Snapshot: The CRO Industry Today

Industry strengthens relationships with sponsors, learns the benefits of flexibility and moves more trials out of the developed world

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The CRO industry is growing up. According to the Tufts Center for the Study of Drug Development (TCSDD), by 2002, this comparatively nascent industry accounted for 10% of the worldwide annual R&D spending by sponsoring drug companies. By 2007, Frost & Sullivan reports that the industry will rake in nearly $14.4 billion, compared to the nearly $7.8 billion in revenues reported for 2002. Despite dire pipeline predictions for many large pharma companies, the CRO future appears rosy, due to improving relationships with sponsors, a commitment to expanding global services and learning to be flexible in an ever-changing R&D paradigm.

The Four-Step Program

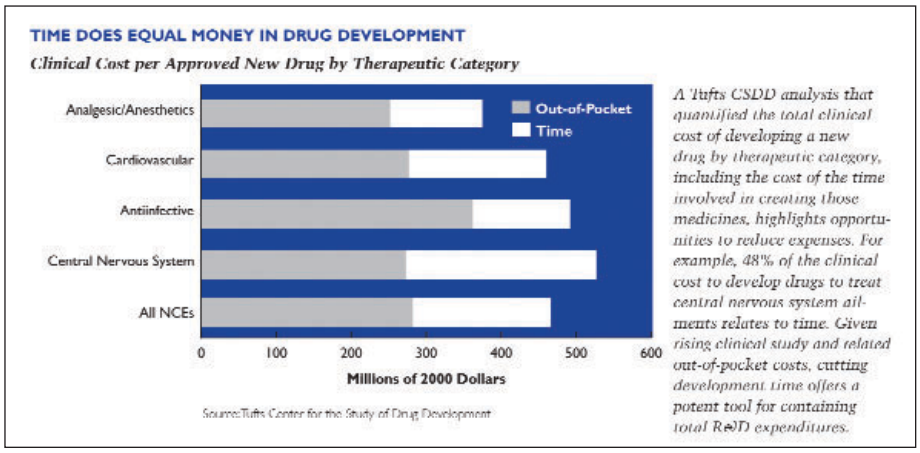
In its September 2003 research report on "Pharmaceutical Services," Goldman Sachs laid out the pattern of "traditional outsourcing integration." The first stage of the pattern was characterized by transactional work between the sponsor and provider.

Currently, much of the CRO industry remains at this stage. One executive at a major CRO characterized the past relationship of sponsors and providers as a "master/slave" relationship. For years, CROs were at the whim of their sponsors. Trials were cancelled and projects were halted, leaving CROs to pick up the pieces. CROs devoted resources to attracting and retaining business, trial-by-trial, project-by-project. Without a concrete promise of future business, this type of relationship made it difficult for CROs to make investments in improving technology and their processes.

Joe Herring, president and chief operating officer of Covance, said, "I think that our clients have come to realize that hiring someone as a vendor, treating them like a vendor, not sharing information, is very time consuming and very expensive. If you get mad at this CRO and place the next study with the next CRO and get mad at them, and then go to the next one, you're not creating value for your company. A number of large pharmaceutical clients right now are saying, 'Stop the madness. Let's pick one or two or three companies that we make part of the team.'"

The preferred provider relationship is the next stage of the outsourcing pattern. More than a handful of companies are now becoming preferred providers of service for pharma and biopharma companies. For example, in September 2003, Goldman Sachs reported that Johnson & Johnson had established a list of five preferred providers, whittled down from three times that many suppliers. Covance also announced in July 2003 that it had been selected by a top 10 pharmaceutical firm to provide all of that company's toxicology work.

Mid-size pharma companies and biotechs are also looking to form stronger relationships with CROs, since those companies do not have CRO capabilities in house. Some of these agreements include risk-sharing opportunities for CROs, so



that both companies become more vested in the success or failure of a compound. Becoming a preferred provider gives CROs the opportunity to make more investments in technology and improvement of their own processes, as the promise of future business from these sponsors becomes more clearly defined.

Currently, Wyeth is in the process of narrowing its list of service providers. The company recently closed the gap from 45 CROs down to five. Dr. Christopher Gallen, vice president and clinical operations head at Wyeth Research, commented, "We started out looking at about 45 different CROs. We went through a very detailed process examining their capabilities, costs, performance records with us and their references. We matched them up against our specific needs in the particular therapeutic and geographical areas that we focus on. In the first cut, we had to figure out who had the capabilities and who seemed like a reasonable possibility."

He added, "There were interviews with different teams and different groups within CROs to determine who's really qualified for our therapeutic areas. We also reviewed past performance, since we worked with most of them; that drilled it down to about eight. Then there was an even more intensive period of going through the financials, what they would agree to, what we thought their performance was likely to be. Based on further qualifications, and we narrowed it down to five."

Wyeth didn't just stop there. In its clinical data management area, the company began a new partnership with Accenture in 2003. The partnership phase is the third step in the aforementioned pattern of outsourcing. This relationship is characterized by "incorporating the client into strategic planning, assigning dedicated relationship management, making directed investments and building strong collaborative mechanisms." From the looks of it, the Wyeth and Accenture partnership aims to do exactly that.

According to the agreement, Accenture has become a long-term, sole-source provider of data management for one of the world's largest drug companies. Dr. Gallen stated, "We are optimizing the CRO relationship line by line in order to make it work for both of us in order to achieve our objectives." He added, "Accenture has basically become our data management group. Their employees are in our buildings, working side by side with our staff, as well as working with their colleagues all over the world to run data management."

The 10-year agreement helps free up some of Accenture's resources that would normally be allocated to sales, as the company no longer needs to chase continued business from Wyeth. Dr. Gallen said, "The work will be coming to them for a 10-year period, so they can therefore make investments in productivity enhancements and have a sufficient period of time to recoup over the period of the contract."

And while he couldn't say whether Wyeth would be pursuing this type of relationship with other, "typical" CROs, he stated, "It [the partnership with Accenture] is quite a radical and creative endeavor with its design driving them to fundamentally improve the entire data management process for our mutual benefit. I believe this sort of partnership is the next stage that the CROs should be shooting for."

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— Joe Herring, president, chief operating officer, Covance

The fourth stage of the outsourcing pattern is achieved with strategic alliances, bringing partnered companies closer together to achieve shared endpoints and goals through strategic planning and open-ended agreements. And so far, the CRO industry appears to be following this four-step pattern. Mr. Herring commented, "It's an incredibly exciting time. If some of the discussions that are going on right now bear fruit, it's going to be a tremendous growth opportunity, because I think CROs will have deeper, more meaningful relationships with pharma clients." He added, "Pharma is going to find it much easier to outsource to someone whom they know and trust over time rather than treating CROs like vendors whom they don't know or trust."

Likewise, some see CROs taking on greater and greater roles for sponsors. Alan Horgan, vice president of late stage development at MDS Pharma Services, conjectured, "I think there'll be more outsourcing of whole programs to the CRO industry. I think there'll be some enlightened companies that actually hand over all of their development work to CROs, but not many." So far, the industry seems to be following the outsourcing pattern to the last stage, but it's anyone's guess as to when they'll get there.

Covance Expands In China

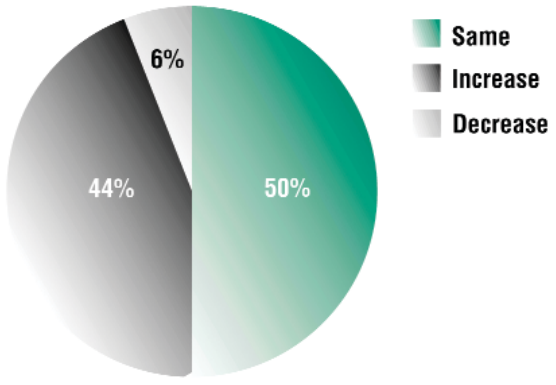
COVANCE INC. IS EXPANDING its clinical trial operations in China through a collaboration with Excel PharmaStudies, Inc. to support the international biopharmaceutical industry's drug development needs in China. According to the company, the collaboration will strengthen Covance's clinical capacity in China to conduct global studies. Excel PharmaStudies, with headquarters in Beijing, is the largest domestic contract research organization (CRO) in China, providing full clinical development services. "By partnering with Excel PharmaStudies, we are able to offer our global biopharmaceutical clients faster local patient recruitment across a wide spectrum of therapeutic areas, combined with strong project management and process controls required to meet their drug development needs," said Dr. Alan Wood, general manager of Covance's Global Clinical Development Services unit. According to industry sources, China is the fastest growing pharmaceutical market in Asia Pacific with market growth rates of approximately 15%. China offers significant opportunities for global clinical research and development including world-class research and laboratory facilities, availability of internationally trained scientists and medical professionals, and access to a large "treatment-naïve" patient population. Covance will provide ongoing investment in training to Excel PharmaStudies. Lyle Holm, vice president, clinical and periapproval service delivery Asia Pacific at Covance, commented, "By instituting an integrated business approach with Excel PharmaStudies, we will avoid the communication and process breakdowns that might occur in typical multi-vendor trials. Our mutual clients will benefit through faster and more accurate gathering of trial data and study results for their clinical programs in China."

At Your Service

So how does a CRO go from a preferred provider, to a partner, to one half of a strategic alliance? It all comes down to one word: Flexibility. Being able to provide the sponsor with what they want and when they want it, with everything in-between. It's not an easy task, but as with any service industry, that's what it takes. But is it possible for large multinational CROs to be as flexible as smaller organizations? Some say yes, others say no, and some are waiting to see.

In July 2003, Dr. Christopher Milne, assistant director of the TCSDD, wrote a report on a study he conducted on the impact CROs had on the R&D environment. In an interview for this article, he said, "As the CROs get large, they do have to worry about maintaining a pool of resources they can bring to bear when a sponsor is coming to them. If a sponsor's in-house capacity is exceeded, they don't want to hear, 'Well gee, *we* don't have anybody in that area either.' CROs are going to have to either develop some sort of backup plan, which may be some sort of network themselves, or develop a cadre of consultants or people that are out in the clinical research centers that they can draw on in times of need. It's developing competencies and maintaining them ahead of the demand curve. It's a difficult thing to do, but it's how CROs maintain their position in a difficult and evolving R&D paradigm."

U.S.-based CRO Survey Respondents Reporting Foreign Clinical Trials, 2000-2002



Source: Tufts Center for the Study of Drug Development

Others believe that the drive towards obtaining all these services will leave CROs bloated, "cracked," and in need of subcontractors to spackle inevitable holes or inefficiencies. In CONTRACT PHARMA'S March 2004 issue, Steven Heffner, acquisitions editor of Kalorama Information, a division of MarketResearch.com, wrote, "The consolidation and maturation of the CRO sector will lead to the kinds of big-organization inefficiencies that made big pharma look to CROs in the first place." He added, "This drive toward CRO service expansion will inevitably leave cracks in competencies to be filled by subcontractors."

Many in the industry don't see it that way, pointing out that the CRO industry is structured differently than the pharma industry. Mr. Horgan disagreed, stating, "The silo structure that you get in a pharma organization is not applicable in our business; ours is a very, very flat structure which allows it to be more flexible and responsive." He concluded, "I believe there is a good, strong future for the larger CROs." After all, would Dennis Gillings have paid millions of dollars of his own money to take Quintiles private if he didn't believe there was a future for the largest CRO in the world? Exactly.

Another way of looking at it is, for instance, when a CRO partners with a niche company (or even its competitors) to provide services that it does not ordinarily perform, it demonstrates how flexible that CRO is. Josef von Rickenbach, chair-

man and chief executive officer of Parexel International, stated, "Our view is, we are here to serve [the sponsors]. What they want, they get."

He added, "We have decided, up to this point, that we are not providing our own central lab services. We are partnering, even with our competitors, if it's in the interest of the client. We are partnering on a geographic basis. We're partnering with several technology companies. Our goal is not to become a fully integrated everything." Through partnering, smaller, specialized companies can help larger companies build their flexibility and attract more preferred provider relationships, hastening the end of the transactional stage of business for the CRO industry.

As Dr. Milne put it, "The sponsors are using 10 different organizations and have the flexibility of going to other providers. If you can't provide those services, then you're going to lose out. CROs, by the same token, if they're big, have the resources and relationships to call on when those demands are exceeded." However, if larger CROs do not bend over backwards for a sponsoring company, there are plenty of medium-sized providers that are waiting to show clients just how flexible they can be.

So, what does a sponsor look for in a preferred CRO provider? What qualities make one CRO more attractive than the next? According to Wyeth's Dr. Gallen, flexibility is key, but "The main quality that determines the CROs that you ultimately select is their consistent user-friendliness!" As Dr. Gallen and other industry insiders have said, one bad experience will poison people within an organization against a particular CRO.

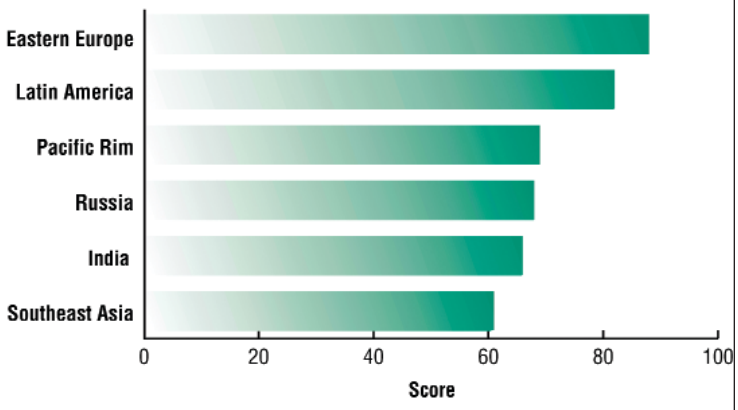
He added, "User-friendliness is by far the real psychological driver of how you distinguish between these otherwise fairly comparable organizations." When it comes to cost and time savings, other insiders have claimed that there is not much of a significant difference between CROs. What it comes down to is the company that provides that best service. It *is* a service industry, after all.

Going Global

CROs have learned to be flexible and go where the patients are. While many CROs have been multinational corporations for years, once untapped regions of the globe are becoming more and more attractive to sponsors. In recent years, areas such as Eastern Europe, Latin America and now Asia are becoming increasingly popular due to improved access to naïve patient populations, easier recruitment of patients, a more facilitative regulatory environment and, in some cases, lower costs.

According to the TCSDD's Impact Report on CROs, "As patient recruitment has become increasingly difficult in the U.S., western Europe and Japan, other parts of the world offer better access to subjects, especially in certain therapeutic areas." Part of being flexible and staying ahead of the "demand curve" is to determine where the patients are. In the past two to three years, CROs have either partnered with local companies or set up their own facilities in these regions of the world (See "Covance Expands In China," p. 44 and "PPD Opens Office in India, p. 47).

Attractiveness of Geographic Regions for Patient Recruitment



Score: 100 = area of highest potential; 0 = area of least potential

Source: Tufts Center for the Study of Drug Development

Companies are taking advantage of willing patients in these areas. Through its partnership with Apex, a CRO that provides services in the Asia-Pacific region, Parexel is able to offer expanded services to clients. The lower costs and willingness of participants is hard to pass up, Mr. von Rickenbach says. "A lot of these people are relatively underserved in terms of healthcare. They have a high motivation for participating in clinical trials because it's a way to get free healthcare." He added, "The costs are lower. For a particular patient in one of those countries [India and China], the costs for the data from one of those patients used in the clinical trial is substantially less that it would be in say, Germany."

Or is it? Some say the buzz around the lower costs of trials in India and China has yet to really materialize. Dr. Milne said, "Whether it's less expensive seems to be a bit of a wash right now. I think once you're set up there and once you have the infrastructure in place, it probably is cheaper. That's where some of the hype comes in, as far as seeing some figures about how it's x percent cheaper to do trials in India, but that all


Photo courtesy of Wyeth Research

PPD Opens Office in India

PPD, Inc. has opened a new office in Mumbai, India. The new drug development site in Marol, Andheri (East), provides patient recruitment and clinical monitoring for Phase II-IV studies in certain therapeutic areas. Fred Eshelman, chief executive officer of PPD, commented, "The Mumbai office expands our geographic footprint in Asia and enhances our ability to conduct global studies in industry-targeted therapeutics." He added, "Extending our drug development expertise to this part of the world allows us to assist clients in offering cost-effective clinical research opportunities to treatment-naïve patients for a number of therapies, including oncology and metabolic disease, such as diabetes." Recent regulatory reforms have made India an important new market for clinical research. CenterWatch reports that India's pharmaceutical market is the second largest in Asia, increasing by more than 9% annually. Some experts project total clinical research spending will grow more than 30% annually for the remainder of this decade, resulting in revenues for clinical research services potentially reaching $75 million in 2005 and $300 plus million by 2010. According to a report in CenterWatch, patients can sometimes be recruited in India three to four times faster than in the West, including a heightened acceleration for oncology studies, due to the unmet needs in this therapeutic arena.

depends on what you've got set up there." However, if time is money, and the recruitment of patients in these developing countries is faster and easier, then there may be some truth to the hype.

It has also been said that the regulatory environment in these new hotbeds is an attractive characteristic of conducting trials in the developing world. Dr. Gallen stated, "The ever-growing bureaucratic burden in the developed countries basically slows down your ability to get trials started and going, which has created a very strong incentive to go to other countries where it is simply more efficient to do the research."

He went on, "I have been impressed by the quality of the data from studies conducted in the developing countries. I think CROs and the sponsor companies both need to be developing capacity there. This is a huge opportunity for the CROs. While many of the mid-size companies have enough staff to run trials in the large market countries, very few of them have enough staff to run their trials in the developing countries. The big companies may have enough staff to do it, but even there, it's questionable for many of them. So I think that that's a huge market opportunity for the CROs in the future. And I would not be surprised if, somewhere down the line, investigators in western Europe and the U.S. eventually begin to be concerned about the fact that so much of the clinical work is moving out of the developed countries into the developing countries. The shift is basically driven by the national requirements and industry is responding rationally to be as efficient as possible."

He concluded, "In some regions, the regulatory burden is really growing quite large and is quite discouraging, particularly in western Europe. It's a very big problem."

Others are wondering what effect the new additions to the EU are going to have on member nations. Dr. Milne said, "Eastern Europe is still in a building stage and that area has certainly been hottest over the last few years. People may have some concerns there with regard to what's going to happen when they fully accede to the European Union, because in some ways that may be good and in some ways that might be bad. You may start to get more western Europe-type restrictions on what you can and can't do. Over the next few years it could go either way."

Mr. Herring concluded optimistically, "Getting proof of concept to the geographical regions of the world that have naïve patients and great infrastructure for doing clinical studies is a great opportunity where technology, process and global reach have all come together and can make a difference. And that has been the biggest issue facing clinical research: how you get access to patients, get them on a study, get clean data more quickly."

CROs are continuing to improve the relationships it has with sponsors, locking down future work and moving out of the transactional, piecemeal work stage. Companies are learning to be ever more flexible by adding capabilities of their own or partnering with niche providers and sometimes even their competitors to offer as much value as they can to a sponsor. According to sponsor companies, a CRO's ability to please the client will ultimately secure future business, and possibly stronger, preferred provider-type of relationships. As these relationships improve, the CRO's ability to make further investments in technology and improving processes will lead them to provide better services to their clients, as well as secure a fixed space in the "ever-changing R&D paradigm." ■

Photo courtesy of Parexel International