CHAPTER 1

Clinical Research - Clinical Investigator's Perspective

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1.1 Introduction

Clinical research / trials require a substantial commitment of both time and effort as participation may continue for months or years. Though financial rewards are limited for participating in a clinical trial, there are other incentives like:

- The chance to collaborate with other clinical investigators.
- Experience of clinical research methods for study site personnel.
- Opportunities to enhance knowledge of the disease and the treatment under investigation.
- In some trials, exposure to new investigative techniques or access to specialized equipment or facilities.

The scientific, practical and financial implications should be weighed before considering participation in a clinical research / trial.

It may be prudent to consider and address the following aspects before an investigator decides to undertake a clinical research project.

1.2 Scientific Aspects and Practical Aspects

- It is important to determine that the trial addresses a question of clinical and scientific relevance. Some trials permit a commercial sponsor to apply for an extension to the marketing authorization of an investigational product but do little to improve the understanding of disease and therapeutics. The same question is sometimes addressed by different sponsors and the proposals may be redundant as the information is readily available.
- Investigator must discuss clinical trial design and statistical issues and should assess whether the protocol is likely to confirm or refute a trial's hypothesis. An important consideration for an investigator is whether the required number of clinical research participants stated in the protocol can be enrolled in the defined time frame. The requirements for follow up of patients must also be considered, e.g., the duration and frequency of follow up and the data to be collected.
- Investigator must carefully assess the eligibility criteria as the number of patients at a study site, who might be eligible for a trial may be overestimated. Some study sites keep records of admission to tackle this problem. More experienced study sites can often use information from previous trials that had similar eligibility criteria as a guide. Investigators should be confident that sufficient eligible patients will be recruited for the study. It is advisable to survey and maintain a log of potentially eligible study participants. This will provide a guide to estimate recruitment rates.
- An investigator's primary obligation is to protect the welfare of his/her participants. An investigator should consider how much time he/she will have to devote to the study, and compensation they may receive. Will the patients be required to undergo investigations that would not be considered part of routine care, and if they have to, will they be painful or put the patients to additional risk? The Ethics committees pay particular attention to these issues when reviewing a research study protocol.
- Data collection is a time consuming task, especially if case report forms ask for vast amount of data, much of which may contribute little to the study results. It is important to address how the data will be amassed and recorded. Procedures for processing adverse events may be very time consuming and this may not be clear at the outset of the trial.
- It is essential to ensure that the study site and institution have staff available to run the trial and that these people are sufficiently experienced in clinical trials before committing to participation in a clinical trial. This is particularly true of the study coordinator and any co-investigators who will be assigned the task of running the trial on a day to day basis. Curricula vitae is usually requested by the study sponsor because it is a requirement of the International Conference on Harmonization, Good Clinical Practice (ICH,

GCP) and Indian GCP guideline, to ensure staff are appropriately qualified and adequately trained. It is important to assess the amount of time required for patient enrolment, data collection and follow up and to consider whether study staff will have time to fulfil these obligations.

When calculating the staff costs, it is important to consider the following questions:

- How many personnel will be needed to fulfil the requirements of the protocol?
- Are the salary levels of team members identified?
- What proportion of their time will be spent on the study?

- It is further essential to address the issue of post-trial access of study medication for the participating subjects.
- It is important that investigators sort out publication related issues before start of any study and the same be clearly mentioned in the clinical study agreement.

1.3 Financial Considerations

Payments to study sites vary from study to study but the principles applied when reaching a decision to participate in a trial should remain the same.

- Most institutions now may set up a specific department, or appoint an external group to review studies and ensure that local health service resources are not used inappropriately to subsidize research. Prior to submitting a study for review by such groups, investigators should perform a financial review themselves and ideally develop a local budget. Local costs are usually predictable. However, it is important to remember that there may be many 'hidden' costs of drug storage, ethics committee review and provision of laboratory certificates. If specimens are to be sent to a central laboratory it is important to ensure that costs of local processing, storage and shipping are covered.
- Investigators should also consider the structure of the payment schedule. Most research studies pay a set amount of money per subject recruited, but the timings of such payments may vary. Possible payment schedules are:
  - One payment per patient when the patient is recruited.
  - One payment per patient once certain pre specified data have been declared clean i.e. from omissions or inaccuracies, and hence appropriate for statistical analysis.
  - One payment per patient at the time that the entire dataset has been received and declared 'clean'.

- A structured payment schedule whereby set amounts are paid at recruitment for the receipt of data from various follow-up visits and at the time that the entire dataset has been declared 'clean'.

The investigator should make sure that all eventualities have been considered when agreeing to undertake a study where the payments are based upon receipt of 'clean' data and/or are tied to follow up visits. Investigators must be aware that there is a potential for payments to be withheld if there is poor or no recruitment. Further, if payments are dependent on patient follow-up, then it is vital that these follow-ups take place. Also, contracts should be examined to ascertain what will happen in circumstances that are beyond the control of the investigator e.g., death of a patient.

Many protocols are amended one way or the other during the course of the study and extension to recruitment periods is a real possibility. Investigators should be realistic in the financial planning of a project whilst ensuring that the costs are adequately covered by the contract.

Decide! To participate or not

Finally, clinical investigators may choose to take part in a study because they appreciate the scientific or clinical importance of the research project. However, they may be willing to subsidize research that is not adequately funded, though this is less usual. Equally possible is the fact that they may decide to participate simply because they feel that the study is well funded.

Suggested Reading

1. Spilker B. Guide to clinical trials. New York 1991, Raven Press.
2. Tony Craig. Factories, call centres —— and now clinical trials outsourced to India. National Review of Medicine, July 30, 2004; 1 (4).