

Key Elements of a Clinical Research Protocol and Informed Consent

A Clinical Research Protocol is a formal design of an experiment. It is the plan submitted to an Institutional Review Board for review and to an agency for research support. The protocol includes a description of the research design to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

A Clinical Research Protocol should include the following:

1. **Protocol title and date**
2. **Name, address and phone number of the principal investigator and co-investigators, if applicable**
3. **Site(s) where the study will be performed**
4. **Sponsor of the study**
5. **Introduction:** Background-Rational-Literature Review: Describe the background, including human subjects or animal research studies, results and references that are relevant to the design and conduct of the study. Where new techniques or procedures are to be used, a description of preliminary or early work should be provided. If a FDA Investigational New Drug (IND) is to be used, animal data on the drug should be included. If a study is one for which a Clinical Investigator's Brochure (CIB) is provided, one copy of the CIB must be submitted to the IRB when the protocol is submitted for review. A summary of the relevant features of the CIB should be included in the protocol.
6. **Research Objectives and Hypothesis:** State the precise objectives of the study in the form of a hypothesis. The protocol should be designed to answer the questions posed by the objectives.
7. **Study Design and Research Methods:**
 - **Study Design:** Describe the involvement of human subjects including initial evaluation procedures and screening tests, phases, procedures, and sequence of the study as much as possible. Describe alternatives to experimental therapy, if they exist. Give detailed procedures for the treatment and dose adjustments. Describe the randomization procedure, if applicable. Address the experience of the investigators if procedures are to be performed for which the investigators have not been specifically credentialed. This section should also include some or all of the following:
 - **Primary and secondary endpoints**
 - **Design of the study (double-blind, placebo controlled, etc.)**
 - **Measures taken to minimize bias (randomization, blinding)**
 - **Study treatments or interventions**
 - **Expected duration of subject participation (what is done and when)**
 - **Stopping rules or discontinuation criteria**

- **Selection and Withdrawal of Subjects:**
 - Selection (Insert justification for use of special or vulnerable subject populations, if applicable)
 - Inclusion Criteria
 - Exclusions Criteria
 - Withdrawal Criteria: describe the types, frequency, duration of tests, admissions, outpatient visits and procedures that a research participant should expect during the protocol. Define stop points and criteria for withdrawing subjects from the study. In studies done with therapeutic intent, the protocol should clarify what the off-study criteria for “deterioration” or “inadequate control” are. The protocol should also clearly state that voluntary withdrawal from the protocol is always an option for the research participant.
- **Human Subject Protections:** Provisions for the protection of the subject’s privacy and confidentiality
- **Rationale for Subject Selection:** State the rationale for research subject selection based on a review of gender/ethnic/race categories at risk for the disease/condition being studied. Include justification for exclusions, if any. If the protocol involves subject enrollment at multiple sites, describe plans for ensuring appropriate IRB review and approval at each site.
 - **Include procedures for recruitment, including advertising, if applicable.**
- **Evaluation of Benefits, Risks and Discomforts:** Describe the potential benefits to subjects or to others that may reasonably be expected from the research. Describe any potential risks (physical, psychological, social, legal or other) and assess their likelihood. Describe provisions for managing subject adverse reactions. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects. Describe the procedures for protecting against or minimizing any potential risks, such as violations of confidentiality, and assess their likely effectiveness. Where appropriate, describe the risks associated with the collection, storage, and future use of samples or data. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to result.
- **Informed Consent and Assent Processes and Documents:** Describe the consent procedures to be followed, including the circumstances in which consent will be sought and obtained, who will

seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. Children are not legally empowered to give consent, but depending on their age, they may have the ability to give assent. Every protocol involving children should include a discussion of how assent will be obtained.

- **Documentation of informed consent** (who will obtain informed consent, provision for a witness as needed, signatures of the subject or the subject's representative, signature of investigator, signature of person obtaining consent, signature of witness, use of short form if needed, providing the subject a copy of the informed consent information). A "short form" states that the elements of informed consent have been presented orally to the subject. When a short form consent document is used, the IRB will review and approve the written summary of the full information to be presented orally to the subject. A witness is required to attest to the adequacy of the informed consent process and to the subject's voluntary consent.
 - **Compensation:** if applicable, specify what compensation clinical research subjects will receive. Compensation may be provided for their time and inconvenience, and for their travel and escort needs while participating in the protocol.
 - **Efficacy Assessment:** Ensuring optimal efficacy is an important facet of patient safety during the conduct of a clinical trial, if, by "safety," we mean the anticipation, prevention and assessment of any event that can have an unfavorable impact of the enrolled patients.
 - **Safety Assessment,** including recording adverse events
 - **Statistical Analysis:** Delineate the precise outcomes to be measured and analyzed. Have a data collection tool that you will use for the statistical analysis. Describe how these results will be measured and statistically analyzed. Delineate methods used to estimate the required number of subjects. Describe power calculations if the study involves comparisons. This section should also include some or all of the following:
 - **Statistical methods including interim analysis if appropriate**
 - **Number of subjects to be enrolled**
 - **Rationale for choice of sample size (power calculation and clinical justification)**
 - **Level of significance to be used**
 - **Criteria for terminating the study**
 - **Procedures for reporting deviations from the original plan**
 - **Selection of subjects for inclusion in the analysis**
8. **Anticipated Results and Potential Pitfalls**
9. **Discussion of Next Steps**
10. **Appendices:** Supplemental material of documents such as flow diagrams or work-up tables may be added to the protocol. A properly constructed flow diagram can greatly clarify complex interactions.

11. **References:** References should be used for any point that can be attributed to a specific source. They should be sequentially numbered throughout the protocol.