-ingelheim.com) follows the one-stop-shop concept with a list of clients that range from small research-based operations to large pharmaceuticals.

"All elements required for outsourcing biopharmaceutical development and production, from high expression system to fill-and-finish, can be found within the corporate capabilities of Boehringer Ingelheim," states Rolf G.

Werner, corporate senior vp, biopharmaceuticals.

“We constantly improve our development and production processes and we continuously invest in our facilities. The current capacity adds up to 180,000 L for mammalian cell culture processes and 12,000 L for microbial processes. Our partners know that they can rely on us to respond to their needs by creating flexible and integrated biopharmaceutical solutions, which minimize their initial investment risk.”

Laureate Pharma (www.laureatepharma.com) is working with Boehringer Ingelheim to offer full service capabilities from small-scale to commercial production. “We have entered into a preferred partnership agreement with Boehringer Ingelheim to provide our clients with a complete path from clinical-scale production at Laureate to large-scale commercial manufacturing at Boehringer Ingelheim.” states Mike Cavanaugh, vp of sales, marketing, and business development at Laureate.

In addition to working with Boehringer Ingelheim, “We have added a new pilot plant to Laureate’s manufacturing facility for early engineering runs and producing product for uses such as formulation and toxicological testing. The equipment in our pilot plant facility is designed to facilitate a direct, seamless scale-up from development to cGMP production for our clients’ projects.

“With the new pilot plant in operation, we can accelerate our manufacturing of preclinical material and save on several months’ worth of product development time, which is critical to our clients.”

Time Is of the Essence

Finally both CMOs and clients must remember that time is of the essence. With many project milestones on the critical path, a delay in resolving a minor issue may adversely impact project schedules.

“Both parties need to follow up on issues in a timely manner,” states Nasir Khan, project manager, **Thallion Pharmaceuticals** (www.thallion.com). “For a biotechnology company, a new project may have a time schedule of two or three years. This may seem like there is a lot of time to complete your tasks; however, every single day is important to the project.”

Overall responsibility for meeting project goals rests with both the CMO and its client. The client can improve the chances for success of their project by fostering a collaborative working relationship, investing the time and effort for full communication, and setting realistic schedules and goals. In return, CMOs are adopting new technologies, investing in new capacity, and expanding their service offerings.

■ ■ ■

William Downey is president of HighTech Business Decisions, which published Biopharmaceutical Contract Manufacturing 2007: Quality, Capacities and Emerging Technologies. Web: www.hightechdecisions.com. E-mail: wdowney@hightechdecisions.com.