



Raising the Bar

Alan Morgan of ICON Clinical Research, Europe, assesses how best to implement new standards in patient recruitment in order to achieve beneficial and effective practice



Alan Morgan is President of ICON Clinical Research, Europe. Alan is responsible for the Phase II/IV business in the region. He joined the company in August 2006 as Vice President for Process Development. He was Global General Manager of the Phase II/IV business of MDS Pharma Services from August 2005, having joined MDS in September 2002 as General Manager of their European, Latin American and Asian Clinical Development operations. Alan's initial career was in pharma, including seven years with Glaxo Wellcome and two years with ICI Pharmaceuticals in various business financial roles. He is a graduate of the City University Business School in London and a Fellow of the Chartered Association of Certified Accountants.

The patient recruitment methods increasingly being used by CROs involve a more scientific and targeted approach, which should become a new standard for best practice within the industry. This approach involves the use of a comprehensive in-house database covering a wide range of countries and therapeutic indications, and also includes performance data on investigators. By systematically searching the database at both a macro (country) and micro (within a specific country) level, a CRO can start the process to identify the best countries, sites and investigators in order to ensure optimum patient recruitment for a client. The use of performance data is a major step forward in terms of how CROs operate. This approach relies on both the quality and quantity of the data in the database; it can therefore be used most effectively by larger CROs that have more extensive global and therapeutic indication coverage. Traditional feasibility studies are still required, but the focus on investigator performance can make this approach much more effective in identifying motivated investigators who have access to appropriate patients.

PREPARING THE DELIVERY STRATEGY

In order to successfully execute and deliver an effective clinical trial programme, a CRO needs to invest considerable time and effort preparing a delivery strategy prior to being awarded a contract. The most important part of this process is the initial identification of the best investigator sites in an attempt to ensure optimum patient recruitment. This process is aided by having experienced and empowered project managers in charge of patient recruitment. Other key aspects are to have contingency plans in place in order to deal with any problems or issues that may arise, and a 'toolkit' of tactics and approaches to enhance patient recruitment. Preparation of the delivery strategy should include an assessment of the trial protocol(s) and timelines, and as much knowledge as possible of trials that will be competing for patients and/or trials that will be jostling for the investigator's attention. The strategy should also include a delivery risk assessment of the protocol – for example clinical feasibility, especially the

inclusion/exclusion criteria, motivation for patients and investigators, and the availability of suitable patients. Ideally, a CRO should prepare, present and discuss two delivery strategies: one that meets the sponsor's RFP requirements, and one that the CRO would recommend as being better able to meet the sponsor's needs based on their experience and the information provided by the sponsor.

Both the macro and micro approaches should be defined: for example a cost-effective country distribution based on the required timelines, the most suitable countries to use, including any sponsor preferences and, for each country, a patient recruitment plan, which will vary from country to country since the approaches taken will be different. Starting at the micro level, the patient recruitment plans are built up on a country-by-country basis. This approach allows some of the risks and challenges involved to be assessed for each country. Best practice has moved away from simply using a list of investigator names in different countries towards a more scientific

approach, which utilises in-house data on investigator performance in previous studies. Thus, investigators with a proven track record of previous good performance, which is the best indicator of good future performance, can be initially selected. Such a database allows the performance of different investigators in a particular study within a single country to be compared and assessed. However, performance assessment at the investigator level across different countries is very difficult to achieve due to differences in drug availability, standards of medical practice and so on. Due to the restrictions imposed by data protection legislation, all the data contained in the database must be factual and made available to the investigator. All the information in the database is, therefore, objective.

Having conducted the initial assessment, best practice dictates that an external feasibility exercise should be conducted to validate the information obtained from the database. This enables the CRO to get a good sense of the investigators' scientific interest in the study and how the planned study might compare with other competing studies. Since many sponsor companies have unrealistic timelines for the production of a detailed proposal, with CROs generally being given less than 10 days to formulate a clinical trial programme, there is usually very little time to conduct a full external feasibility exercise at this stage. However, because there is increasing willingness within the pharmaceutical industry to pay for these studies on a stand-alone basis, there is more recognition of the importance of this critical stage and the need to allow more time for the development of a proposal.

CRITICAL PATH RISKS AND CONTINGENCY PLANS

The identification and evaluation of critical path risks and the preparation of contingency plans should initially be conducted before any pre-study site visits and refined for each investigator site after the first pre-study visit. Once the patient recruitment plan has been developed, this will also need to be adapted and refined, as needed, as the clinical trial programme progresses.

After being awarded a contract, but prior to the start of the study, there should be an agreement between the CRO and the sponsor as to what the key risks are and, for each key risk, what the contingency plan is and what the trigger point is for implementation of the contingency plan. This is an important agreement to have in place for the CRO. Key risks include such factors as approval timelines, ethics issues, protocol amendments and drug and equipment supplies. Contingency plans can include having back-up countries and investigator sites in place, and having advertising strategies ready to help recruit additional patients. For a large, complex study there will typically be a number of back-up sites both in the countries included in the programme and in back-up countries. These sites need to be ready to start as soon as possible after being included in the clinical trial programme and, to facilitate this process, should have been subject to initial ethical and regulatory approval at the planning stage.

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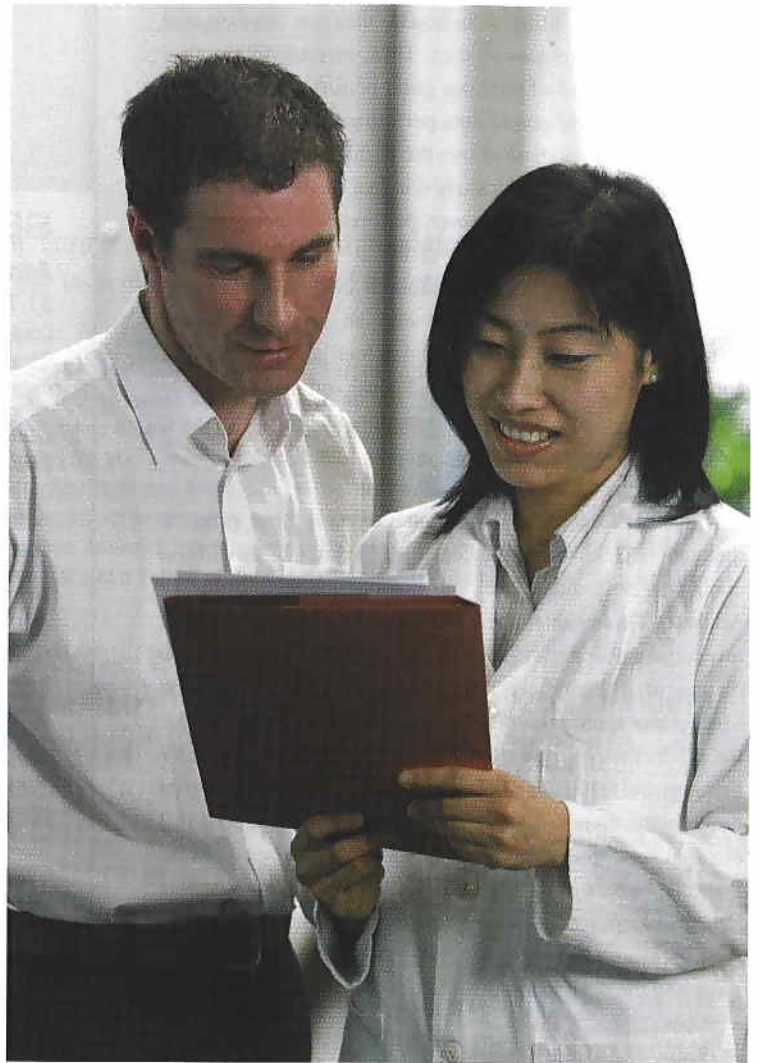
As important as having back-up countries available is having prior agreement with the client on the trigger point for closing a poorly performing site, as this can be an effective way of saving money and improving patient recruitment.

The key to the smooth running of this process is for the CRO to have upfront transparent discussion and agreement with the client as to what is and is not included in the core plan, what the contingencies are, and who pays for which items. In addition, it is important that there is transparent communication with all the investigators so they know that if they have not recruited the required number of patients into the study before a particular date, then the CRO may recommend to the sponsor that the site is closed and resources focused on sites that have patients identified and ready to enter the study.

EXECUTION, REVIEW AND ADAPTATION

Once a study is underway, there needs to be a comprehensive set of metrics that are pertinent to the agreed trigger points so that the status of the trial can be constantly monitored and assessed. In reality, all plans undergo adaptation once they are underway and changes are constantly being made.

Accountability and responsibility for running the clinical trial programme lies with an individual project leader who, ideally, should have easy access to a management system that includes a repository



of knowledge built up by other managers and project leaders within the company, so that the project leader can tap into the expertise available within the CRO. An effective management system is an important asset for a CRO, and technological advances have made this much easier to use. A patient recruitment 'toolkit' can assist project managers by providing them with all the information they need in order to manage the process more efficiently. A toolkit should include a variety of information such as a list of potential recruitment/retention tactics by country and by therapy area, support documents including templates, links to useful websites, decision trees and process flowcharts, and a list of routine tactics used for most studies.

CONCLUSION

Best practice for patient recruitment should utilise a scientific and targeted approach with a comprehensive in-house database supplying information on countries, sites and investigators, including investigator performance data. Such an approach enables the best countries, sites and investigators to be objectively chosen in order to ensure optimum patient recruitment. The use of objective performance data is a major step forward in terms of how CROs operate. ♦

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