New Ways to Recruit Trial Subjects

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To minimize time to market, sponsors must explore new subject recruitment techniques.

Clinical trials are a vital step toward bringing new drugs to market. U.S.-based clinical trial activities increased by 6% in 2001, the largest rise since 1990.[1] But although pharmaceutical companies pay close attention to the science when designing their clinical trials, few consider how they will get enough subjects to participate. As a result, most trials are plagued by delays that can cost pharmaceutical companies millions of missed sales. Delays in getting a drug to market are estimated to cost companies around $1 million a day.[2]

In fact, despite technological advances in pharmaceutical R&D, nearly 80% of all clinical studies for new products fail to finish on time, and 20% of those are delayed six months or longer.[3] Given that, on average, 40% of pharma companies' R&D costs are devoted to clinical trials, and that R&D expenditure is increasing by around 10% a year, companies can ill afford such a situation.[2]

Here, we focus on some new approaches that recruitment agencies have recently adopted to enroll subjects and expedite clinical trials.

Why recruitment matters

Time to market is one of the most important phrases in clinical research. The faster you can get a product approved, the more financial value it will have for your company. The successful clinical development of any drug relies upon several key factors. One is to recruit the necessary number of subjects within the project time frames to meet development and regulatory milestones. This creates a challenge for both sponsors and contract research organizations (CROs), because the typical new drug application (NDA) needs data from approximately 4000 subjects. Other factors can also cause poor accrual, such as competition between trials for the same subject population, a decline in specialist referrals, and generally smaller health-care budgets.

Finding, screening, and recruiting clinical trial subjects at multiple research sites is a challenge for even the largest pharmaceutical sponsors and CROs. U.S. data indicates that the number of clinical trials per NDA more than doubled in the decade 1985–1995. The NDAs approved in 1994–1995 were based on an average of 68 clinical trials.[2,4,5] Some researchers suggest that increasing the number of subjects required for NDA clinical trial databases could reduce post-marketing adverse events, thus making recruitment strategy crucial to a trial's success.[2,4,5] Others point out that the nature of the drugs being tested affects the number of subjects needed for a trial.[2,4] In 1998, for example, the number of trial subjects ranged from an estimated 212 for Xeloda (a breast cancer drug that received accelerated approval based largely on a 162-subject Phase 2 study) to the 16,000 subjects enrolled worldwide for Actonel, a drug for treating Paget's Disease.[2] CMR International analyzed 23 clinical dossiers submitted to regulatory authorities in Europe, the United States, and Japan between February 1995 and April 1999. That analysis showed that the average dossier contained data from 35 clinical trials involving more than 4000 subjects each.[2,6]

Achieving realistic recruitment rates

Many companies follow a strategy of compressing the enrollment period to improve clinical cycle times. They recognize that the nature of a trial affects the recruitment period.

Therefore, the degree of improvement that can be made will differ from trial to trial.

An analysis of 1577 Phase 2 and 3 clinical studies active in 1997, for example, showed that the median time for subject enrollment varied with the therapeutic class.[2] For drugs in the anti-infective and antiviral classes, median times for recruitment were five and six months, respectively, whereas for cardiac therapies (not including antihypertensive therapies), median time for enrollment was much longer at 16 months. For trials involving antihypertensive therapies, the median enrollment time was only 8 months. The finding that the enrollment time for cardiac therapies was nearly double that for antihypertensives was associated with the availability of subjects; hypertensive subjects were being seen and diagnosed more frequently by primary care physicians during standard appointments. Understanding the frequency with which clinicians see the desired subjects can therefore lead to a realistic assessment of the recruitment rate possible at trial centers for a particular study.

Interestingly, the same analysis showed that the largest trials, those with over 400 subjects, had a shorter interval between first subject enrolled and last subject enrolled. This may be due to the considerable resources allocated to subject recruitment for these large studies, which are usually run by the major companies. In any case, the results illustrate the complexity of the parameters involved in subject recruitment.

Understanding the investigator's role

A clinical investigator plays an important role in subject recruitment. According to E. Panacek and R. Lewis, "As growing numbers of medical products or devices undergo evaluation and are brought to market, the number of investigators involved in clinical trials is expected to grow."[10] The increase in products—accompanied by an increase in the number of trials per NDA filed, a rise in the number of subjects per trial, and pressure to reduce the time required for trials—means that investigators will be under increasing pressure to recruit subjects.

Investigators constitute a key asset to subject recruitment for three reasons.

- They add credibility and medical expertise in the clinical area and mediate the study discussion between subject and coordinator.
- They have access to information pertaining to subjects whose characteristics are more appropriate to the study conducted.
- They have daily exposure to potential subjects and are able to introduce information about the trial and ask for their participation during these visits.

Because of several potential conflicts of interest between investigators and industry sponsors—in large part because of the sponsors' financial stake in clinical trials involving their products—a productive relationship between the two parties can be achieved only through honesty and openness. The same goes for subject recruitment. A clinical trial starts with developing a protocol that is feasible without being too restrictive in its inclusion/exclusion criteria.[11] Even though avoiding analytical bias through precise protocols is important, a realistic approach is also necessary. After being selected, all study participants—including investigators and subjects—should be fully briefed with trial literature and study materials that are user friendly. When subjects and site staff both have a clear understanding of the study protocol and of what is expected of them, that aids recruitment and helps guarantee the success of the trial.

Experimenting with recruitment options

One strategy that sponsors and CROs can use to boost subject recruitment is to contract with a recruitment specialist. During the past few years, several have begun to provide subject recruitment campaigns to accelerate enrollment. The campaigns entail media planning, communication strategies, and field-based recruitment methods. A growing number of pharmaceutical companies are adopting this new approach in hopes of achieving greater accuracy in forecasting budgets and timelines for each protocol and trial. Properly implemented, such campaigns allow clinical trial planners to model various resource investment scenarios, to estimate specific costs, and to forecast timetables.

Protocol review. Project leaders must conduct a thorough protocol review from clinical and general demographic perspectives, including site qualification, evaluation of the target patient population, confirmation of subject accrual timetables, existence of other drug trials competing for similar subjects, and disease prevalence within the general population.

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Funding. Project leaders need management confirmation that funding levels will match recruitment efforts and expectations. This includes both the understanding that some costs may not be known at the beginning of the campaign and an understanding of the timelines of each subject recruitment initiative.

Communication. Project managers should establish strong communication with clinical managers and those involved in the enrollment process, in order to expedite decisions and the recruitment progress between the sponsor and recruitment consultants.

Getting the message across

Another issue involves marketing. Because recruiting subjects has become as competitive as marketing products, some defining characteristics of a comprehensive recruitment program are similar to those of a strategic marketing program.

Advertising costs are the single greatest expense for many subject enrollment programs. Therefore, it takes expertise in media buying to realize the lowest cost per qualified referral. Advertising for each study requires a focus centered on either subjects or the clinic. That focus, in turn, determines whether

clinical trial planners will use recruitment and retention approaches based on mass media advertising or on an investigator database and community referral. Enrolling subjects successfully depends upon the recruiters' ability to reach potential subjects through a broad range of messages. Recruiters do that through television, radio, and print advertising; direct mail campaigns; public service announcements; clinical educational presentations; Internet and Web site programs; and community outreach initiatives.

In recent years, consumer media have covered most aspects—good and bad—of development-stage medical devices. This has led to an increase in the number of self-referred subjects participating in clinical trials.

"This phenomenon may be attributed to a change in the way device manufacturers are promoting their investigational products," according to a March 2001 report in *The Gray Sheet*.[7] Subjects have more access to data through the Internet than they used to, and some device companies have followed the lead of the pharmaceutical industry by implementing direct-to-consumer (DTC) marketing schemes. In addition to improving subject awareness about devices, DTC advertising and subject recruitment can help manufacturers avoid potential conflicts of interest on the part of investigators.

Potential trial recruits must be reassured that they will not suffer as a result of their participation and that they won't be treated as guinea pigs.

Project management software is essential to help identify and plan for recruitment and study milestones, including the approval of campaign materials by institutional review boards and the timing of "deliverables" to prospective subjects and other members of the trial team. Enrollment programs must track each study site's response to the referrals generated by the recruitment campaign. Such tools can also help refine tactics throughout the program, while customizing elements of the recruitment program to each investigator's preferences.

Using technology

Analyzing recruitment performance by site helps sponsors identify the top performing sites. It also uncovers signs of decreasing lead generation and the need to reallocate resources and provide additional on-site support. As a result, more recruitment consulting firms are developing simple-to-use, Web-based data collection systems that make it easy for sites to input current data.

The Internet offers an ever-growing wealth of information about health care; an estimated 12,000 sites (both suspect and reliable) are dedicated to health and medical topics. In the United States, sponsors and CROs now post information about their clinical trials on the Internet, usually on Web sites of research centers, patient associations, and advocacy groups. When potential subjects surf the Internet, they are usually highly motivated and self-selecting.

Another crucial element of the recruitment process is in-depth knowledge of the subject profile. Enrollment consultants can provide special expertise in this area by working with therapeutically focused clinicians who review historical data and demographic factors before initiating any recruitment programs. It is important for trial planners to understand the clinical trial's market demographics, the subject population, and the possible barriers to the study.

Increasing public confidence in trials

Clinical and community outreach initiatives can also be helpful for enrolling subjects in clinical trials with narrow inclusion criteria. Target populations for the outreach programs may include clinically defined patients, caregivers, families, support groups, and community-based referral sources. Such initiatives can include educational and medical information programs delivered on site at hospitals, residential care facilities, community health and senior centers, and affinity group meetings run by skilled MDs, PhDs, and other experts trained in the specific clinical trial protocol. Study planners can also enlist community support groups to reach potential subjects who suffer from specific ailments, and their families.

Several factors contribute to the lack of subject participation in clinical studies. According to an online study of 2031 adults conducted by Harris Interactive in February 2002, only a minority of the public is confident that clinical trial subjects

- are not treated like guinea pigs (24%).
- do not suffer more pain or side effects than they would from standard treatments (13%).
- receive high quality care (32%).
- receive honest and accurate information (25%).

However, most survey respondents believe it is "essential" (43%) or "very important" (40%) that all new pharmaceutical products be tested on humans before they are approved for general use.[8]

Some experts suggest that a public education campaign may help turn those who are "somewhat confident" into "very confident." The main challenge is to reassure potential trial recruits that they will not suffer as a result of their participation and that they won't be treated as guinea pigs.

But such reassurance is hindered by the fact that so few protocol developers are able to write consent documents that comply with the directive in 21 CFR 50.20 that "The information that is given to the subject or the [subject's legally authorized] representative shall be in language understandable to the subject or the representative." Institutional review boards do their best to correct the problem, but putting technical medical terms into easily understood language is a rare art form.

One way to boost public confidence in participation is for pharma companies to sponsor education for trial site staff, such as the courses offered by National Institutes of Health's Human Participants Protection Education for Research Teams.[9] These courses are designed to augment policies established by medical center institutional review boards and regulations enforced by federal, regional, and local agencies. Participants learn how

to cost effectively maximize recruiting efforts; clarify FDA policies and considerations regarding review of subject recruitment materials for clinical trials; organize case studies of recruitment for a variety of clinical trials; compete for a limited number of subjects; use proven methods developed by sponsors to increase subject enrollment; enhance communication strategies for clinical trial recruitment; and improve minority recruitment initiatives.

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To minimize time to market, sponsors must explore new subject recruitment techniques.Â Â© 2020 MJH Life Sciences and Applied Clinical Trials Online. All rights reserved. Spotlight. Patient Participation. Regulatory, Other. TopicSee All >. Clinical Trial Supply Chain. "The trial found assigning a male name to a candidate made them 3.2 per cent less likely to get a job interview. Adding a woman's name to a CV made the candidate 2.9 per cent more likely to get a foot in the door." LOL.Â Professor Hiscox said he discussed the trial with the ABS and did not consider it a rigorous or randomised control trial, warning against any "magic pill" solution. permalink. embed. Often promoted as a great way to recruit those hard-to-pin millennials, social media recruiting has become commonplace for many companies. Even some of the more old school companies are latching on to the idea. When the class of 2016, freshly graduated, checked on their Snapchat stories, they found something new: a job opportunity.Â Using your employees to find new ones will save money and give you a better sense of your workplace culture. If a steady stream of your employeesâ€™ friendsâ€™ resumes are coming in, your employees must like working there. On the other hand, if the resumes are trickling in, you should ask yourself: why donâ€™t your employees want to subject their friends to your company? Many traditional recruiting practices do not work well when recruiting gen Y. Here are 3 ways to recruit this new generation Y.Â Now, how does this impact the recruitment of Gen Y talent? For one, here are 3 traditional recruiting practices that Gen Y does not respond well to: 3 Ways to Recruit Employees. 1. Where do you see yourself in 5-10 years from now? Gee, do you have any idea how that sounds to a generation that isnâ€™t even sure about tomorrow?