CHAPTER THIRTEEN

Participant Recruitment and Retention in Clinical Trials

At the conclusion of this chapter, readers will be able to:

- Identify special populations for inclusion in clinical trials.
- Describe a variety of recruitment methods and the potential benefits and disadvantages of each.
- Define the IRB role in the review of advertising materials.
- Understand the need to set realistic recruitment and retention goals for clinical trials.

Introduction

In 2010, pharmaceutical and biotechnology companies spent more than $60 billion on research and development, including a large amount for clinical studies.[1] The average cost of developing one new drug has increased to over $1.24 billion, and the development process time from the pre-clinical stage to FDA approval averages about seven years.[1] Around the world, more than 80,000 study sites a year are involved in carrying out research, based on 5,000 to 6,000 unique protocols. More than one million volunteers will participate in these trials. The largest numbers of volunteers are needed for phase III programs.

Given the enormous development costs, companies obviously want to speed the process as much as possible, allowing for more marketing time before their patent protection for the product expires. The timely enrollment of appropriate participants into trials is critical to managing the timelines for a development program. Finding, enrolling and retaining study participants are some of the largest and costliest challenges facing clinical research professionals today.

The majority (nearly 86%) of clinical trials fail to enroll the desired number of patients within the contract specified enrollment period. This failure rate is up from 80% of trials in the late 1990s.[1] Clearly, these enrollment delays result in significant direct development costs for the study sponsor and, even more importantly, they delay the introduction of promising new therapies for patients' unmet needs. Recruitment efforts fail for a number of

reasons including poor protocol design, conflicting clinical trials for similar treatments, new and competing products becoming available on the market, workload of the study investigator and staff and negative public perception of and lack of trust in clinical research.

The investigator should be realistic when determining the feasibility of recruiting participants prior to conducting a study.

Education of Potential Participants

One of the key components of successful recruitment stems from educated patients who understand clinical trials, their roles in the clinical trial and how they may or may not personally benefit from participation. Educating potential participants takes time, resources and patience.

In past years, there have been reports of negative occurrences in clinical trials, including deaths and injuries, undermining public confidence in research and making it more difficult for investigators to recruit participants. Ultimately it is the investigator's responsibility to address any safety concerns a potential participant may have. This is best done by ensuring the study design does everything possible to protect the safety and welfare of research participants.

Why Patients Join Clinical Trials

Patients join clinical trials for myriad reasons, including wanting to help advance the science of their diseases, a lack of available therapies, a desire to obtain improved medical care, lack of health insurance, advice from a primary care physician or financial or other reasons. The decision whether to participate is a very complex process that involves not only what is known about a drug, but also the patient's reaction to his disease, his relationship with his doctor and his cultural roots. Understanding why a patient chooses to participate is helpful and will aid with both recruitment and retention of participants for the full duration of the trial.

The well-discussed phenomenon of "therapeutic misconception" must be considered among the reasons patients volunteer for trials. Simply put, despite cautions about lack of direct benefit in the consent forms and verbal statements from investigators confirming the questionable nature of benefits, many patients still believe clinical trials are "treatment." This is particularly evident when patients have serious diseases, such as cancer or AIDS. Investigators must guard against overstating the benefits of research and should ensure that patients make a realistic assessment of benefits and risks before volunteering.

The most frequently mentioned concern as to why people do not par-

ticipate in clinical trials is the fear of receiving placebo instead of the active drug. Another concern is the fear that study drugs may cause risky side effects. With increased effort focused on education regarding clinical trials, individuals who agree to join should have a better understanding of the risks and benefits of participation.

Recruitment of Special Populations

It is important to include a representative population in most clinical trials. This generally means the study should include men, women, minorities and age-appropriate participants, in keeping with the proportion of individuals afflicted with the disease or condition being studied. In many cases, including a representative population is not only important but also mandatory. For example, the National Institutes of Health (NIH) has made the inclusion of appropriate numbers of women and minorities an explicit criterion to be considered when reviewing grant applications. Similarly, the FDA now requires data being submitted in support of a new drug application (NDA) include an appropriate number of female and minority participants, and that the data are analyzed to determine differing effects on these populations.

The following are specific considerations for recruitment of various populations:

Minorities

Much has been written about the lack of participation by minorities in clinical trials in the U.S. Barriers include economic factors, mistrust and lack of awareness about clinical research. These barriers often can be surmounted with careful planning, including efforts to address minority participant concerns prior to participation via educational materials, the availability of transportation, meals and child care services as needed, the use of home visits or study centers with convenient locations, participation by minority researchers and research staff, the use of study materials in other languages, investigator or other study staff of the same ethnicity and efforts to educate and develop trust with potential participants.

Barriers to recruiting minorities can be surmounted with careful planning, time and effort upfront to better understand the needs and concerns of the targeted populations.

Women

Today, in many studies, women make up 50% or more of the study cohort. This has not always been the case. As recently as the early 1990s, it was the