# Clinical Trial Recruitment Practices: The Evolution of Ethical Considerations

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*Over the last few decades, the process of clinical trial conduct has evolved significantly. Clinical trial recruitment is one of these key areas. In addition to the advances in recruitment advertising through social media and other technologies, there are a number of practices that used to be considered acceptable, and even standard, which are no longer considered acceptable. In many cases, this is related to an increasing awareness and effort to avoid potential conflicts of interest for investigators, study teams, and referring physicians. At the same time, other practices, such as study sponsors providing direct staffing support for busy clinical sites, have become more popular.*

*This paper reviews practices related to clinical trial recruitment, with consideration of which are considered acceptable under current best practice, ethical and regulatory standards.*

## Generally considered acceptable:

### Payments to referral sources based on time and effort

While the payment of "finder's fees" to referral sources is considered unacceptable, it is usually considered appropriate to compensate a referral source for the time and effort that they spend on the referral process. For example, if the nurse at a primary care center spends 6 hours looking at medical records to identify patients who may be eligible for the study, and calling those patients to tell them about the study and how to get more information if they are interested, it would be appropriate to compensate the nurse's time at fair market value. It is important to remember that the compensation would be paid, regardless of whether any of the referred patients end up enrolled in the study, or even whether they screen for the study. Although this is generally considered acceptable by most oversight bodies (such as Institutional Review Boards (IRBs)), there are some ethicists who disapprove of this practice.

### Assistance with trial-related site travel expenses

For many years, study sites have reimbursed trial participants for expenses related to study visits including such things as parking fees at the clinical site, cab fare to the clinical site, meals during long study visits, and sometimes even expenses like child care. For some studies, this may even be extended to include reimbursements for air travel and hotel stays when study participation requires long distance

travel. Generally, researchers, IRBs and sponsors agree that participation in clinical research should not incur additional expenses for the trial participant that they would not have encountered had they not been in the study. Therefore reimbursement of these expenses, or providing services to avoid the expenses (like giving meal or taxi vouchers), is both respectful and appropriate.

More recently, sponsors and sites have tried to facilitate the participation in research by providing transportation to clinical sites for study visits through third-party ride-service vendors like Uber™ or Lyft™, where the cost of the transportation can be directly billed to the site or sponsor. Although this is essentially the same concept as providing reimbursement for parking, or a taxi voucher, some IRBs and sites have been hesitant to use these services for reasons that are not clear. Although these on-demand services are novel for many people, there is no unique ethical or regulatory concern introduced that should prevent the use of these services to reduce the burden of participation.

## Support for site study activities including recruitment

In studies with biopharma or other sponsors who provide funding, indirect costs in the contract often go toward the salary support for study staff who are tasked with multiple study-related activities, including subject recruitment/enrollment. In some cases, the study site contract may provide salary support as a direct cost, with team members assigned to the project for a certain percentage of time proportional to that support.

It is also fairly common for sponsors or CROs to provide extra temporary staffing support to a study site when activity is high; for example, to send a Clinical Research Associate to the site to help enter data into case report forms or answer data queries in advance of a data base lock deadline when the site finds itself understaffed. FDA has considered and accepted this practice of having study staff that is not in the direct employ of the investigator.[1] The appropriate participation of these supplementary team members requires that they work under the direction of the investigator, who remains responsible for all site activities related to the study, that they are trained for the tasks they are conducting, and that their responsibilities are documented as necessary in the delegation of authority log at the site.

An emerging type of support for study activities is the use of enrollment assistants at clinical sites. These are study team members who have salary support from the sponsor, but are assigned to, and work under, the direction of the site staff or investigator to support activities related to identifying potential study participants. Depending on the site needs and the study, their activities may include contacting referral sites to make them aware of the study, reviewing medical records to identify potential participants, outreach to potential participants, and pre-screening or screening activities. As with support for other study site functions, there are no regulatory or ethical prohibitions on staffing of this kind, assuming that the financial

support of these staffers are time-based (not based on referrals or enrollment numbers), and that there are no other direct or indirect incentives related to enrollment which could create a conflict of interests.

## Generally Considered Problematic:

### Site payments based on enrollment numbers

Several years ago, it was not uncommon for sponsors to include recruitment-based incentive gifts or payments incorporated into study site contracts. These incentives could be seen in several forms:

- As a "per subject" payment for study costs which increased in amount after a certain enrollment target was reached (e.g., $2000/ subject for the first 10 subjects, $3000/subject for the next 10 subjects)

- As a bonus payment either to the site or directly to a member of the study team when an enrollment target was reached, or for the first site in a multi-center study which reached an enrollment target (e.g., first site to randomize 10 participants got a $5000 bonus to the study staff)

    > Sometimes there were efforts to make bonuses more acceptable by providing them as reimbursement for travel to a conference, or as equipment or educational materials for the study site or study team, (textbooks, etc).

Essentially, these kinds of bonus payments are now considered unacceptable. It is now recognized that providing direct financial incentives to the study staff for the enrollment of participants creates an unacceptable conflict of interests. Even without consciously doing so, the staff may encourage or pressure potential study participants to enroll, so that they can obtain the financial rewards. They may even be motivated—again, perhaps even without consciously doing so—to assess eligibility criteria less rigorously, or to be less critical in assessing the signs or symptoms of a potential participant that would otherwise be exclusionary or questionable, when rewards are promised.

Both sponsors and research sites, for the most part, now recognize this conflict and neither offer nor expect this kind of recruitment bonus. Recruitment plans that include these incentives are still occasionally seen, often when the study is being sponsored or managed by a less-experienced team, or when recruitment plans are developed by firms that specialize in marketing and commercial projects outside of the health sciences field, and when these teams have not thought through the conflicts these situations present.

### Payments to referral sources based on successful enrollment of referrals (finder's fees)

In some studies, the study site may encourage the referral of potential study subjects from other physicians or healthcare facilities. For example,

a psychiatrist participating in a study for a new antidepressant might send a letter to local primary care physicians, suggesting that patients in the primary care practice who are not responding well to standard therapies may be candidates for the clinical trial, and that the primary care doctor provide information about the study to these patients.

Payments for successful referrals—referrals that result in enrollment of a study subject—are often referred to as "finder's fees." While there is no specific regulation that prevents the payment of finder's fees, they are generally considered inappropriate because they create a conflict of interests. The promise of payment for successful enrollment may induce the referring physician to strongly encourage a patient to join the study even if the patient expresses doubts, or even to refer patients who aren't really appropriate for the study but might slip through the screening process. These payments also conflict with the Code of Ethics of the American Medical Association, which prohibits referral payments to physicians, specifically stating that, "Offering or accepting payment for referring patients to research studies (finder's fees) is also unethical."[2]

## Conclusions

Study site recruitment practices have evolved over the last several years, with a broader overall view in the industry of the issues of conflict of interests and the protection of research participants from the impact of these conflicts. Most of the practices that historically raised concerns are rarely seen in the conduct of clinical trials today. Newer models of supporting recruitment efforts, such as supplementing site staff with additional staff focused on enrollment efforts, are generally considered to be ethically appropriate as long as payment is not based on recruitment efficacy, and the investigator retains oversight of all site activities.

## References

[1] Guidance for Industry- Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects, Department of Health and Human Services, Food and Drug Administration, October 2009. Section III(A)(4)(a), What Are an Investigator's Responsibilities for Oversight of Other Parties Involved in the Conduct of a Clinical Trial?

[2] American Medical Association Code of Medical Ethics, Opinion 6.02; Fee-splitting: Referral to Health Care Facilities

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