Accelerating patient recruitment

Advice on how to tackle one of the industry's major problems.

The annual cost of clinical trials in the US is $7 billion; the estimated cost of patient recruitment is $1.89 billion. These costs are subject to further increases with each day's delay in bringing the product to market. Industry sources claim that for every day lost in development, it costs $1 million in lost sales. A recent article claimed that only 15% of clinical trials are completed on time, with over 50% of delays attributed to patient recruitment and 25% of investigator sites failing to recruit a single patient.

Contributing to the mounting pressure for effective patient recruitment is the rising demands of regulatory bodies for an increase in the number of trials per NDA filed and a rise in the number of patients required per trial. The average regulatory submission contains data on over 4,000 patients; however, the time available to recruit these patients has gone down as the industry has to maximise its ROI by reducing the time it takes to complete product development programmes.

The situation is further complicated by a combination of factors that have resulted in the general public – and hence the pool of potential trial participants – becoming more discerning in their assessment of medical profession and pharma industry and subsequently reluctant to 'sign up' for clinical trials. In many countries, the industry has a less than perfect reputation, deserved or not, and more patients are increasingly unwilling to take part in company sponsored clinical trials when media scares about drug safety or 'dirty' dealings of clinicians being 'paid' to take part in clinical trials are an almost daily occurrence. The release of vast quantities of information in the patient population. Consideration should be given to the use of competitive enrolment policies to be implemented in the field. For example, we have noticed an increasing tendency towards over-restrictive inclusion/exclusion criteria in trial protocols. There is an understandable desire to maximise treatment differences and avoid analytical bias through 'clean' protocols. However, the clinical reality is full of 'grey' areas. A more pragmatic approach is also important. In a trial we recently conducted, the protocol specified a laboratory parameter in the inclusion criteria for which there was little background information in the patient population.

Realistic expectations

With a well thought out protocol in hand, the next consideration for the success of your recruitment strategy is setting realistic expectations. It is important to get a good sense of the incidence and/or prevalence of the disease in question. This may vary from one geographical area to another, even within a single country there may be local differences. One can estimate the effect of the protocol criteria on reducing the total patient population based on the performance of similar trials in the past and by entering into an effective dialogue with investigators. You need to consider what variations may occur in patient populations due to cultural or ethnic differences and the spread of individual sites in relation to patient populations, as well as the internal healthcare facilities in different countries and the impact this has on the site's ability to recruit patients and conduct the trial.

The impact of local regulatory policies should also influence the decision on which sites to work with. This should be supplemented with an audit of sites, patient records or registries, previous experience and any historical recruitment metrics they have for similar trials to aid the process of identifying what sites can meet your recruitment needs. Analysis of medical journals, databases and published papers from conferences and meetings can help identify potential investigators, rising stars and opinion leaders – pharma industry should also consider the experience of their study site staff as these are the individuals who often carry over the reputation of the study.

We find that too often sites overestimate the number of patients they can recruit because they are not initially familiar with the protocol and the effect its selection criteria will have on the total patient population. We therefore suggest a protocol synopsis and one-to-one discussions between sites and an experienced clinical researcher are required in order to estimate realistic numbers and secure agreements on the expected performance of individual sites. In addition, we strongly advise the use of competitive enrolment together with the inclusion of back-up sites so they can be brought on board should individual sites drop below their agreed target levels. This is sometimes perceived as causing potential difficulties for a company wishing to work with that site in the future; however, our experience is greater patient exposure to the drug for regulatory submission.

- Patient and clinician satisfaction with current therapies.
- Competitors with trials in the same disease indication.
- Tying up investigational sites by CROs/SMOs.
- Poor planning or lack of specific recruitment policies.
- Lack of patients coming forward for or aware of clinical trials.

Leveraging the opportunities for success

Having selected your pool of investigators, make the investment in terms of time and money to ensure they are fully briefed with trial literature and study materials that are user friendly to both investigator and patient. Consider the use of educational material for both patients and site staff; this will aid recruitment by offering reassurance and information to all participants in the study. Make sure that they have a clear understanding of the study protocol and that they have bought into what is expected of them. The format and timing of your investigator meeting should be designed to both inform and motivate and help provide an early impetus for patient screening and the entry of patients into the trial.

The timing of the meeting should form part of an integrated range of activities designed to maximise the opportunity for patient recruitment and communication with the widest patient population. Consideration should be given to the utilisation of the following activities based on the needs of the individual trial:

- Promotion via patient organisations, newsletters and websites.
- Advertising in local media (press, TV, radio, poster sites). This will be subject to ethics committees approval, but all materials should be designed and approved in advance so they can be implemented.
can be used in the recruitment activities
• Production of posters, flyers and leaflets for
  surgeries, local clubs/institutions and locations
  that match the patient profile
• The use of appropriate Internet portals and
  websites promoting and providing information on
  clinical trials currently being undertaken and the
  opportunity for patient enrolment, such as www.
centerwatch.com. This can be used to
  both boost recruitment and provide details of
  investigators to potential patients
• The launch of a dedicated website for the
  therapeutic area or promotion on appropriate
  consumer healthcare sites, supported by
  information about these sites within all your
  other promotional activities
• An educational campaign targeting the public
  and communicating the need and nature of
  clinical trials and calling for patients to
  participate and help in the development of
  successful medicines
• The placing of articles in targeted newspapers
  or magazines written by well-known clinicians or
  a relevant celebrity, linked to a website or free
  phone call centre
• The use of research centres and SMOs – by
  using these facilities one can boost recruitment
  by opening out the study to a larger number of
  patients with whom they already have contact, and
  take advantage of local knowledge, which
  can be vital if conducting a trial on a global basis.

For the first seven options, in order to aid the
recruitment process, information directing the
patient to a call centre or website for pre-screening
could be part of the process and hence facilitate the
speed and accuracy of recruitment.

An important element to the success of a study’s
recruitment strategy is regular and optimal access to
information about what is happening at individual
sites. This is especially true with regard to the
management of global trials where day-to-day
contact may not be practical and the time delay
between monitor visits can impact on the
identification and solution of problems that could
have a dramatic impact on patient recruitment.

Consideration should therefore be given to the
use of electronic clinical trial management systems that
allow real-time access to study data and the
performance metrics of individual sites. Some
systems offer the use of secure websites as an
integral part of their system for communicating with
sites. These can vary in their functionality and can be
developed to meet the need of individual studies. On
a daily basis, clinical research personnel at both the
sponsor company and the CRO can gain access to
this information and be in a position to:

• Have daily access and regular communication
  with investigator sites
• Monitor on a daily basis the number of patients
  recruited, their eligibility, screen failures and to
  obtain feedback that will allow them to identify
demographics of Internet users – how
trends and demographic variations in the
the Internet for the management
clinical trials and recruitment of patients
these facilities one can boost recruitment
the need for clinical trials
faster.

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Fig 2. Options for enhanced patient
recruitment

Daily access to this information provides
sponsors with the opportunity to identify what
activities need to be leveraged or modified to
ensure sites meet their recruitment targets and
improves the speed and efficiency of the
clinical trial process.

The use of the Internet for the management
of clinical trials and recruitment of patients
has increased dramatically over the past five
years. Specialist companies offer a variety of
‘pay for’ services designed to facilitate
patients and investigator access to enrolment
in clinical trials. This approach has offered
the opportunity for communicating with a wider
patient population and has the potential to
increase the size of the patient pool. The
Internet can be utilised in a variety of ways;
however, the following points should be
considered:

• The use of on-screen, screening
  questionnaires that are user friendly to
  ensure patients are sufficiently eligible for
  pre-screening telephone contact
• Provision of instant feedback to potential
  trial participants with a methodology to
guide them to the relevant participating
  site with the understanding that there may
  be limitations on enrolment due to the
distance between the site and potential
  participant
• Potential selection bias due to the
demographics of Internet users – how
close does this fit your patient profile?
• The variation on the use of the Internet in
different countries and the stance of
different ethics committees on its use for
  recruitment
• The need for security and confidentiality
  of patient data.

The Internet should be considered as a poten-
tial weapon in the industry’s armory of tools
for accelerating patient recruitment, its utiliza-
tion based clearly on defined objectives and
on evidence that it can be shown to have a pos-
tive impact on patient recruitment.

The options that should be considered in the
development of a study’s patient recruitment
strategy are summarised in Fig 2. The activi-
ties used as a consequence of the strategy
adopted should form part of an integrated
approach that will accelerate patient
recruitment and provide the opportunity to
increase the size of the patient pool available
for participation in the clinical trial. This inte-
grated approach will lead to an increase in the
efficiency, precision and speed of clinical tri-
als, reducing the time required for clinical
evaluation and bringing the product to market
faster.

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Time, as the saying goes, is
definitely money.

Never has this been so true as it
is in today’s clinical research
environment, where many factors
can impact on the time it takes
to get your product to market.

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by several orders of magnitude.

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with fewer queries, faster database
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