CLINICAL TRIAL PROTOCOL

➢ INTRODUCTION:

-As per ICH E6 Guideline, Trial protocols are documents that describe the objectives, design, methodology, statistical considerations, and aspects related to the organization of clinical trials.

- It provides the background and rationale for conducting a study, highlighting specific research questions that are addressed, and taking into consideration ethical issues.

- It must meet a standard that adheres to the principles of Good Clinical Practice and is used to obtain ethics approval by local Ethics Committees or Institutional Review Boards.

➢ WHO READ PROTOCOL?

The protocol language/ content should be understood by

- Other physicians
- Nurses/CRAS (Clinical Research Associates)
- IRB (Investigational review board) members
- Scientific reviewers
- IC (Informed Consent) for a layperson

➢ PREPARATION OF PROTOCOL:

➢ It needs approval from Ethical committees & Health authorities (before the commencement of the Clinical Trail) to ensure that Protocol follows prescribed guidelines and Applicable regulatory requirements.

➢ The poorly designed protocol can lead to

- Rewriting or modification of the protocol.
- Misinterpretation of study-related aspects which may lead to inappropriate data collection and wrong outcomes.
- Risks to patient safety
- Hold on to the whole trail.

➢ Mostly created by Sponsoring companies.

- Clinical Trial Protocol is **unique** for each clinical study. Hence, it is **difficult to use one standardized protocol for all studies.**

- However, certain common sections and information are contained in all protocols.

1. Title Page (General Information)
2. Background Information
3. Objectives/Purpose
4. Study Design
5. Selection and Exclusion of Subjects
6. Treatment of Subjects
7. Assessment of Efficacy
8. Assessment of Safety
9. Adverse Events
10. Discontinuation of the Study
11. Statistics
12. Quality Control and Assurance
13. Ethics
14. Data Handling and Record
15. Publication Policy
16. Project Timetable/ Flow Chart
17. Reference
18. Supplements/ Appendices

Title Page

- Title page introduces the document, its title, precise number, sponsor, and author to the reader.
- Protocol identifying number and date. Any amendment should also bear the amendment number and date.
- The protocol number must clearly indicate the version number, whether it is final or draft, and the date of this version.

Background Information & Rationale

- All protocols require a section detailing the scientific rationale for a protocol and the justification in the medical and scientific literature for the hypothesis being proposed.

- The introductory section should be organized in a logical, sequential flow.

Objective

- Objectives should be stated clearly as hypotheses to be tested.
- Each objective should have a corresponding discussion in the statistical section.

Study Design

- The study design section of the protocol should contain a stepwise description of all procedures required by the study.
- A good study design section includes sufficient information for the participating site.
- Parts of the study section may include:
  - Initial evaluations
  - Screening tests
  - Required lab tests.
  - Details of treatment or procedures
  - Device specifications
  - Dose scheduling and modification
  - Calendars

Adverse Events/Safety

- Adverse effects and side effects are terms commonly associated with drugs.
- They are used by nurses and doctors to refer to undesirable effects of a medication on a patient.
- The Safety (or Adverse Events) section should include:
  - Detailed information for reporting adverse events, including reporting to the FDA and/or the sponsor.
  - Unblinding processes (if applicable)
  - Lists of expected adverse events.

Statistics

- The study objectives and study design elements in the statistical section should be described in the Objectives section.

- The descriptions and definitions of toxicities in the statistical section match those in the Safety/AE section.

Need of Protocol

- It required an element of the protocol (submitted for funding).
- It provides a detailed clinical trial plan which guides how the trial should be carried out.
- It also ensures each step is conducted, analyzed, and presented in a scientific and ethical manner.

➢ IMPORTANCE OF PROTOCOL

- helpful in maintaining compliance with applicable regulations and prescribed guidelines.
- helps in safeguarding the health of the research subjects.
- ensures all communications are done in a complete, proper, and timely manner to all stakeholders.
- helpful in understanding trials for proper execution.

➢ PROTOCOL AMENDMENTS

- is defined as Revision, Change, or Addition (addendum) to approved research protocol.
- Implantation and communication can be costly affairs.
- Can introduce challenges in data analysis and result production.
- There are 3 different types of Protocol amendments:

NEW PROTOCOL	CHANGE IN PROTOCOL	NEW INVESTIGATOR
• When a sponsor plans to conducy a study that is not covered by a protocol which already contained in their IND application	• When there are changes in exsisting protocol that significantly affect safety of subjects, scope of investigation, or scientific quality of the study	• When a new Investigator is added to carry out a previously submitted protocol

➢ PROTOCOL EXCEPTIONS, DEVIATION, AND VIOLATIONS:

Protocol exceptions- intentional deviations from the approved protocol

Protocol deviations- accidental or unintentional change and non-compliance with a protocol that does not increase risk or decrease benefit or significantly affect the subject's rights, safety, or welfare. and/or on the integrity of data

Protocol violations- include accidental or unintentional change and non-compliance with protocol; Violations generally increased risk or decrease benefit affect subject's rights safety, or welfare, or data integrity.