I. **Purpose**

To ensure study site staff adequately review clinical trial protocol. The SOP may also be used as a guide for writing or review of investigator-initiated clinical trial protocols.

II. **Other Related Procedures**

SOP P3: Review of Protocol Amendments
SOP P12: Ethics Committee/Institutional Review Board Application and Communications

III. **Background**

N/A

IV. **Procedures**

A clinical trial protocol is a document that describes the objective(s), endpoint(s), design, methodology, study procedures, statistical considerations and organization of a trial. It also states the background and rationale of the trial.

The information listed below is the required contents of a trial protocol according to ICH GCP E6 Guideline. Some of the information regarding the investigational product may also be contained in other protocol referenced documents, such as an investigator’s brochure.

1. **General information**

   a) Check the title of the protocol and identify the protocol number and date.

   b) Ensure the name and address of the sponsor and monitor (if other than sponsor) appear somewhere on the protocol. It is usually on the title page or in appendix.

   c) Identify the name and title of the person(s) who are authorized to sign the protocol and the protocol amendments.

   d) Check that the name, title, address and telephone number(s) of the sponsor’s medical expert (or dentist when appropriate) for the trial is documented on the protocol.
e) Check that the protocol also includes the name and title of the investigator(s) responsible for conducting the trial, and the address and telephone number(s) of the trial site.

f) In addition to the above, ensure that the name, title, address and telephone number(s) of the qualified physician (or dentist, if applicable) who is responsible for all trial-site related medical decisions (if other than Investigator) is clearly stated.

g) If clinical laboratories are used, ensure that the name and address of the laboratory and any other medical and/or technical department(s) and/or institutions involved in the trial are identified.

2. **Background Information**

   a) Identify the name and description of the investigational product(s) from the protocol.

   b) Read the summary of the findings from non-clinical studies that are potentially clinically significant and relevant to the trial.

   c) Review the summary of the known and potential risks and benefits, if any, to human subjects.

   d) Review at the description of and justification for the route of administration, dosage, dosage regimen and treatment period(s).

   e) Check to see if there is a statement that the trial will be conducted in compliance with the protocol, ICH GCP, Declaration of Helsinki and the applicable regulatory requirement(s).

   f) Identify the description of the population to be studied.

   g) Briefly review the references to literature and data that are relevant to the trial, and provide background for the trial.

3. **Trial objectives and purpose**

   Review the detailed description of the objectives and the purposes of the trial.

4. **Trial design**

   The scientific integrity of the trial and the credibility of the data from it depend substantially on the trial design. Therefore, a description of the trial design should be reviewed in detail:

   a) Specific statement of the primary endpoint, and secondary endpoint(s) if any, to be measured during the trial.

   b) Description of the type/design of trial to be conducted e.g. double-blind, placebo controlled, parallel design and a schematic diagram of the trial design, procedures and stages.
c) Description of the measures taken to minimize/avoid bias, e.g., randomization and blinding.

d) Description of the trial treatment(s) and dosage regimen of the investigational product(s). Also, a description of the dosage form, packaging and labeling of the investigational product(s).

e) Expected duration of subject participation and description of the sequence and duration of all trial periods, including follow-up, if any.

f) Description of the “stopping rules” or “discontinuation criteria” for individual subjects, part of trial and entire trial.

g) Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.

h) Maintenance of trial treatment randomization codes and procedures for breaking codes.

i) Identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data.

5. Selection and withdrawal of subjects

a) Identify the subject inclusion criteria for the study.

b) Identify the subject exclusion criteria for the study.

c) Check the subject withdrawal criteria (i.e., terminating investigational product treatment) and procedures specifying:
   • When and how to withdraw subjects from the trial/investigational product treatment;
   • Type and timing of the data to be collected for withdrawn subjects;
   • Whether and how subjects are replaced; and
   • Follow-up for subjects withdrawn from the trial/investigational product treatment.

6. Treatment of subjects

a) Understand the treatments to be administered including the names of all products, dose, dosing schedule, route/mode of administration and treatment periods including follow-up period for subjects for each the investigational product treatment/trial group/arm of the trial. If the sponsor does not provide all treatments (e.g., if licensed product is to be used as a comparator), understand how this will be made available at the site.

b) Identify medications/treatments permitted (including rescue medication) and not permitted before and/or during the trial.
c) Check the procedures for monitoring subject compliance.

7. **Assessment of efficacy**

   a) Check the specification of the efficacy parameters.

   b) Understand the methods and timing for assessing, recording and analyzing the efficacy parameters.

8. **Assessment of safety**

   a) Check the specification of the safety parameters.

   b) Understand the methods and timing for assessing, recording and analyzing safety parameters.

   c) Identify the procedures for eliciting reports of and recording and reporting adverse events and inter-current illnesses.

   d) Ensure that the type and duration of the follow-up of subjects after serious adverse events is known.

9. **Statistics**

Read the following information regarding statistics in the protocol:

   a) Description of the statistical methods to be employed, including timing of any planned interim analysis.

   b) The number of subjects planned to be enrolled. In multicenter trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on or calculations of the power of the trial and clinical justification.

   c) The level of significance to be used.

   d) The particular criteria for the termination of the trial.

   e) The procedure for accounting for missing, unused and spurious data.

   f) Procedures for reporting any deviation(s) from the original statistical plan; any deviation(s) from the original statistical plan should be described and justified in the protocol and/or in the final report, as appropriate.

   g) The selection of subjects to be included in the analysis, e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects.
10. **Direct access to source data/documents**

Check if it is specified in the protocol or other written agreement that the Investigator/Institutions will permit trial-related monitoring, audits, institutional review board (IRB) review and regulatory inspections, providing direct access to source.

11. **Quality control and quality assurance**

Review the protocol to ensure that it includes plans for quality assurance and quality control, such as, site monitoring, audits, standard operating procedures for quality management.

12. **Ethics**

Check if the ethical considerations relating to the trial are specified. This section includes, but is not limited to, the guiding ethical principles being followed by the study, e.g., Declaration of Helsinki, ICH GCP, etc.

13. **Data handling**

Check if the type of data capture and data handling procedures to be used for the study is described.

14. **Finance and insurance**

Check the arrangement related to finance and insurance for the study. If the information is not stated in the protocol, this will normally be addressed in a separate agreement with the Investigator.

15. **Publication policy**

Check the publication policy stated in the protocol. If this is not documented in the protocol it should be addressed in a separate agreement.

16. **Supplements**

Review supplementary information usually presented as appendices of the protocol.

V. **References**


VI. **Appendix**

N/A