



Long Distance Relationships: Finding the Right Partner

As trials become increasingly global, the question is more often not whether to outsource but to whom. John V Farinacci at ResearchPoint leads us through the relative advantages of global and network CROs

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The International Conference on Harmonization E5 opened up the use of non-US data for pharmaceutical product approvals in the late 1990s, increasing opportunities to develop pharmaceutical products on a worldwide basis (1). Global clinical trials are now quite common, and the pharmaceutical, biotechnology and medical device industries have embraced global business practices mirrored in many technical and service industries. Simultaneous development across different countries has reduced bottlenecks and resulted in more productive, efficient methods to contain rising costs. Gone are the days of sequential development where clinical trials were conducted first in one country and then the next.

To increase capacity and support investigator sites, pharmaceutical, biotechnology and medical device developers often use contract research organisations (CROs) as they are equipped with the regional resources, diversity and expertise to conduct trials in countries where they have little or no presence. There are real economic advantages of conducting trials in new and emerging markets and a ready supply of treatment-naïve patients. Partnering with local sources increases efficiency, particularly when there are differences in language, infrastructure, and cultural and business practices. CROs established in regional markets have the regulatory and clinical insight to liaise with Ministries of Health and ethics boards, and have established strong relationships with specialised medical centres and investigators.

While most principal investigators are fluent enough in English to communicate with the sponsoring company or CRO tasked with conducting the trial, the importance of native speakers, including co-ordinators, should not be underestimated. Language-related misunderstandings do occur and can compromise the integrity of the study. Literal translation of local expressions may mislead data analysts, prolonging project cycle times with endless queries (1). In contrast, co-ordinators and investigators have a thorough understanding of the regional standards of care and cultural sensitivities that may influence the execution of a clinical trial. A standardised glossary to prevent misunderstandings should be part of every investigator's meeting, in order to proactively address communication errors. Informed consents are always translated into local languages, and native-speaking study co-ordinators play a key role in interaction with patients and collection of study data.

MULTIPLE OPTIONS

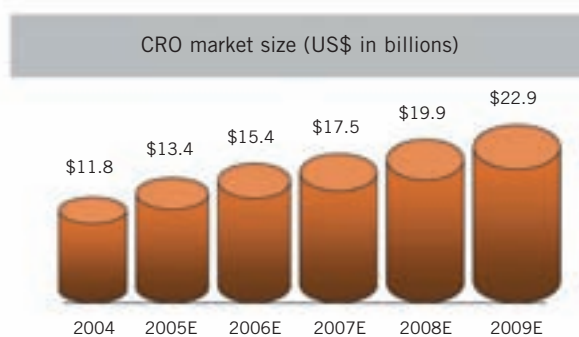
Sponsors have a number of options when considering providers in offshore countries for their development programmes. Depending on the sponsor's study plans, choices include: a panoply of specialised, niche providers; large global CROs; or more increasingly, networks of small-to-mid-sized organisations with like-minded business practices and specialised expertise.

Managing multiple CROs in different countries is often problematic for sponsors. Clients that prefer a 'one-stop shop' strategic mentality are unlikely to desire management of many small, niche providers. Instead, they may opt for either large global CROs or a closely aligned network of mid-sized providers that includes a single, dedicated international project manager who serves as the focal point of contact with management authority over the entire network. Each choice has its strengths. The success of any international trial requires a clear strategic vision, strong management and proactive communications.

WHY USE GLOBAL CROs?

Global CROs became a phenomenon primarily in the late 1980s and early 1990s when pharmaceutical companies launched outsourcing as a business practice, and regulatory authorities around the world became more accepting of non-US data in country-specific drug applications. There are a handful of CROs that claim global status with a presence throughout

Figure 1: Worldwide CRO markets



Source: Korieth K and Zisson S, *Top CROs Report Strong Growth Amid Warning Signs*, CenterWatch Monthly 13(4), April 2006

Western and Eastern European countries, Asia, Australia, South America and Africa. Emerging markets, including India and China, have affiliate offices opening up as clinical trial activities extend to those countries.

The advantages of working with a global CRO include: centralised logistics, monitoring, data management, financial management, biostatistics and regulatory or other additional services. Typically, a single international project manager directs the clinical trial across the CRO's locations and ancillary services (for example central laboratory, imaging studies, interactive voice response systems (IVRS), health economics and so on), and is responsible for day-to-day operational decisions. The team meets periodically, with or without the client, via teleconference or webcast, for communication and status updates.

There is an assumed connectivity among the country affiliates of a global CRO to synchronise all activities for a particular study programme. Local technology assets consistent with corporate systems may not exist in emerging countries and therefore require extensive modifications or importation. Enormous investment is incurred to facilitate transparent communications, establish consistent processes and standard operating procedures (SOPs), and build information technology or other infrastructure for a sponsor's smooth outsourcing experience.

ITEMS FOR FURTHER CONSIDERATION

All clinical trials require SOPs to ensure study subject safety and maximise clinical development. Global CROs focus theirs primarily on a US-centric model consistent with Food and Drug Administration (FDA) regulations, International Conference on Harmonisation (ICH) and Good Clinical Practices (GCP). Other countries may need more country-specific SOPs and SOP training to tailor their processes to local medical standards, ethics boards, Ministry of Health requirements and practices common in their region, otherwise they risk non-compliance.

Substantial investment in infrastructure and set-up of regional offices is buried within a global CRO's financial statements. Typically, upon start-up, an affiliate office is staffed by a single or small number of employees with supplementary contract resources – clinical research associates (CRAs), data management and regulatory – available on a contract basis. Sponsors are often unaware that a single person may fulfil multiple roles providing clinical data and regulatory services. Country-specific offices are under pressure to maintain positive cash flow. Eager to discontinue slow business cycles or promote service in a particular region, a global CRO may be encouraged to select countries with less-than-optimal patient populations. Like any large business, a global CRO is forced to pass along its fixed infrastructure costs.

Care must be exercised when selecting CROs that use acquisitions as a strategy for building its global base. The acquired companies may be market leaders, but their successful processes, systems and infrastructure may be quite

different from the acquirer. Integration often takes years, is frequently challenging, and rarely without obstacles.

ATTEND TO THE INFRASTRUCTURE

Despite 'standard' infrastructure (wide area networks) throughout an organisation, communication is still challenging as much of it is disseminated in piecemeal fashion and not all affiliates or support services utilise the same common systems. Local technical service support is often necessary and care must be exercised that regulatory requirements are not compromised (2).

As a global CRO grows, it is inevitable that its size will contribute to an hierarchical structure involving multiple layers of communication that, in turn, often impact responsiveness and flexibility. Pragmatism is stripped, urgency dissipated and a sense of complacency ushered in (3). Special client requests may be pushed back against the 'tried and true' processes and experiences of the vendor.

WHY USE GLOBAL NETWORKS?

Strong relationships form the foundation of successful biopharmaceutical or device development. Increasingly, small to mid-sized CROs are forming global joint ventures to extend the reach required in modern pharmaceutical, biotechnology and medical device development (4). Successful networks take a customer-centric focus and have similar values, corporate cultures and standards of quality. Agreements are not exclusive, but in some instances can be binding, and include shared revenues or other financial incentives for business leads and collaborative opportunities. Strategically structured networks offer services and deliverables that can be mixed and matched according to sponsor requirements, and have advantages over CROs without a local presence.

Senior managers in a global network often have the requisite global CRO backgrounds, but have chosen to be in an environment that is more customer-centric, less hierarchical, and where they can truly make a difference. Their involvement provides insight and expertise in removing obstacles and avoiding pitfalls. These leaders have the opportunity to mentor and coach the next generation of drug development professionals, and build upon past successes in new projects. Their presence is experienced at all levels of a development programme.

Some successful networks meet on a regular basis in order to share information, discuss project-specific issues, review proposals, redefine strategies and discuss new opportunities. Here, feedback on collaborative work and process improvements are exchanged. A proactive, pragmatic approach to provide creative and innovative solutions often delivers faster results, with the same or better quality than global CROs. Networks are able to accommodate special requests often unaddressed by larger CROs because of the entrepreneurial spirit, flexibility and service mentality of its partners.

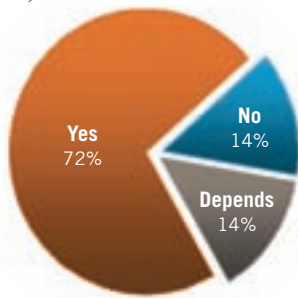


Figure 2: Is it important for a CRO to be global?

Note: 21 responses

Source: Krueger J, CRO Quality Survey, William Blair & Co. Industry Report 06-030 CRO Industry Update, March 2006

Table 1: Leverage the advantages

Global CROs	Networks
Centralised 'one stop shopping'	Flexibility in level of service and geographic location
Single project manager/ point of contact	Single project manager/ point of contact or multiple points of contact, as desired by the sponsor
Experienced corporate infrastructure	Experienced, senior management involvement
Reputation/experience	Responsive
Corporate stability	Financial incentives to partner effectively and deliver quality services

Sponsors are not restricted to global CRO-driven options, but rather can pick and choose geographic regions and country-specific companies to enhance patient enrolment. Regionally networked CROs, like their global CRO counterparts, know the microclimate, often have wide therapeutic expertise, have access to willing patient populations, as well as strong physician relationships, and knowledge of local standard healthcare practices and feasibility; all of which results in accelerated enrolment and better quality data. Each brings knowledge of their unique regulatory environment, importation laws and guidelines. In addition, they have established, local, and proven database pools of development talent in clinical monitoring, data management, regulatory and biostatistics.

Many network partners have a long history of working regionally with pharmaceutical, biotechnology and medical device corporations on projects due to their local expertise and regional advantages. For instance, Russia offers a host of primary care systems with large populations of cardiovascular, oncology, and diabetes disease states. Australia has world-renowned research and medical investigators, as well as institutions enhanced by rapid trial approval processes. Regions such as Australia and South Africa offer inverse seasonality (for example influenza studies) and diverse populations (for instance Caucasian, African and Asian). Disease states of both third world (malaria, tuberculosis and so on) and westernised nations (diabetes, cardiovascular disease and so on) are found in South Africa.

LEVERAGE A NETWORK'S STRENGTHS

Closely aligned networks offer flexibility and favourable costing for drug development programmes, and costs are often more competitive than that of global CROs. Local CROs know prevailing market rates for the best investigators and are in a better position to amortise those relationships into win-win scenarios for both sponsor and investigator. Clients are not tied to 'blended billing rates', which increase complexity, and for single country or region-specific projects, compensation is made in local currencies.

In an ideal network model, rather than having the sponsor oversee each separate company, a single international project manager is selected from among network partners to manage study conduct. Just as with the larger global CROs, there is a single point of contact and accountability.

CONSIDER THE STRUCTURE

Despite the numerous benefits of the network model, sponsors often perceive these partnerships to entail more management time

on their behalf than with global CROs. Indeed, a great deal of commitment among network partners is necessary to ensure communication and choreography challenges are met. However, if the network is properly structured, a transparency exists amongst member companies, and sponsor management requires no more than would be expected for a global CRO.

Each individual company selected as a functional service provider for the network should be independently financially viable. Participation in the network builds the business base, offers opportunities to pursue new leads, and amortises individual strengths, without succumbing to the pressures of publicly traded company shareholders.

Technology platforms are flexible and adapted to client requirements rather than wedded to internally developed systems. Further, network SOPs are generically constructed to meet country-specific concerns, yet are strong enough to maintain GCP. Ultimately, it will be the sponsor who determines which SOPs, data management process, information technology or electronic data collection systems are applied.

CONCLUSION

The global development environment perpetually changes and with it traditional business practices. Outsourcing continues to be part of the sophisticated developer's plan and has steadily grown more strategic (4). Sponsors now look to CROs, large and small, with the regional insight of local businesses and cultural practices for partnerships to advance their product development.

Global CROs and CRO networks are conducting GCP trials in more places than ever as infrastructure and technology extend access to emerging countries and treatment-naïve patient populations. Each model has perceived advantages. Global CROs have resources and geographic reach under a single corporate structure and years of stability. Networks have been in existence for over a decade and have enjoyed success on a par with those of global CROs. Properly structured networks offer service flexibility, metric-driven results and sponsor value at competitive prices.

Success with any outsourcing provider is ultimately a function of relationship management, realistic expectations and outstanding communication with the sponsor, regardless of CRO structure. ♦

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