A New Paradigm

Survival in difficult times has been something of a mission statement for many in the last couple of years. Nevertheless, CROs are doing their bit to help biopharmaceutical companies adapt to the global recession.

While the global recession has exacerbated financial pressures on biopharmaceutical companies, these pressures create opportunities for the industry to re-examine and revamp the drug development process. Consequently, clinical trial sponsors are increasingly relying on CROs to help them accelerate drug development and make it more cost-effective. At the same time, CROs are working with sponsors to develop new relationship paradigms for streamlining product innovation and development. By forming broader, long-term partnerships with industry, as well as by implementing innovations such as electronic data capture, flexible staffing and risk-sharing models, CROs are adding measurable value to drug development.

The failure of the US bank Bear Stearns in the third quarter of 2008 was one of several events that set off a global credit crisis, which applied recessionary pressures to every major economy worldwide. As credit became less available and more restrictive, funding for biotechnology ventures dried up and, as a result, some biotech companies disappeared. Earnings pressures, exacerbated by the burgeoning recession, drove massive change across the biopharmaceutical industry, signalling the final death knell for the blockbuster era. Faced with high development costs, scientific challenges, changing regulations and a number of high-profile product withdrawals, many companies felt compelled to devise a new drug development model, even as they continued to pour money into R&D. Despite the general economy, US-based biopharmaceutical companies invested a record $65.3 billion in 2009 – an increase of $1.5 billion on 2008 (1). Indeed, over the past 25 years, R&D spending by biopharmaceutical companies has exceeded that of all other sectors in the US (1).

Nevertheless, the recession has had a profound impact on CROs. Rationalisation of biopharmaceutical companies’ pipelines resulted in a higher rate of project cancellations and initiation of fewer projects in 2008 to 2009. Additionally, many awarded projects were delayed as budgets were reviewed. As the industry began to tighten its belt, CROs looked inward to find ways to optimise their internal processes and become more efficient. This introspective process has yielded a renewed focus on technology, development of new business models and strengthening of continuous improvement initiatives as CROs help biopharmaceutical companies devise new strategies to rebuild their pipelines.

Cost Cutting and Risk Management

The financial pressures engendered by the recession created a unique opportunity for the biopharmaceutical industry to revamp the drug development process and strengthen product pipelines. Many companies implemented cost-cutting and risk management strategies that focused their energies on compounds and therapeutic areas with greater potential or unmet medical needs. Biopharmaceutical companies also deployed variable cost structures, which are less prone to pipeline variations, by increasingly using outsourcing to shift fixed costs onto CROs. Others, in an effort to rationalise their pipelines and therapeutic focus, have dropped compounds or even entire therapeutic areas, and in some cases have reprioritised development projects. Many companies have undergone organisational restructuring, which has led to significant headcount reductions and facility closures.

In addition to cutting costs, many companies are spending differently. Some are moving more aggressively to restock their pipelines through acquisitions, licensing deals and partnerships. Others are shifting their focus from discovery to development or from small molecules to biologic products. In some cases, organisations are creating entire departments or business units that primarily use external expertise and manpower to provide operational and intellectual ‘muscle’, thus acting as ‘virtual’ pharma companies.

Rethinking the Innovation Process

As companies seek to accelerate drug development, many are taking a fresh look at the innovation process. In some cases this has led to a relaxed ‘guardianship’ of intellectual property (IP), with information shared more freely (2). Several of the largest biopharmaceutical companies have established collaborations to share assays and compound libraries with government and academic research organisations, as well as with smaller biotech companies, in an effort to identify drug candidates earlier. This relaxed approach to guarding and sharing IP is taking place even as the industry continues to consolidate – a trend that was evident before the recession. Many companies view consolidation as a means to obtain size,
scale and market share, thus shoring up their competitiveness amid economic uncertainty.

Such rethinking of the innovation process goes hand-in-hand with more aggressive outsourcing strategies. Partnering with CROs has become more prevalent as drug makers continue to seek ways to cost-effectively increase the volume of quality clinical and preclinical data while reducing time to market (3). This trend has led to a stronger focus on preferred providers with whom companies can leverage relationships and infrastructure to create integrated systems to share information, along with harmonised standard operating procedures and business practices.

There has also been a greater focus on private-federal partnerships – as exemplified by cooperative research and development agreements (CRADAs) – as drug makers tap into federal laboratory expertise while sharing development costs.

All these efforts to revamp the innovation process have largely been fuelled by an intensifying focus on technology, as evidenced by widespread adoption of genotyping for pharmacogenomics, personalised medicine initiatives and exploration of nanotechnology. Rather than employing technology to speed up what was essentially a shotgun approach, companies are increasingly using advanced technologies to quickly and efficiently target drug candidates to specific disease pathways, thereby facilitating development of therapeutic compounds with favourable efficacy and safety profiles in specific patient populations.

Yet, even as consumers worldwide continue to feel the pinch of economic stress, the recession appears to have bottomed out in most countries, and some economies are experiencing modest growth. Consequently, biopharmaceutical companies are executing previously announced strategies and programme priorities have been clarified, resulting in more focused pipelines and an improvement in projects across the industry. As shown in Figure 1, investment in biotech rebounded strongly in 2010 (particularly during the second quarter), aided in no small part by the Affordable Care Act, through which the US government granted a $1 billion tax credit to biomedical companies with fewer than 250 employees (4,5). Thus, as the nascent signs of an economic recovery become more evident, the industry is looking to CROs for more efficient and effective buying processes and methods to streamline development.

At the same time, CROs need to rethink their relationships with sponsors to address their new approaches to product innovation and development. Some CROs are adopting risk-sharing models whereby they invest in the development of novel drug candidates, thus fuelling the hiring of CROs. In the second quarter of 2010, the CRO hiring rate significantly outpaced pharma hiring, and was 250 per cent greater than those of medical device and supply firms (6). The growth in CRO hiring is largely due to a strong recovery in late-stage development (Phase 3 to 4 studies), although this is slightly offset by a slower recovery in Phase 1, as well as a flat to slightly declining market for toxicity studies. Project

The Impact on CROs

As noted above, outsourcing has emerged as a crucial cost-containment strategy for biopharmaceutical companies, thus fuelling the hiring of CROs. In the second quarter of 2010, the CRO hiring rate significantly outpaced pharma hiring, and was 250 per cent greater than those of medical device and supply firms (6). The growth in CRO hiring is largely due to a strong recovery in late-stage development (Phase 3 to 4 studies), although this is slightly offset by a slower recovery in Phase 1, as well as a flat to slightly declining market for toxicity studies. Project cancellations have normalised across the industry and in the third quarter of 2010, the top 10 CROs all reported strong book-to-bills ranging from 1.0 to 1.5, with an average of single-digit revenue growth across the industry (7).

Many CROs, by virtue of their diverse client rosters and range of therapeutic experience, can often cast wider nets than some biopharmaceutical companies, and usually have more recent experience in a particular area of research. Consequently, clinical trial sponsors increasingly recognise that working with CROs is key to developing sound protocols and boosting patient recruitment (8). CROs can help sponsors adapt to the changing clinical trial environment through greater use of technology, flexible staffing approaches, novel approaches to registrational trials and assistance with Phase 4 studies. Unlike Phase 3 studies, which generally have complicated protocols designed to secure marketing approval, Phase 4 trials are often meant to answer questions about a product’s post-marketing use, safety and effectiveness. CROs with the right expertise can thus help companies streamline Phase 4 studies to address the protocol objectives in a more focused manner, making these studies’ designs far less complicated to implement.

Emerging Markets

Biopharmaceutical companies continue to invest in R&D on a global basis, as lacklustre growth in traditional markets is offset by rapid growth in emerging
markets. CROs with a presence in emerging markets are well positioned to capitalise on this trend. The BRIC quartet (Brazil, Russia, India and China) is expected to dominate future R&D growth. Supported by improving infrastructure, emerging economics in Asia are expected to have double-digit growth (15 to 20 per cent), compared to the one to two per cent expected in traditional markets (9). Some Asian countries are already reaping the benefits of clinical trial activity. Clinical trial initiations in South Korea rose by 150 per cent from 2006 to 2009 (10). In India, R&D spending by the top 25 drug companies rose by nearly 17 per cent between 2008 and 2009, and the country’s pharma market is predicted to reach the $55 billion sales level by 2020 (11,12). Additionally, the Indian government plans to establish a $640 million venture capital fund to encourage drug discovery and strengthen the country’s pharma infrastructure (12).

Meanwhile, pharma investment in emerging markets continues apace. Eli Lilly has invested $1.27 billion in the US-Russia Health Sciences Forum (13). GSK acquired the Argentine firm Laboratorios Phoenix in 2010 (14). Sanofi-aventis opened an R&D centre in China in 2010 and is pursuing R&D activities in Russia, South Korea and India (15). Merck CEO, Kenneth Frazier recently hailed the one to two per cent expected in traditional markets (15 to 20 per cent), compared to the growth (15 to 20 per cent), compared to the traditional markets (9). Some Asian countries are already reaping the benefits of clinical trial activity. Clinical trial initiations in South Korea rose by 150 per cent from 2006 to 2009 (10). In India, R&D spending by the top 25 drug companies rose by nearly 17 per cent between 2008 and 2009, and the country’s pharma market is predicted to reach the $55 billion sales level by 2020 (11,12). Additionally, the Indian government plans to establish a $640 million venture capital fund to encourage drug discovery and strengthen the country’s pharma infrastructure (12).

Preferred Supplier Relationships

Preferred supplier relationships are a key strategy of biopharmaceutical companies as they seek to maximise the outcomes of their partnerships with CROs. These alliances allow the partners to make use of business processes, joint accountability, information technology infrastructure and communications across projects, thereby enhancing efficiency. In a recent Avoca Group survey of 88 CROs, more than half indicated they were increasing their pursuit of preferred providerships (see Figure 2) (18). The Avoca Group also polled management personnel at 72 biopharma-sponsor companies; 69 per cent responded that they presently had preferred provider arrangements and 42 per cent indicated that at least three quarters of their clinical research expenditures in 2009 went to preferred providers. When asked what they expect from preferred providers in 2010 and beyond, more than half of respondents from sponsor companies cited factors such as discounted rates, increased senior management oversight, formal performance measurement/management, and preferred access to specific staff members (see Figure 3). Notably, the percentage of sponsors that always expect formal relationship management programmes from preferred providers has doubled since the 2007-2009 period. Additionally, 55 per cent of sponsor respondents indicated that they currently use measurement of key performance indicators (KPIs) to evaluate clinical service providers’ performance; however, only 30 per cent of those who use KPIs felt those indicators...
provided an adequate reflection of providers’ true performance, including the quality of deliverables (18).

The Avoca Group data underscore the importance of establishing the right partnership structure, with shared governance and sponsor access to CRO management. While metrics provide an indication of performance, other ‘softer’ factors may also affect the relationship. Experience suggests that a more subtle approach to relationship management can have a positive impact on the success of the partnership. Such an approach depends on robust business systems supported by operating procedures that clearly define roles and responsibilities. Successful relationship management must also take into account the vested interests of team members, both within the sponsor company and the CRO. Project teams must be empowered to resolve issues in a collaborative way, and team members must be encouraged to avoid assigning blame and to share successes.

**Conclusion**

In the past year and a half, the biopharmaceutical industry has undergone a historic period of change. Evolving business models are being developed to accelerate drug development and make it more cost-effective. As those business models become more widely adopted, sponsor companies and CROs need to address new relationship paradigms for preferred partnerships, which appear to be gaining favour as the clinical trials environment continues to change. The changing environment places a premium on performance metrics and CROs can add measurable value to the drug innovation and development process. As the role of CROs continues to expand, CROs will increasingly be regarded as an extension of their sponsors, a characterisation that should help the industry continue to thrive well into the 21st century.

**References**

10. Taylor N, Trial initiation in S Korea rose by 150 per cent from 2006-2009, Outsourcing Pharma, 8 September 2010
17. Pesic A, Pfizer plans more partnerships in Asia, Outsourcing Pharma, 23 September 2010, www.outsourcing-pharma.com/ Preclinical-Research/Pfizer-plans-more-partnerships-in-Asia

**About the author**

Dalvir Gill, PhD is President, Late Stage Development at PharmaNet Development Group, Inc. Dalvir has more than 20 years of experience in international clinical research. In his current position, he has overall responsibility for PharmaNet Phase 2 to 4 services. Prior to PharmaNet, he spent nine years in various leadership roles at Rhone-Poulenc Rorer (RPR, now Sanofi-aventis) in the US and Europe. During his tenure at RPR, he played a key role in the submission of a number of successful regulatory filings and also held positions in Process Improvement and Corporate Marketing. Email: dgill@pharmanet.com