Entering a New Era of Clinical Trial Outsourcing

a report by

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Outsourcing Is Key to Research and Development Strategy

Successful pharmaceutical and biotech companies are those that have adaptable research and development (R&D) and commercialisation strategies. Given that at the beginning of 2007, R&D spending by the top 10 biopharmaceutical companies was close to US$60 billion and yet new drug productivity remained modest,[1] questions have been asked about the current management strategies of those running R&D programmes.

The modern pharmaceutical market is global and highly competitive, requiring a quicker ability for companies to adapt. By 2008, the top 10 biopharmaceutical companies are predicted to spend close to US$65 billion on R&D, which will represent over 80% of total industry R&D spend.[1] As many large pharmaceutical companies fully realise, investors and industry observers will not be content with continuing stagnation in new drug productivity.

Outsourcing to contract research organisations (CROs) is one area that is being used more proactively by pharmaceutical and biotech companies and should help them meet their productivity targets. Outsourcing enables pharmaceutical and biotech companies to reduce overall costs, cover gaps in capacity and improve their skill base.[1] It also allows them to concentrate their in-house efforts on the parts of the R&D process with which they are most familiar and can adequately resource. Meanwhile, the CRO can use its existing global R&D infrastructure to ensure that it covers the remaining needs of the sponsor company.

A key area that has driven the use of outsourcing has been clinical trials. At present, it is common for clinical trials to account for at least 40% of total company R&D costs (see *Figures 1* and *2*). Large, global clinical programmes are required for major products to be developed successfully to the satisfaction of regulators and patients, yet clinical trials are difficult to co-ordinate and the larger the trial, the more investment in time and resources is needed.[1] Therefore, in order to maximise the chances of success at this critical point of the R&D process, pharmaceutical and biotech companies have partnered with specialist CROs.

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The Relationship Is Key

Although drug development is often characterised in terms of cost, quality and timelines, if it involves more than one party then the strength of the relationship between these organisations is the key to success. Initially, there was some resistance to using CROs due to a feeling that companies would lose control over the development of their products. Many pharmaceutical and biotech companies, particularly larger ones, would outsource with extreme reluctance and would treat the CRO more like a 'hired hand' than a true partner. With this negative attitude it is hardly surprising that many relationships failed and conveyed the idea that outsourcing was an inferior option to carrying out all activities in-house. However, companies that took a more objective view to outsourcing have reaped the benefits. By understanding that they needed to establish a true partnership with the CRO, over time their outsourcing strategy was fine-tuned until it paid off.

All that these companies required were outsourcing managers to oversee the work of the CRO, rather than large numbers of staff being involved in every procedural step. Furthermore, CROs were able to improve their own processes to suit the client's objectives and develop the role of the project manager who would oversee work from their end. This sponsor-focused approach appears to have worked, given that many CROs have achieved high growth rates from gaining repeat business from their clients.

The CRO industry is now considered a mature sector, with many CROs having considerable experience in carrying out clinical trials on an international basis and in a range of therapeutic areas. This means that

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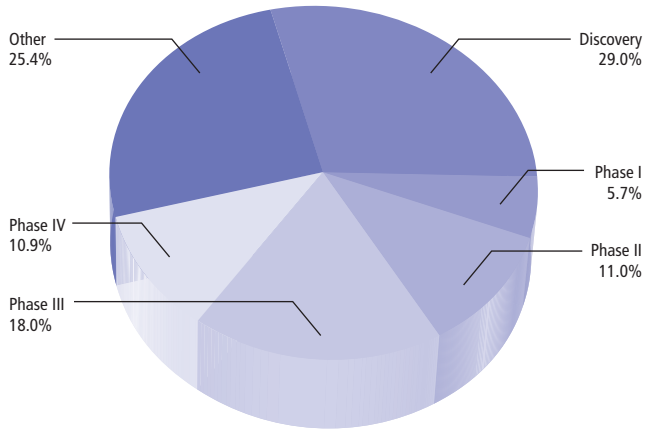
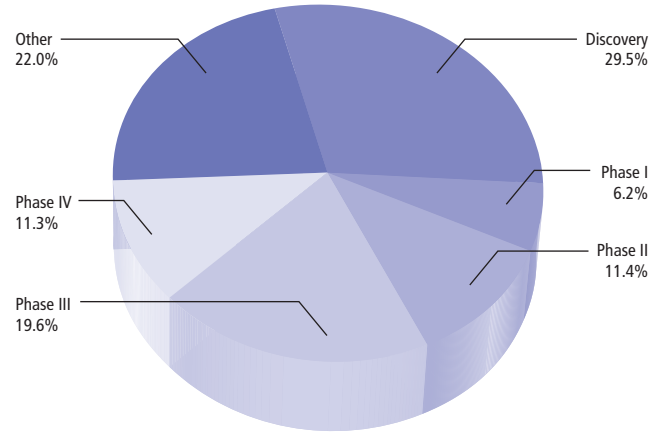
Figure 1: Global Pharma R&D Expenditure by Function (2006)



Source: PHARMBIOSYS Pharmaceutical and Biotechnology Systematic Intelligence.

Figure 2: Global Pharma R&D Expenditure by Function (2008)



Source: PHARMBIOSYS Pharmaceutical and Biotechnology Systematic Intelligence.

not only are CROs capable of running a variety of clinical trials, they can also provide companies with valuable input when planning clinical development programmes.[1]

As trials become more complex for new-generation drugs, improvements in clinical development are taking place through closer partnerships between CROs and sponsors. The clinical programme will depend on factors such as the therapeutic area of investigation, how the drug is to be used, the nature of the disease and the recruitment of suitable patients.[1] Company requirements, such as the number of indications, route of administration and dosage forms to be pursued, will also determine the make-up of the clinical programme and are areas where the CRO can advise.

In 2004, it was estimated that leading CROs managed around 23,000 phase I–IV clinical trials worldwide.[2,3] An additional boost for the reputation of the CRO sector was the 2006 report by the Tufts Center for the Study of Drug Development (CSDD) that company sponsors who were more extensive users of CROs tended to complete their projects faster, with this being particularly noticeable during the study close-out period.[2,3] A further feature of these findings was that quality comparable to submissions involving minimal use of CROs was maintained.

Global Clinical Trials

The pharmaceutical market is truly global, with companies striving to operate in as many national and regional markets as possible to drive their growth. This globalisation of the pharmaceutical market has been accompanied by a similar trend in clinical research. The findings generated by clinical trials will define a product's chances of success far beyond its initial launch. Relying on home markets alone will not be sufficient to generate the type of clinical research data required to support global commercial objectives.

Companies believe that international trials will help them gain rapid access to more patients and also allow them to control trial costs.[1] In many of the so-called emerging markets, clinical trial costs are frequently lower than in Europe, the US and Japan due to fast patient recruitment and lower operating costs. As these clinical trials will necessitate working with local physicians, an added commercial benefit is that the medical community in these countries will be experienced with the company's products when they reach the national market. In fact, in some countries regulators expect to see some local clinical development of a product to have taken place. In particular, Central and Eastern Europe, Latin America, India and China have grown in prominence as locations for clinical trials.[1]

Many trials in emerging market countries are now generating clinical data that can be used to support companies when dealing with regulators in established markets, such as the US and Europe, as well as for local efforts.

The demand for global clinical trials places additional demands on CROs. To take on such large projects they must have the technical expertise, but also be able to relate this to each of the countries in which they must oversee the trial in question. Many large CROs have built their reputation on the ability to co-ordinate international clinical development programmes effectively. Key to the success of these CROs has been their expertise in dealing with the different regulatory processes in each country. In many cases, although perhaps familiar with the pharmaceutical market, the sponsor will be unaware of the complexities of clinical trial regulations in these countries and how quickly they can change. In contrast, the CRO, through having conducted previous clinical trials, tends to be in a much stronger position. Therefore, sponsors should expect a CRO to understand the clinical trial environment in sufficient detail and to have also built up important relationships with the local regulators. This can be tested by asking the CRO to carry out an initial feasibility study for the proposed trial and to suggest what the international focus should be. The results can be compared with the viewpoints in-house. If the logic of the CRO is sound, this should be a good basis on which to judge the organisation, rather than it agreeing

Large CROs have built their reputation on the ability to co-ordinate international clinical development programmes effectively.

with every facet of the viewpoints in-house. The ability of a CRO to be objective and provide constructive criticism should be considered a strength. Simple agreement with a sponsor may indicate nothing more than desperation to win the outsourcing contract.

As the pharmaceutical industry comes under greater scrutiny over its commercial activities, it must ensure that it is seen as operating ethically when carrying out clinical trials in emerging markets.[1] Since working with a CRO involves some delegation of responsibilities, companies must be sure that they work with organisations that understand the high standards required for their clinical trials.

In the major world regions for drug development, clinical trials are run to International Conference on Harmonization Good Clinical Practice (ICH GCP) standards.[4] ICH GCP is an international ethical and scientific quality standard to ensure that clinical trials involving human participants are designed and carried out in an ethical manner. Since companies are accustomed to following ICH GCP in the major world regions, they use the same approach in emerging world regions. Yet, although ICH GCP standards would be desirable in order to generate data that are acceptable to both regulatory authorities in ICH regions and to national governments, developing countries were not involved in the development of ICH GCP and so its application in these countries should not be taken for granted, nor should it be expected.

It is imperative to pay adequate attention to informed consent procedures so potential patients understand their involvement in a clinical trial.[4] As part of this, it may be necessary to consult with community representatives to develop innovative and effective means to communicate necessary information in a manner that is understandable to potential participants.

Potential participants should be allowed sufficient and adequate time to confer with anyone else of their own choosing to discuss the particular features of the research and to minimise the possibility that they may be subjected to undue influence or coercion. Recently, there has been considerable media coverage of clinical trials in India, with allegations that some organisations have behaved unethically when dealing with poor and illiterate patients.[5]

Working with CROs who have local experience is the best way of ensuring that clinical trials are run to the required standards worldwide. However, this does not necessarily mean working with the largest international CROs. If a company has good managers to oversee and co-ordinate the outsourcing process, they can partner with a series of niche CROs for the different markets in which they wish to conduct clinical trials.

Outlook

Pharmaceutical and biotech companies operate globally, and as they have expanded into foreign markets the importance of running local clinical trials has also grown. However, in their pursuit of commercial benefits, companies must ensure that they operate ethically. In their efforts to control the rising costs of clinical trials, most companies are now outsourcing their projects to CROs. Since it will be the CRO that oversees much of the clinical trial work in foreign markets, pharmaceutical companies must have absolute confidence in the CRO's approach as any mistakes could prove disastrous both financially and for the company's reputation. The CRO must provide value for money but also operate in a manner that maintains high standards. Only in this way can pharmaceutical companies make a success of their global R&D efforts. ■

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Diary

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The Burlington Hotel, Dublin, Ireland
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