CRO Industry Rides High on Emerging Opportunities in Eastern Europe

by Ajit Baid

A perceptible sense of optimism infuses the global contract research organizations (CRO) market. According to the latest research from Frost & Sullivan, revenues are forecast to increase at an annual average of 13.1% in 2002–2007, reflecting a climb from US$7.78 billion to $14.37 billion (1).

As biotech companies try to maintain greater ownership of their drugs, they are increasingly redirecting R&D funds from their pharmaceutical partners toward CROs. Through 2007, CRO revenue growth from biotech is expected to surpass that from pharmaceuticals.

Growth in all regions continues to be fueled by the need for drug developers to contain costs and speed products to market, increasing globalization of pharmaceutical and biotech companies and technological demands from drug developers.

Costs and Speed

Dwindling revenues, a softening global economy, and rising R&D expenses are exerting cost containment pressures on drug developers. This is providing further impetus to outsource R&D services.

CROs now conduct preclinical safety assessments as well as phase I, II, and III clinical trials for pharmaceutical and biotech drug developers. Such outsourced studies are often performed more than 30% faster and at lower absolute costs than comparable in-house efforts. For instance, pharmaceutical companies usually take 88 weeks to complete phase I trials, whereas CROs complete the same task in 66 weeks. CROs are also able to prune 56 weeks from phase II trials and 43 weeks from phase III studies.

In an industry where each day of market delay costs nearly $1.3 million in lost sales, such time savings are critical. Thus it is no surprise that about 18% of all drug testing done worldwide is outsourced to CROs, and that percentage is expected to grow as the benefits of outsourcing become more apparent (1).

Clinical testing expenses, already a major proportion of in-house R&D outlays, are rising by an estimated 11.8% annually, forcing drug developers to look for more economical alternatives (1). Contract research companies can offer decreased testing costs through economies of scale and access to low-cost test sites.

Eastern Europe Ready for Testing: Some CROs have reduced testing expenses by conducting trials in regions where patient reimbursements are significantly lower than in the United States or Western Europe. Eastern Europe, in particular, is emerging as a hub for outsourced clinical trials. Patient compensation, which accounts for the lion's share of clinical trial costs, has grown increasingly expensive in Western Europe. Compensation of volunteers and medical staff in the region is now comparable to US rates.

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In contrast, volunteer fees in Bulgaria, Romania, and Croatia average around $2000 per person instead of the $5000 per person generally paid in the United States. Increasing regulation often compels multiple trials, and many trials require a sizable volunteer

base, so the savings accrued can be considerable.

The advantage of conducting trials in Eastern Europe is compounded by the significantly lower fees charged by physicians who have skill levels comparable to their counterparts in the United States and Western Europe. In addition, trial centers in Western Europe regularly bill for all their expenses whereas trial centers in Eastern Europe generally levy charges only for costs incurred outside their standard operating expenditures. This situation has caused a shift in clinical development from Western Europe to Eastern Europe.

Price Controls: Another factor driving change in the European CRO industry is the ongoing use of government price controls, which has served to depress R&D activity in Western Europe, especially in the high-cost area of preclinical research.

In 1990, European pharmaceutical companies allocated nearly three-quarters of their research budgets domestically for in-house and CRO development projects. By the end of the decade, they had drastically reduced that share to 59% (1). Much of that shift results from price controls.

Governmental healthcare expenditures in Western Europe have soared, at least in part because of the practice of providing partial or total reimbursement for the cost of prescription medicines. Most governments have resorted to price controls to stem excess spending. The cascade effect of those price controls has been dwindling company revenues, reduced R&D funding, and increasing pressure to curb drug development costs. Many manufacturers have reacted by shifting sales and R&D activities to the United States, where drug prices are linked to market conditions.

In the United Kingdom, a pharmaceutical price regulation system controls drug-manufacturing profits. In addition, the National Institute for Clinical Excellence (NICE) limits the use of expensive new drugs in the country through published protocols regarding the cost-effectiveness of novel medications and procedures. In France, price-cap increases on prescription drugs are regulated at the national level. If German physicians exceed state-determined limits on prescription spending by more 25%, they are compelled to make good the difference from their own pockets. In Italy, the cost of a reimbursed drug is based on government-determined prices in other EU countries. New Italian legislation has reduced the prices of all reimbursable drugs and has altered reimbursement processes for new medicines.

The outcome of such strict price control measures has been to reduce the use of expensive new drugs and encourage the use of older, more economical alternatives. Although that has compromised the quality of patient care, public efforts to rescind such restrictions have been futile in the face of spiraling drug costs, soft economies, and shrinking government budgets.

Preclinical research has been negatively affected in such circumstances. Because this phase of the drug development process is cost-intensive, relying on sophisticated science and expensive testing equipment and facilities, developers are reluctant to commit to high capital expenditures, especially when revenues are relatively stagnant.

Also, because preclinical testing needs to be located close to central development efforts, US pharmaceutical and biotechnology companies are unlikely to outsource preclinical work to European CROs. This contrasts with the growing movement to outsource clinical work to Eastern European CROs.

Favorable Environment for Clinical Research: As already mentioned, the primary attraction of outsourcing clinical trials to Eastern Europe is the low cost of patient reimbursement. Similar cost savings can be had in other regions. But trials in Eastern Europe have the additional advantage of being faster than those in other developing regions of the world: Patient recruitment is easier because of the region's racial similarities with the United States and because of the region's healthcare structure and economic realities.

Centralized healthcare systems that provide fairly straightforward access to sizable, homogeneous patient populations have aided recruitment drives in Eastern Europe. Individuals in this region are relatively undermedicated, and compliance with study protocols is exceptionally high. This reduces the risk that patients might use competing drugs that could distort the data. High quality patient populations have contributed to superior quality data collection, which has helped expedite regulatory approval.

CROs on the Move: Many leading CROs have established bases in Hungary, Poland, and the Czech Republic. Attracted by the prospect of even greater savings, CROs are exploring possibilities of setting up facilities in Russia, Bulgaria, Romania, and Serbia as well. Already, Quintiles Transnational Corp. (www.quintiles.com) has opened offices in Bulgaria, Russia, and Croatia, and ICON Group International (www.icongrouponline.com) and Parexel

The Kremlin in Moscow at night PHIL SIGIN (WWW.ISTOCKPHOTO.COM)

International Corp. (www.parexel.com) have set up sites in Latvia and Lithuania, respectively.

Nonetheless, some clinical development activity is expected to continue in Western Europe. Deep-rooted cultural and linguistic similarities with the United States and highly skilled medical personnel are likely to maintain the region as a key global research base.

Besides not offering these benefits, Eastern Europe also suffers from a reputation of being somewhat untested. Because time to market is critical and delays resulting from inconsistent results or other problems could result in a significant loss of income, some sponsors prefer to take the safer, tried-and-true route of using Western European trial centers.

PHARMACEUTICAL AND BIOTECH GLOBALIZATION

The pharmaceutical and biotech market is becoming increasingly globalized, creating a demand for global CRO services. Although the United States remains the world's largest drug market with more than $400 billion in annual sales, Europe and Asia are close behind. Pharmaceutical companies such as GlaxoSmithKline and Eli Lilly are consequently establishing their presence in Europe.

The biotechnology industry likewise has expanded from the United States to Europe, Australia, Japan, and other Asian countries. Nearly 1000 biotech companies are active in Europe, and the success of several biotech drugs discovered in Europe is likely to encourage and amplify further start-up activity in the region.

Europe is the second largest pharmaceutical research market globally, representing about one-third of drug development R&D. Drug development efforts in this region have closely paralleled those in the United States and have been characterized by an increasing complexity of disease targets, more sophisticated research, tighter regulation, and the need to reduce development times and costs.

As global drug R&D continues to increase, CROs are expected to expand their geographical reach through both organic growth and acquisitions. Leading CROs have now set up offices throughout Eastern and Western Europe. Many have also ventured farther afield into the relatively untapped regions of Israel, Scandinavia, Latvia, Lithuania, and Russia.

Entry Barriers: Despite the promising outlook for Eastern Europe and other untapped regions, CROs need to be cautious about entry barriers. Patient populations are extremely small in Eastern Europe, so most countries can support only one or two trial centers for each CRO. For instance, Bulgaria has a population of about 8 million, and the entire Eastern European region, with the exception of Russia, has a total population of just 50 million. So trial providers must look for untapped countries in the region.

In addition, each country has a distinct language, patient demographics, currency issues, and regulatory and political regime. Thus, expansion is complicated and many CROs wishing to avail of the advantages offered in the region, particularly the smaller firms, tend to do so through partnering relationships with established providers rather than set up their own facilities.

With a population base of 150 million, cost-effective structure, and lack of competition, the Russian market for contract research services offers exciting expansion opportunities. But even though the market is ripe for the picking, CROs have to assess how best to begin and sustain operations in its unstable economy.

Low costs notwithstanding, Eastern Europe has not been a favored destination for Asian pharmaceutical companies. In large part, this is because of the racial differences between the regions. Effective drug testing requires the test patient population to be genetically and racially similar to the intended final users. Consequently, clinical trials for drugs meant for Asian markets tend to be conducted in that region itself.

TECHNOLOGICAL DEMANDS

CROs are developing particular areas of expertise to encourage pharmaceutical companies to depend on them rather than perform clinical studies in-house. Improved capabilities in cutting edge data management tools and technologies at CROs are facilitating the move to outsourced testing.

An escalating number of drug candidates has compelled the creation of screening procedures that rapidly and cost-effectively identify the most promising leads for further development. CROs that specialize in early stage assessments and have sophisticated technology

can often provide more rapid and efficient screening than drug developers themselves.

As clinical trials become ever more complex, sponsors are realizing the value of the advanced technological competence of CROs. Some CROs have concentrated on particular areas such as statistical analysis and data management, gradually building their proficiency in those fields. Others have chosen partnerships or have acquired pioneering technology providers to enhance their services. The result has been continually reduced trial times and the capable management of spiraling volumes of data — both of which have added to the appeal of CROs.

Competitive Strategy

The European contract research industry parallels its counterparts elsewhere in the world: It encompasses dedicated contract research companies, universities, hospitals, and clinical diagnostic laboratories. A small number of large global players generate annual European contract research sales of more than $50 million. Besides that, several midsized companies turn over between $10 million and $50 million, and many small CROs have annual profits of less than $5 million.

Many market participants maintain offices in multiple countries because regulations tend to be country-specific. MDS Pharma Services, for instance, has two offices in Switzerland, three facilities in France, and four sites in Germany.

With nearly 375 companies headquartered in Western Europe and Eastern Europe, the European CRO market is the world's second largest. The US market generated revenues of $4.18 billion in 2002, and Europe racked up an estimated $2.60 billion. The region is set to grow at a compound annual growth rate of 10.4% to reach an estimated $4.26 billion in 2007, accounting for nearly 30% of total worldwide CRO revenues (1).

Potential growth will be constrained by the migration of pharmaceutical and biotech research facilities from Europe to the United States. Compensating for that is an anticipated increase in research activity within Eastern Europe.

At present, the leading trio of CROs — Quintiles, Covance, Inc. (www.covance.com), and PPDI (Pharmaceutical Product Development, Inc., www.ppdi.com) — account for nearly 30% of all sales in Europe. Their dominance is cemented by a strong presence in Eastern Europe, the United States, and Asia as well as the ability to offer a wide range of services including preclinical and clinical testing and commercialization. Covance and PPDI are forecast to make strong gains based on their solid performance records.

Mergers and Acquisitions: Most of the biggest companies have used acquisitions to rapidly expand their market share. During 2001 and 2002, buy-outs spiraled as the large US-based CROs attempted to strengthen their presence in the European market.

Among the more notable acquisitions, mergers, and alliances in recent times are Inveresk's acquisition of ClinTrial Research Solutions to penetrate the US market; ICON's purchase of UK-based Medeval Group, Ltd.; and Charles River Laboratory's buy out of Ireland-based Biological Laboratories. Also, Quintiles and UK-based BioFocus have entered into an alliance for a new screening service for the rapid and early detection of potential cardiac side-effects caused by drug candidates and lead molecules.

As new players enter the market and competition intensifies, success will be determined by a quartet of factors: an established track record for research quality and thoroughness, time for project completion, competitive pricing, and familiarity with local regulations, language, and culture.

Although many competitive factors in Europe are similar to those in the United States and Asia, particularly a company's ability to deliver top-quality data within ever-shorter periods of time and at lower costs, Europe's unique multicultural geography creates several other key points of differentiation.

Sponsors often request that trials be performed in certain locations. So in this context, companies able to offer broad geographical coverage and tackle linguistic differences, divergences in business practices, and varied regulatory regimes are likely to enjoy an advantage over those that can function in only a few regions.

Although some CROs enter into partnerships with other companies to provide wider coverage, CROs with their own facilities appear to have the edge in terms of inspiring client confidence. Not surprisingly, they tend to win more business than counterparts without their own facilities.

Price also continues to be a key competitive differentiator in the European CRO market. The ability to offer clinical studies in low-cost Eastern Europe continues to be an advantage for Western European CROs without this capability. Even within Eastern Europe, however, some areas offer lower cost structures than others and give some study providers a competitive edge. All this will need to be backed by strong global capabilities, patient and staff recruiting and retention capabilities, and strong client relationships.

Reference

1 Frost & Sullivan. *World Contract Research Organisations*, code A547, http://healthcare.frost.com.

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