OUTSOURCING
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First part of a multi-issue series

As some companies tighten their belts, CROs across the globe are enjoying this growing business trend

BY DAVID HUTTON

AMID THE CHOPPY WATERS of the international economic seas in recent years, many pharmaceutical businesses have been tightening their belts to weather the stormy tide, and drug development has felt the pinch.

One sector of the industry has found itself swimming against the tide—contract research organizations (CROs), which have seen a steady increase in business over the last several years, tough financial times notwithstanding.

According to market research firm UBS Global Healthcare, the value of the global CRO industry is estimated at between $15 billion and $24 billion, with growth rates in the neighborhood of 15 percent annually. Biopharmaceutical companies spend $20.2 billion on drug discovery research annually, according to Barclays Capital, with $1.6 billion being outsourced today.

According to a 2005 Thomson CenterWatch survey, the $15 billion CRO industry was growing at a rate of 12 percent annually, but over the last two years, statistics point to a significantly greater rate of growth of nearly 17 percent. In 2007, of the approximately $60 billion biotech and pharmaceutical companies spent on drug development, $15 billion, or about 25 percent, was outsourced.

In this story, the first in a multi-part series, we take an in-depth look at the geographical roots of outsourcing and where the business trend has spread, and we also examine the advantages and challenges of sending work outside your company's walls—and potentially, your nation's borders.

Where it all began

If you think the rise of CROs is a phenomenon that has taken off in the last five years, you would be mistaken.

Dr. J. Fred Pritchard, vice president of drug development services at Celerion in Lincoln, Neb., says CROs first emerged in the 1980s in North America in North Carolina, California, Pennsylvania and New Jersey areas, as well as Wisconsin, Texas and Nebraska.

"In Europe, CROs emerged in the major scientific centers of the United Kingdom, France, Germany, Netherlands and Switzerland, often evolving as spinouts of prior pharmaceutical operations," Pritchard points out. "In Asia, CROs are emerging in India, China and there has always been some activity in Southeast Asia. Australia, South Africa and South America have small industries by comparison."

Pritchard says CRO locations are often dependent on the type of services they offer.

"Other factors include the need to have access to talent for recruitment into their organizations and being close to the client base," he notes. "They are often close to major pharmaceutical or biotechnology hubs."

Domestically, Pritchard notes that preclinical CROs tend to be located near areas that train people in veterinary sciences, while Phase I CROs are often located near areas that recruit volunteers successfully and also have a steady supply of scientifically trained workforce such as university centers. Late-stage clinical CROs have locations near major university clusters, such as Research Triangle Park in North Carolina, can feed the need for statisticians and medically trained professionals.

"Laboratory-based CROs need to consider transportation needs for efficiency as well as access to analytical chemists and bioengineers," he says.

Drug discovery beyond borders

Officials with Amarex, a global CRO based in Germantown, Md., see outsourcing on the rise not only globally, but also on a domestic level.

Patrick J. Burke, senior director of business development at Amarex, says that domestically, the majority of CROs are located in regions of the country where the majority of drug development companies are located.

"One reason for locating near the drug development companies is that there are some advantages to the drug company being close to their vendor to facilitate communications, particularly to facilitate face-to-face meetings to review complex clinical trial projects," says Burke. "It also benefits the CROs to work near the drug companies to give them access to a supply of trained employees that migrate between working for drug companies and CROs."

According to Dr. Michael Schlosser, president and founder of Midwest BioResearch, most CROs are located in the United States, China and Japan, locating there because of access to major pharmaceuticals and biotech markets and to incur spending within region registering products, which is particularly important for China. Schlosser points out that in the United States, new CROs and expansion of existing CROs are tending to locate/expand in western areas (e.g., Covance, CRL), closer to biotech centers like San Diego and San Francisco.

Celerion is a privately owned CRO formed through the acquisition of the development and regulatory services consultancy and early clinical development operations of MDS Pharma Services. Dr. J. Fred Pritchard, vice president of drug development services at the Lincoln, Neb.-based company, says CROs first emerged in the 1980s in North America in North Carolina, California, Pennsylvania and New Jersey areas, as well as Wisconsin, Texas and Nebraska. Many of the companies that are based in these areas often choose locations that are close to major pharmaceutical or biotechnology hubs, Pritchard observes.

Dr. Lee Babiss, executive vice president of global laboratory services at PPD Inc., a global CRO with offices in 41 countries, agrees that most large, global CROs have a strong presence in North America and Western Europe.

"Yet, they also have established operations in Asia, Eastern Europe and Latin America, three fast-growing, emerging markets where we are seeing strong growth in drug discovery and development," Babiss says. "Clinical trials have become more complex and costly because of the need to satisfy stricter regulatory requirements and to ensure efficacious data. These regions have become increasingly important because they offer highly qualified investigators and large, targeted patient populations. For example, about 80 percent of Brazil's residents live in urbanized areas, making patient enrollment, retention and post-trial communication easier."

Advantages in key geographic areas

Burke notes that many CROs exist in the same region as their drug company partners because CRO founders may have worked for the companies in the past, and they start their business near where they live.

Accessibility to patients is an important consideration in order to enroll patients in clinical trials quickly. In addition, expansion into areas such as China and India has been occurring, driven by both cost efficiencies, which can be realized by both CROs and their clients, and access to well-educated and trained scientists.

"Our clients are expanding their programs into these areas because these regions offer large patient populations and well-educated, experienced investigators," Babiss says. "China, for example, offers strong scientific talent. China's pharmaceutical industry has experienced a 21 percent compounded annual growth rate over the past five years, and the drug discovery market is very strong. Asia Pacific is an important region for PPD, and an area where we have made long-term investments."

Sekhar Medisetti, a healthcare analyst with GBI Research, says outsourcing is an attractive option for myriad companies because the time needed to recruit patients in Latin America continues to be very fast, leading to time and

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—Dr. J. Fred Pritchard, vice president of drug development services at Celerion

cost savings for companies, he explains.

"One reason that outsourcing is such an attractive option is the availability of a pool of available patients to participate in clinical trials," Medisetti says. "Going forward, I see the shift to low-cost regions such as Eastern Europe and Latin American countries, Brazil and Mexico."

Babiss says PPD's acquisition of BioDuro, located in Beijing, enabled the company to offer preclinical small molecule drug discovery services to multinational and local clients.

"We gained more than 650 highly skilled chemists, biologists and quality scientists," he says. "Combined with our acquisition of Excel PharmaStudies, we have expanded our capability to deliver global central laboratory, drug discovery, regulatory, Phase II-IV clinical development, data management and quality assurance services to biopharmaceutical companies in China, Japan and the entire Asia Pacific region. We are now the largest contract research organization to offer discovery and clinical development services in China."

In Europe, CROs tend to be more regional in nature and cater to clients' cultural and regulatory needs. Asian CROs are emerging quickly and offer lower costs; however, the industry is watching to see if they can consistently meet the rigor of western quality audits by sponsors and regulators, Pritchard adds.

"For European and North American clients, the time difference and distance can be a factor in ensuring good communications and oversight of the work," Pritchard says.

Pitfalls and challenges

There are, of course, challenges facing outsourcing that can vary in certain geographic regions.

Jeremy Spivey, a senior research analyst at Cutting Edge Information (CEI), which recently produced a report on the outsourcing market, "While most companies see India and China as potential areas for large growth going forward, the perspective we heard is that they can still present problems if the trials aren't managed extremely well. In some cases, regulatory hurdles or infrastructural issues can delay trials for many months.

"In North America and Europe, the cost of the CRO workforce is often high, so pricing tends to be increased on a per-patient or per-study basis," Spivey adds. "However, other value-adds tend to be better, such as access to specific expertise, knowledge of the science, up-to-date equipment and methods of working."

For some companies, even the most minor issues can become major when trials are running worldwide, according to CEI's report.

"One top company realized they had a serious logistical issue when trial protocols were having to be translated into 33 different languages and dialects," Spivey says. "Another found that the Spanish dialect used led to an improper protocol interpretation on a major element of the trial when read by those speaking a different dialect."

Schlosser says other challenges impacting the outsourcing trend can include access to established CROs with depth of expertise, and the protection of intellectual property within the United States.

Burke agrees: "The biggest challenge is likely access to experienced staff, e.g., a region that might be very affordable in terms of living and business expenses is also likely to be a region without many people that have clinical research experience," he says. "Another challenge would be a region that is not close to a sizable airport, because a certain level of periodic face-to-face meetings is important."

Emerging regions do not have a long history of conducting global discovery and development programs, and Babiss notes that there are sometimes immature infrastructures and facilities, unclear regulatory guidelines and ethics committees in hospitals that are not fully informed about good clinical practice (GCP) guidelines.

"Clients, CROs and regulatory agencies continue to put forth a large effort to increase GCP training and bring more scrutiny and adherence to GCP standards and standard operating procedures (SOP) in this region," Babiss says. "In addition, China has a relatively long regulatory approval process, and it is working to bring regulatory filings more in line with the rest of world. Some of the best young talent, trained as chemists, is based in China. The challenge is that it takes several years of training to transition from a synthetic organic chemist to a medicinal chemist. While these challenges are real, in the end, the value PPD gains by making such investments will clearly be realized for our current and future clients and shareholders."

In Europe, the Clinical Trials Directive was approved in 2001, although it was not fully implemented in most countries until 2006 and then only in the European Union. Babiss notes that the directive attempted to streamline clinical trials processes as multiple requirements made Europe a complicated area for drug development.

"While the directive has improved these processes, there continues to be problems with implementation in some countries," he notes. "In addition, the clinical trials directive is only applicable to countries that are members of the European community. There are different processes for Eastern European countries such as Russia and the Ukraine."

The Clinical Trials Directive was an important step toward creating uniform legislation in Europe, yet companies continue to face different requirements when conducting clinical trials in Europe, as there is not a unified approach to drug development. Babiss notes that an in-depth understanding of the laws of all countries where trials are being conducted is required.

"As an example, when planning trials in Denmark, France, Portugal and Sweden, it is only necessary to apply to one ethics committee," he says. "Yet, Germany, Spain and the Czech Republic have local ethics committees and a central ethics committee, and each give opinions on trial design and conduct, which can slow the start of a clinical trial."

Given today's challenging R&D and regulatory environments, CROs also must understand that the needs of each client may vary. Medisetti cautions that CROs need to remain flexible, and use their global resources and technologies to deliver capabilities that bring both innovation and efficiencies to clients' drug discovery and development programs.

"CROs that build close client relationships through strategic partnerships can become more closely involved earlier in a program and gain a better understanding of program goals," he says. "When CROs work collaboratively with clients to deliver quality standards while meeting timelines and costs, clients want to continue to build upon that relationship."

Regional hot spots

Looking to the future, PPD's Babiss points out that biopharmaceutical companies will come to rely more heavily on the expertise, technologies and global resources of CROs to manage their R&D programs.

"CROs play a strategic role across all phases of drug discovery and development and can ensure patient safety, manage complex multinational trials and navigate changing regulatory environments," he says. "We are also able to provide cost benefits and are more likely to have a deeper understanding of local language, culture and norms, qualities which lead to better relationships with investigators and improved trial execution."

Schlosser believes that over the next few years, key emerging markets for CRO growth will likely be China and India.

"China and India are certainly poised for growth; however, as expertise and quality starts to approach U.S. in these regions, prices which are already trending upward, which may limit the attractiveness for working in these regions by U.S. companies," he says.

Medisetti, however, says he sees the potential for contraction in the CRO segment.

"I think that we are likely to see some consolidation because CROs will pursue mergers and acquisitions," he says. "They will be looking for a chance to add services to their portfolios." **ddn**

EDITCONNECT: E051028

DR. LEE BABISS, EXECUTIVE VICE PRESIDENT OF GLOBAL LABORATORY SERVICES AT PPD INC., a global CRO with offices in 41 countries, says that some of the challenges facing the global outsourcing market are regulatory in nature. Emerging regions do not have a long history of conducting global discovery and development programs, Babiss notes, and adds there are sometimes immature infrastructures and facilities, unclear regulatory guidelines and ethics committees in hospitals that are not fully informed about good clinical practice (GCP) guidelines.

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