

BASIC CONCEPTS OF CLINICAL TRIALS, NEW DRUGS AND CLINICAL TRIALS RULES, 2019

14.5 BASIC CONCEPTS OF CLINICAL TRIALS

A clinical trial is the scientific term for a test or study of a drug, therapy, surgical procedure, medical device, or of nutrition or behavioural changes in people. The tests are done to find out if the drug, therapy, procedure, etc. is safe and effective for people to use.

Objectives of Clinical trials:

1. To evaluate the safety and efficacy of a new medicine or device on specific patients (e.g. patients suffering from Alzheimer's disease).
2. To evaluate the safety and efficacy of varied doses of a commonly used medication (e.g. 10 mg dose instead of 5mg dose).
3. To evaluate the safety and efficacy of a medicine or devices already available in market for new indication.
4. To determine whether the new medication or device is more efficacious for the patient's specific condition than the already available, standard device or medication.

Types of clinical trials:

Clinical trials are used to study many aspects of health care:

- (a) Prevention Trials:** These trials are conducted to find better approaches to prevent disease or to prevent recurrence of disease. These strategies may include lifestyle changes, vitamins, minerals, medicines, vaccines etc.
- (b) Screening Trials:** These trials are conducted to evaluate the appropriate methods to detect certain health conditions or diseases.
- (c) Diagnostic Trials:** These trials are conducted to determine appropriate investigations or procedures for diagnosis of a particular diseased condition.
- (d) Treatment Trials:** These trials are conducted to assess new approaches, new experimental treatments, new combinations of surgical or radiation therapy drugs.

(e) **Quality of Life Trials:** These trials are conducted to explore appropriate methods to improve quality and comfort of life for patients suffering from chronic illness.

Phases of Clinical Trials

Clinical trials are conducted in the following phases with different purpose.

Phase I studies: These studies are performed to know whether the drug is safe.

This phase is first stage of assessing effective doses in healthy human volunteers and to evaluate the safety of a medication with therapeutic dose range, procedure or device and detect any side effects. These studies generally include a few healthy volunteers (20–100). If a medication, procedure or device is found to be safe, it can be subjected to phase II trials. Phase I trials are usually short, lasting a few days to a few weeks.

Approximately 70% of drugs move to the next phase

Phase II studies: These studies are performed to know whether **the drug effective**

These studies are conducted to assess whether a medicine is efficacious in the treatment of the specific disease or not and to further determine its safety. These trials normally involve a few hundred diseased patients (100–300). The safety of the drug also continues to be evaluated. A Phase II trials usually lasts six months to one year.

Approximately 33% of drugs move to the next phase

Phase III studies: These studies are performed to know whether the drug is safe and effective in larger groups of volunteers for longer periods of time?

These studies are carried out on large groups (typically 1,000 to 3,000) of volunteers to confirm the efficacy of a novel medicinal strategy and to determine its benefits and adverse effects if any. They are conducted to compare the novel treatment with alternative treatment already available in the market.

Phase III trials may also include studies in varied dosages and populations to determine the efficacy of merging a novel procedure with other treatment modalities. Phase III trials generally last two to three years

Upon completion of first three phases I, II and III trials, the company or investigator submits the study data to the National Regulatory Body of the respective country. (In India CDSCO) for approval of a new drug or medical approach.

The Drugs Controller General of India (DCGI) is an official of the CDSCO who is the final regulatory authority for the approval of clinical trials in the India.

Approximately 25-30% of drugs move to the next phase

Phase IV studies: (Post-Marketing Studies)

These studies are carried out upon launching of a new medication, procedure or device into the market. These studies are intended to gather additional information regarding the efficacy of the approved drug, device or procedure in different populations and assess any prolonged adverse effects and to compare the approved treatment to a wide-ranging conventional treatment.

In case of emergency needs, there is also a provision of accelerated, or quicker, approval if the drug offers something new or meets a need for people living with pandemic diseases like Covid 19.

However, even if a drug gets accelerated approval, the drug company/investigator must continue to do long-term research (Phase IV trials) on the drug to get full approval.

Regulation, Ethics and Safety

Clinical trials must be conducted in harmony with standard regulations, ethical guidelines, and national laws and codes of conduct. These regulations are meant for ensuring safety of participants, protection of privacy and human rights, responsible research conduct, good clinical practice and quality data collection.

The Central Drugs Standard Control Organization (CDSCO) is the National Regulatory Authority in India for conducting clinical trials. The Drugs Controller General of India (DCGI), an official of the CDSCO is the final regulatory authority for the approval of clinical trials in India.

In USA, applications for clinical trials of a novel medication must be first sent to Food and Drug Administration (FDA) and in Australia it is sent first to national regulatory authority i.e. the Therapeutic Goods Administration (TGA).

All the types of clinical trials must be approved by an institutional review board (IRB) or a human research ethics committee (HREC; as in Australia). The board comprises of researchers, doctors and other members of the community responsible for review and discussion of the clinical trial protocols and other study forms and documents to confirm that the proposed study is ethical and the welfare and rights of the participants shall be protected with reasonable and minimized potential risks when compared to the potential benefits of the study. Upon approval, the IRB / HREC shall continue to monitor the trial.