Clinical trials

An overview

The growing awareness on safety and quality of pharmaceutical products has magnified the significance of clinical trials. These trials are conducted meticulously in different phases, with the aim of determining the safety and efficacy of products before being marketed. Read on for more insights…

Courtesy: Srispharma.com

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As per the Good Clinical Practice for Clinical Research in India (Indian GCP), clinical trials are defined as 'a systematic study of pharmaceutical products on human subjects – (with patients or non-patients as volunteers), in order to discover or verify the clinical, pharmacological (including pharmacodynamics/pharmacokinetics), and/or adverse effects, with the objective of determining their safety and/or efficacy.' Different phases of clinical trials namely Phase I; Phase II; Phase III and Phase IV are well-defined in the Indian GCP. These phases are elaborated below.

Phase I: Human/clinical pharmacology trials

The objective behind Phase I trials is to determine the maximum tolerated dose in humans, pharmacodynamic effect, adverse reactions, if any, with their nature & intensity; and pharmacokinetic behaviour of the drug as far as possible. These studies are often carried out on healthy adult volunteers (tests are conducted on at least two subjects at each dose level) using clinical, physiological and biochemical observations. These trials are usually carried out by doctors/investigators in clinical pharmacology, with necessary facilities to closely observe and monitor the subjects for safety. Usually Phase I trials are carried out in one or two investigational centres.

Phase II: Exploratory trials

In Phase II trials, limited patients are studied carefully to determine possible therapeutic uses, effective dose range and further evaluation of safety and pharmacokinetics. Normally 10-12 patients should be studied at each dose level. These studies are usually limited to three-four investigational centres and carried out by clinicians specialised in the concerned therapeutic areas, having adequate facilities to perform the necessary investigations for efficacy & safety.

Phase III: Confirmatory trials

The purpose of these trials is to obtain sufficient evidence about the efficacy & safety of the drug in a larger number of patients, generally in comparison with a standard drug and/or a placebo as appropriate. These trials may be carried out by clinicians in the concerned therapeutic areas, having facilities appropriate to the protocol. If the drug is already approved/ marketed in other countries, Phase III data should generally be obtained on at least 100 patients distributed over three to four centres primarily to confirm the efficacy of the drug in Indian patients when used as recommended in the product monograph for the claims made.

Phase IV: Studies performed after marketing of a product

Trials in Phase IV are carried out on the basis of the product characteristics on which the marketing authorisation was granted and are normally in the form of post-marketing surveillance, assessment of therapeutic value, treatment strategies used and safety profile. Phase IV studies use the same scientific & ethical standards as applied in pre-marketing studies.

After a product has been placed in the market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc, are normally considered as trials for new pharmaceutical products.

Various stakeholders of clinical trials

Every stakeholder of clinical trial is responsible for producing essential documents of proposed study. There are five major stakeholders for any clinical trial. They include:

Sponsor: A sponsor is an individual or a company or an institution taking the responsibility for the initiation, management and/or financing of a clinical study. The sponsor is responsible for preparing protocol, investigator's brochure, Case Report Forms (CRF), investigational drug, original submission to regulatory authority, assuming responsibility of the study, etc. A sponsor can delegate partial or complete activities to the experts from Clinical Research Organisations (CRO) that can complete the work as per timelines and requirements of the sponsor. However, final responsibility of conduct of any trial always lies with the sponsor.

Clinical investigator: Clinical investigator is a person responsible for the conduct of the study at the trial site. He is responsible for the rights, health & welfare of the subjects. Further he is also responsible for enrolling eligible patients, prescribing investigational product, collecting data and any adverse event pertaining to enrolled subjects as per the protocol in the predefined fields of CRF.

Important documentations required

The sponsor is responsible for preparation of following documents, which serve as the backbone for any clinical trial, apart from being responsible for preparing an informed consent form and patient information sheet for patients.

Protocol: Every clinical trial requires a detailed protocol defining rationale & objective of the trial, ethical consideration and study design giving primary and secondary end-points, if any. It also calls for description of the type of study – random, single blind or double blind, medications & treatment, dosage, route of administration, packaging and labelling of medications, – patient selection criteria as well as withdrawal criteria, handling of investigational product, assessment of efficacy and assessment of safety. Finally, protocol needs to have details on statistics, data handling and management, quality control & assurance.

Investigators' brochure: An investigator's brochure is 'a collection of data (including justification for the proposed study) for the investigator consisting of all the clinical as well as non-clinical information available on the investigational product(s) known prior to the onset of the trial'. There should be adequate data to justify the nature, scale & duration of the proposed trial and to evaluate the potential safety and need for special precautions. If new substantially relevant data is generated during the trial, the information in the investigator's brochure must be updated. Investigator's brochure usually contains physical, chemical & pharmaceutical properties and formulation, non-clinical or animal studies, clinical studies – previous studies carried on human beings, toxicological studies and summary for data and guidance to the investigators.

Case report form: A case report form is a printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

Investigational drugs: An Investigational product is a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Regulatory authority: The Drugs Controller General of India (DCGI) or an office nominated by him is the regulatory authority for the purpose of carrying out clinical trials in India. The regulatory authority approves the study protocol, reviews the submitted data and conducts inspections

Ethics committee: An independent review board or committee comprising medical/ scientific and non-medical/ non-scientific members, whose responsibility is to verify the protection of the rights, safety and well-being of human subjects involved in a study, forms the ethics committee.

Trial subjects / patients: An individual participating in a clinical trial as a recipient of the investigational product.

Why India?

Among Asian countries, India has been attracting a lot of clinical trials due to a large pool of treatment naïve patients and English speaking population, ICH GCP trained investigators, rapidly improving medical technology and hospitals network. Various market research reports indicate a continued healthy trend for clinical trials industry in India.

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