

Good Clinical Practice Q&A: Focus on Subject Recruitment

Are subject enrollment incentives that sponsors offer to clinical trial sites permitted under GGP?

Although site enrollment incentives are not addressed explicitly in FDA or GCP standards, FDA Office of Good Clinical Practice officials have recently cited "minimizing the use of enrollment incentives" as one way for sponsors to discourage—or at least not encourage—fraud by clinical investigators. In reviewing the conduct of investigators found guilty of fraudulent research practices, the FDA discovered that maximizing profits was one of the most significant reasons why these investigators created fraudulent records for nonexistent study subjects.

Still, enrollment incentives are very much a fact of life in an environment that places such a premium on development speed, particularly when subject enrollment is seen as one of the key rate-limiting factors. According to PhRMA's June 2002 (updated in 2004) voluntary "Principles for Conduct of Clinical Trials and Communication of Clinical Trial Results," "when enrollment is particularly challenging, reasonable additional payments may be made to compensate the clinical investigator or institution for time and effort spent on extra recruiting efforts to enroll appropriate research participants."

Rather than taking actions to focus site staff so intensely on enrolling subjects (and possibly away from other important tasks and responsibilities), however, sponsors might be better served to ensure that the site has sufficient access to the appropriate patient population and is adequately resourced to conduct the study. Sponsors should also ensure that site budgets adequately compensate the site staff for the time and effort to conduct the study.

Increasingly, enrollment incentives, or recruitment bonuses, are being viewed as potential conflicts of interest for clinical investigators, and as activities that must be managed and, in some cases, disclosed to clinical subjects.

Are all telephone scripts that clinical site staff use to recruit and inform potential subjects who contact the site to inquire about or express an interest in a study subject to IRB approval? If the script instructs the receptionist to say, "Yes, we have a study about XYZ, and you must have symptoms A, B, and C," is that subject to IRB approval?

There is a subtle difference between recruiting potential subjects and informing potential subjects. Generally, recruiting and selling are involved when a potential subject hears or reads about a study. Materials used in this phase—an advertisement, a letter, or a "cold call"—must be approved by an IRB.

Once a potential subject knows that a study is being conducted and calls the site, the information provided by the site staff (likely a receptionist) must be straightforward and informative, but need not be scripted or approved by the IRB. Typically, a site receptionist's initial responses may include, "You will be called by Nurse Ratchet," or "Please report to a group meeting at 10:00 a.m. on December 7th in Room 123," or "We will mail you a brief questionnaire to see if you are eligible for our study."

Screening scripts or questionnaires developed to "pre-screen" candidates who respond to clinical trial advertisements via a telephone call to the site personnel or a call center are

frequently submitted to IRBs for review as a best practice. This provides the IRB with an opportunity to evaluate the nature and type of information that the potential candidate is being asked to determine study eligibility, and helps ensure that the telephone screeners do not provide potentially misleading or coercive information to the caller.

Any exchange of clinical information, which does not require IRB approval, should be handled by more clinically qualified personnel than the receptionist.

Is enrolling study staff in a clinical study permissible? How about their children?

This practice is highly questionable, and violates, at a minimum, the ICH GCP (E6) guideline's provisions regarding the enrollment of vulnerable subjects. According to the ICH guideline (1.61), vulnerable subjects are "individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group within a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention."

Special protections must be provided to these subjects because their willingness to volunteer in a clinical trial may be influenced by the expectation, real or perceived, of receiving benefits (e.g., promotion, bonus) associated with participation or of being subjected to a retaliatory response from management (e.g., no promotion, no bonus) if they do not participate.

A clinic secretary, a hospital pharmacist technician, and a health care facility parking lot attendant could all be considered "vulnerable" in this sense. It would be prudent for a health care institution that conducts clinical studies to have policies regarding employee participation in these studies. The policies should address the conditions under which staff may enroll in a study and the safeguards that will be implemented to protect them.

Absent written policies, no employees of the institution should be enrolled. An institution's IRB should make this prohibition known to investigators. Investigators need to be highly sensitive to potential conflicts of interest.

Enrolling the children of clinic staff poses similar ethical conflicts. Minors are already included in the ICH guideline's definition of vulnerable subjects. The fact that their parent—the person legally responsible for them—is also a vulnerable individual only adds additional levels of complexity to enrollment issues. Site staff members are well advised to avoid situations that even suggest that they may have enrolled their children based on financial and employment considerations.

Source

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