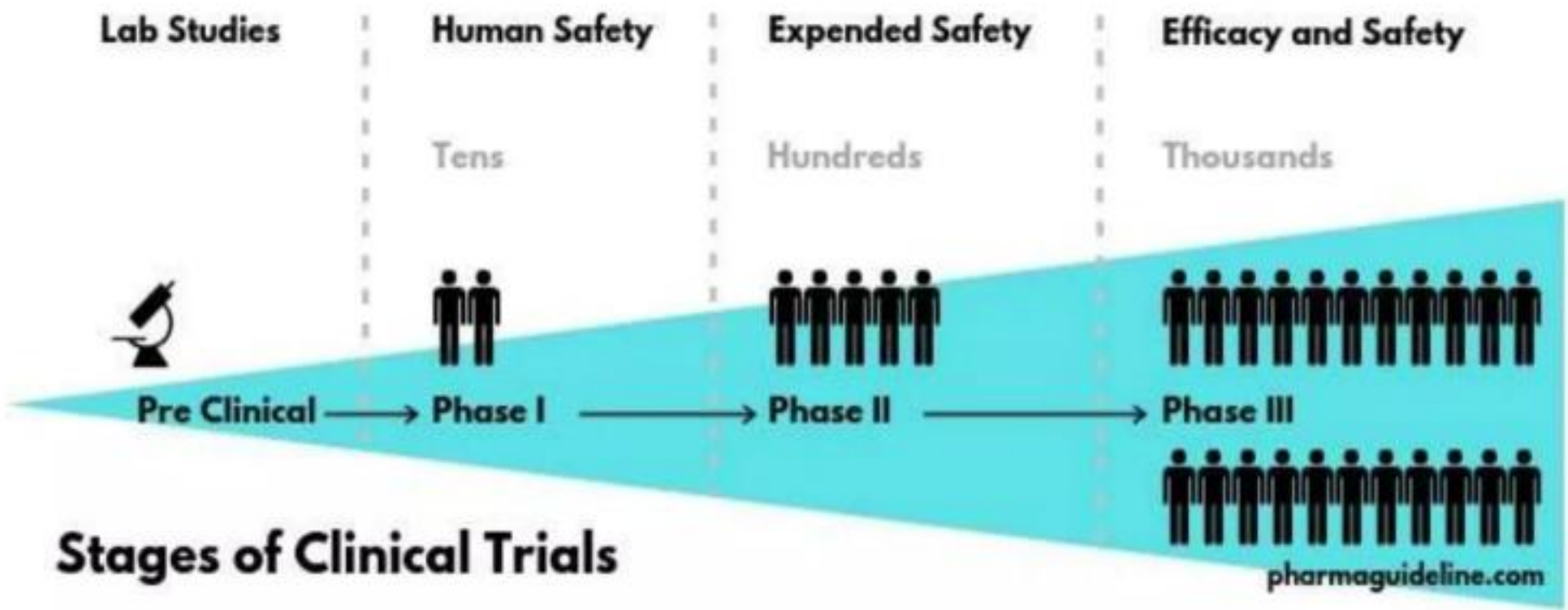
# DEVELOPING CLINICAL TRIALS PROTOCOL

# Definition:

- Clinical trial protocols are documents that describe the objectives, design, methodology, statistical considerations and aspects related to the organization of clinical trials.
- Clinical trial protocol means a written summary description of one or more clinical trials, which generally includes information on the objectives, design, methodology, statistical considerations and organization of the Clinical Trial (and including amendments to such description).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# Aims of Protocol

1. To raise the question to be researched and clarify its importance.
2. To collect existing knowledge and discuss the efforts of other researchers who have worked on the related questions (Literature review).
3. To formulate a hypothesis and objectives.
4. To clarify ethical considerations.
5. To suggest the methodology required for solving the question and achieving the objectives.
6. To discuss the requirements and limitations in achieving the objectives.

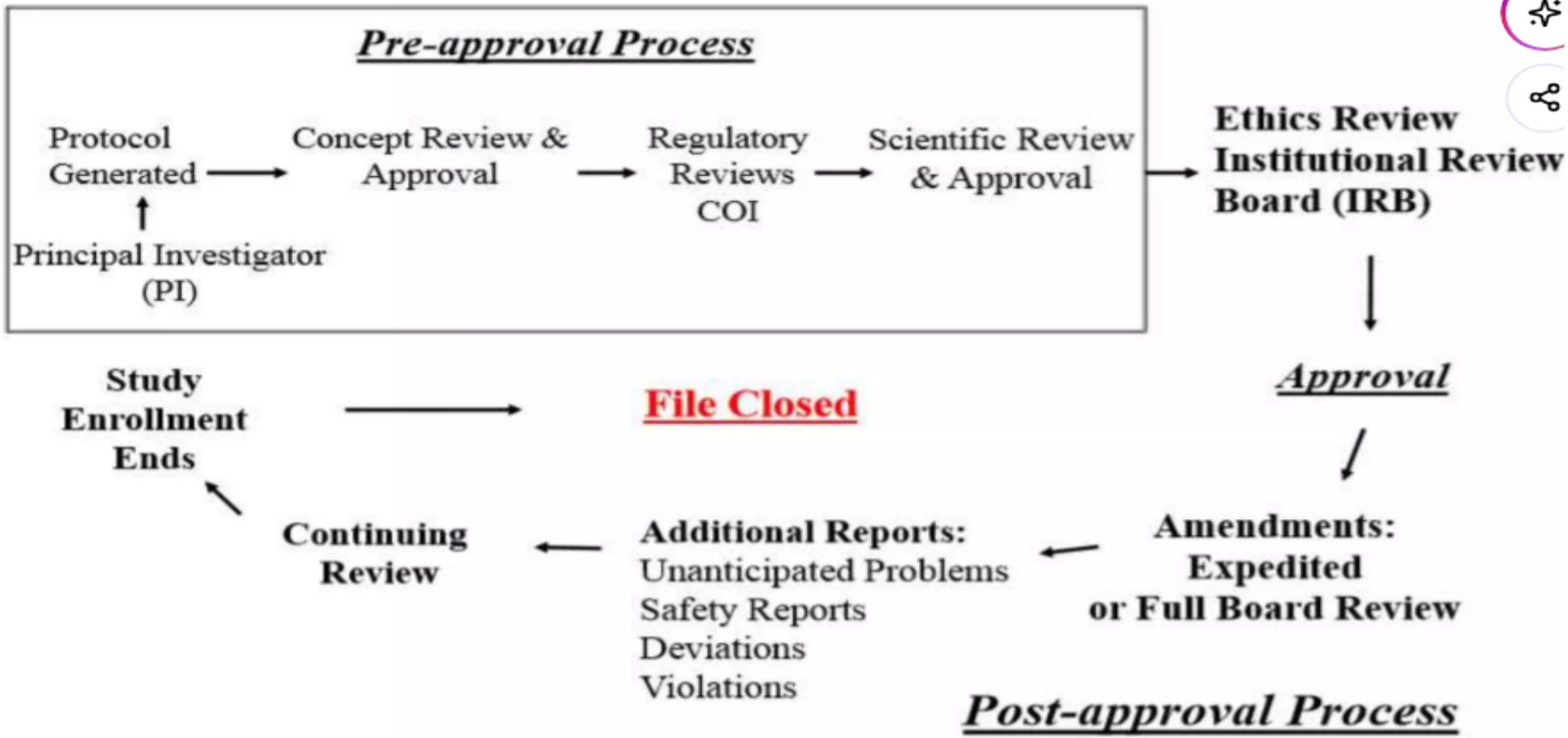
# Key benefits

- Allows the researcher to plan and review the project's steps.
- Serves as a guide throughout the research.
- Forces time and budget estimates.

# Protocol Review

- Clinical trials must be approved and monitored by an **Institutional Review Board** that ensures that the risks are negligible and are worth any potential benefits.
- The committee ensures that clinical trials are **ethical** and that the rights of all participants are protected.
- The board must initially approve and periodically review the research

# Protocol Life Cycle



# Protocol development:

❑Members involve in protocol development

- A chemist
- A pharmacologist/ toxicologist
- A medical monitors
- A data management person
- Potential investigators
- Capable program manager

# Objective and Purpose:

❑A detailed description of the major (primary) and minor (secondary and exploratory) objectives and the purpose of the trial.

# 1. General Information

- Protocol title, protocol identifying number, and date. Any amendment should also bear the amendment number and date.
- Name and address of the sponsor and monitor (if other than the sponsor).
- Name and title of the person authorized to sign the protocol and the protocol amendment for the sponsor.
- Name, title, address, and telephone number of the sponsor's medical expert for the trial.

- Name and title of the investigator who is responsible f conducting the trial, and the address and telephone number of the trial site.
- Name, title, address, and telephone number of the qualified physician who is responsible for all trial-site related medical decisions (if other than investigator).
- Name and address of the clinical laboratory and other medical and/or technical department and/or institutions involved in the trial.

# Title of the study

- Title of proposal should be accurate, short, concise, and identify
- **What** is the study about, **Who** are the targets, **Where** is the setting of the study and **When** it is launched, if applicable.
- It should make the main objective clear, convey the main purpose of the research and mention the target population. Carry maximum information about the topic in a few words; it is a good practice to keep the title to within 12-15 words.
- It should convey the idea about the area of research and what methods are going to be used in a compact, relevant, accurate, attractive, easy to understand, and informative way.

# Administrative details

The following administrative details and a protocol conten
summary should follow the title page:

- Contents page list of relevant sections and sub-sections with
  corresponding page number.
- Signature page is signed by senior members of the research
  team and dated to confirm that the version concerned has been
  approved by them.
- Contact details for the research team members listing postal, e-
  mail addresses and telephone numbers.

# 2. Background Information

- The background to the project should be concise and refer the subject straight forwardly.
- In writing the review, attention should be drawn to the positives, negatives and limitations of the studies quoted.
- Introduction is concluded by explaining how the present study will benefit the community.
- The literature review should logically lead to the statement of the aims of the proposed project and end with the aims and objectives of the study.
- The review should include the most recent publications in the field and the topic of the research is selected only after completing the literature review and finding some gaps in it.

- Introduction should briefly answer the importance of the top the gaps/lacunae in the literature, the purpose of the study and benefits for the society, from the study.
- The research question should be described precisely and concisely.
- It is going to be the basis of designing the project.
- The definition of the problem should be clear so that a reader can straight forwardly recognize the real meaning of it.

**CONTENTS:**

- Name and description of the investigational product.
- A summary of findings from nonclinical studies that potentially ha clinical significance and from clinical trials that are relevant to the trial.
- Summary of the known and potential risks and benefits, if any, to human subjects.
- Description of and justification for the route of administration, dosage, dosage regimen, and treatment period.
- A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement.
- Description of the population to be studied.
- References to literature and data that are relevant to the trial, and that provide background for the trial.

# 3. Trial Objective and Purpose

A detailed description of the objectives and the purpose of the trial.

The aims should be explicitly stated.

These should be confined to the intention of the project and they should arise from the literature review.

State the goal you need to achieve.

- The study aims or objectives emerge from the study questions, hypothesis. They are answers to what are the possible responses to the research question or hypothesis under analysis and measure.
- Aims should be logical and coherent, feasible, concise, realistic, considering local conditions, phrased to clearly meet the purpose of the study and related to what the specific research is intended to accomplish.

# 4. Trial Design

The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design.

A description of the trial design, should include:

- A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
- A description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
- A description of the measures taken to minimize/avoid bias, including:
  - Randomization.
  - Blinding.

- A description of the trial treatment(s) and the dosage a dosage regimen of the investigational product(s).
  - Also include a description of the dosage form, packaging, and labelling of the investigational product(s).
- The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

- Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Maintenance of trial treatment randomization codes and procedures for breaking codes.
- The 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

- Subject inclusion criteria.
- Subject exclusion criteria.
- Subject withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) and procedures specifying:
  - When and how to withdraw subjects from the trial/ investigational product treatment.
  - The type and timing of the data to be collected for withdrawn subjects.
  - Whether and how subjects are to be replaced.
  - The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

# 6. Treatment of Subjects

- The treatment to be administered, including the name of all the product, the dose, the dosing schedule, the route/mode of administration, and the treatment period, including the follow-up period for subjects for each investigational product treatment/trial treatment group/arm of the trial.
- Medication/treatment permitted (including rescue medication) and not permitted before and/or during the trial.
- Procedures for monitoring subject compliance.

# Sample size

- Sample size calculation is recommended for economical and ethical reasons.
- The calculation of the sample size must be explained including the power of the sample.
- The sampling technique should be mentioned, e.g., randomization that will be used in order to obtain a representative sample for your target population.
- Each step involved in the recruitment of the study subjects should be described according to the selection criteria (inclusion and exclusion criteria).
- "Informed consent" should be mentioned (Permission granted in full knowledge of the possible consequences).

# Proposed intervention

- Full description of proposed intervention should be given. Her all the activities and actions should be recorded and thoroughly explained in their order of occurrence.
  - When using drugs, both scientific and brand name should be mentioned followed by the name of the manufacturing company, city, and country.
  - Drug route, dosage, frequency of administration, and total duration of treatment with the drug should be mentioned.
  - When using apparatus its name should be given followed by the name of the manufacturer, city and country.

# Data collection methods, instruments used:

Data collection tools are:

- Retrospective data (medical records)
- Questionnaires
- Interviews (Structured, Semi-Structured)
- Laboratory test (literature or personal knowledge should be referenced, if established test, or description should be provided in details, if not established)
- Clinical examinations
- Description of instruments, tools used for data collection, as well as the methods used to test the validity and reliability of the instrument should be provided .

# 7. Assessment of Efficacy

- Specification of the efficacy parameters.
- Methods and timing for assessing, recording, and analyzing of efficacy parameters.

# 8. Assessment of Safety

- Specification of safety parameters.
- The methods and timing for assessing, recording, and analyzing safety parameters.
- Procedures for eliciting reports of and for recording and reporting adverse event and inter-current illnesses.
- The type and duration of the follow-up of subjects after adverse events.

# 9. Statistics

- A description of the statistical methods to be employed, including timing of any planned interim analysis.
- The number of subjects planned to be enrolled. In multi-centre 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.
- The level of significance to be used.

- Criteria for the termination of the trial.
- Procedure for accounting for missing, unused, and spurious data.
- 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 protocol and/or in the final report, as appropriate).
- The selection of subjects to be included in the analyses (e.g. all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).

# Data Management and Analysis Plan

- This section should be written following statistical advice fro a statistician.
- The analysis plan and which statistical tests will be used to check the significance to the research question/hypothesis with appropriate references should be described.
- Names of variables that will be used in the analyses and the name of statistical analysis that will be performed to assess the outcome should be listed.
- If computer programs are to be applied, it is important to mention the software used and its version.

# 10. Direct Access to Source Data/ Documents

- The sponsor should ensure that it is specified in the protocol other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

# 11. Ethical Consideration

Ethical considerations (issues for ethical Review and Approvals):

- It should indicate whether the procedures to be followed are in accord with the Declaration of Helsinki.
- In any case, study should not start unless approval from ethics committee is received

The following points should be explained:

- The benefits and risks forthe subjects involved.
- The physical, social and psychological implications of t research.
- Details of the information to be given to the study patients including alternative treatments/approaches.
- Information should be provided on the free informed consent of the participants.
  - Information form should contain: Justification for research, outline of study, risks, confidentiality, and voluntary participation should be told patients about the freedom to withdraw from the study whenever they wish to. Confidentiality indicates how the personal information obtained from the patient will be kept secret (Data safety).