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Protocol Development: A Contract between Sponsor and Investigator

R. Santosh Kumar and B. Joshna

GITAM Institute of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam, 530045.

ABSTRACT

The main aim of this review which is published by the European Medicines Agency EMEA and the U.S. Food and Drug Administration (FDA) [1-7] is to describe about the importance of protocol in clinical trials. When developing a successful study design and writing a protocol, the researcher must address various successful components including the type of data being collected, data handling, record keeping, outcome measures. A research protocol is a document that describes the background, rationale, objectives, design, methodology, statistical considerations and organization of clinical research project.

Keywords: Protocol, Clinical trial, Statistical design.

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***Address for Correspondence:**

R. Santosh Kumar, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Gandhinagar, Visakhapatnam-530045, Andhra Pradesh, INDIA.

INTRODUCTION:

A protocol is the most important quality control tool for all aspects of clinical trial. A protocol can be made better by explaining the features of the confirmatory trial clearly during its preparation. It describes how clinical trials are conducted.

It acts as a proof in various research trials as well as in clinical trials. A protocol can be made better by explaining the features of the confirmatory trial clearly during its preparation.

Nature and purpose of a clinical trial:

This review mainly describes about the protocol which shows statistical design and data analysis of a particular experiment. Clinical trials are very complex and different from protocol. While making a protocol, a clinical trial statistician not only should be careful about the design and method of the protocol but also the administrative and organizational purpose of it. A documented contract is done between a sponsor and investigator in the form of a protocol. The agencies and individuals which are involved in the project are identified by the protocol and the responsibilities and obligations are assigned to them.

All pharmaceutical companies name/number their protocol. The various topics in a protocol are:

- Introduction: It gives information about the article, its effect, previous research done and the current topic.
- Objective: It explains about the medical conjecture.
- Subject selection criteria: It explains the criteria for selecting the subject and safety to study the subject.
- Study medication: It explains about the treatment for test, control, packaging , mechanism for masking the treatment.
- Plan and procedure: It makes a schedule of doses, tests, visits which are to be done by the investigative staff, various rules for discontinuing subjects, reports of adverse events, administration of the medicines given in case of emergency.
- Efficacy and safety end point criteria: It includes the safety endpoints of primary and secondary efficacy, collected, monitored, quality control data collection etc.
- Data analysis and statistical considerations: It describes the primary and secondary analyses, variables and statistical design consideration.
- Committees: It identifies different committee. Eg: committee for data monitoring, end point classification, steering and executive committees.[2,4]

- Pharmacokinetic/pharmacodynamic investigation: It consists of sub protocol which includes population pharmacokinetics, exposure-response as secondary analyses.

According to The ICH Section E6 on Good Clinical Practise[1], the sponsor should appoint qualified individuals (eg: biostaticians, pharmacologists and physicians) who will be involved throughout the trial process from designing of the protocol to determine the final report of the protocol.

Content of the statistical section of a protocol for clinical trial:

ICH advices to specify the analysis in advance i.e in order to get the result and conclusion of a clinical trial the extent to which the procedure is followed should be pre planned.

Primary Variable(s) and analyses:

The primary variables which are identified by the protocol should be explained why they were chosen[4].After the analysis the results which can be predicted are included in the protocol[3].

From a given trial many number of analysis can be conducted. In a protocol the trial data which acts a proof and the data which is obtained after analysis should be differentiated.

Primary statistical objective:

In this the primary objective of investigation is converted into statistical terms.

Primary analyses:

These are the statistical data that provide information about the primary investigational conjecture. Different analysts give different judgments and opinions of what principle features should be present in the analysis. Most of the analysts determine the statistics upon which the primary analysis is based on in a protocol. Hence the principle features of analysis should be prespecified in the protocol or else due to different opinions it may lead to confusion.

Decision rules:

A protocol should design the pattern and different methods to combine the data obtained from analysis In order to interpret the results very fast.

It contains information on how a prespecified set of statistics is used to evaluate the primary conjecture. It allows the experimenters to conclude whether the treatment is equivalent. Decision rules about how to conclude the result from the arithmetic.

Error control:

When a number of hypothesis is to be tested the type of errors, the method of controlling, the level to which they are controlled should be stated. The method of controlling type I errors should be stated.

Analyses subsets:

It includes subsets which contain data related to the primary analysis.

Design and number of subjects:

A statistical design should be set in an experiment. It justifies the planned number of subjects.

Sometimes trials are designed in such a way that it is stopped after certain amount of information has been gathered.

Secondary variable(s) and analyses:

Secondary variables are those measurements which support the primary objective or the measurements related to secondary objective.

Interim analyses:

If a particular clinical trial is to be stopped, extended or modified they are based on interim analyses. The criteria for taking the decision should be described in the protocol.

Problem data:

The ICH E9 document says that the specific procedures should be mentioned in the protocol to minimize the irregularities which causes impairment in the statistical analysis.[7]

Safe data:

A safety data summarizes and displays the information. If there are any safety issues the sponsor should prespecify them.

CONCLUSION:

Protocol is a documented proof which clearly specifies about the research plan for the clinical trial. It describes about the safety and risk benefits during a clinical trial. The development of the protocol should be joint effort of representatives from several disciplines such as clinical pharmacologists, pharmacists, biostaticians, physicians and other relevant health care workers as well as experts in traditional medicine.

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