**Clinical Trial Protocol Template**

**Version Feb 2025**

*Adapted from NIH protocol template and ICH Guidelines*

**Guidance for this Protocol Template**

This protocol template is to be used for clinical trials that is, research in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. For observational studies use this template instead - [Observational Study Protocol Template](https://www.uth.edu/ctrc/documents/ProtocolTemplateObservational-Feb2025.docx).

Do not delete any sections of the protocol template as all sections are important for all types of research studies.

This template contains two types of text: instructions/explanatory text and example text.

***Instruction/explanatory text*** *is indicated by italics and in blue font and should be deleted prior to finalizing the protocol. This text provides information on the content that should be included in the protocol.*

[**EXAMPLE text** is included to further aid in protocol writing and should be modified to suit the protocol and it may be deleted if it is not relevant. Example text is indicated by the word “EXAMPLE” and blue font within brackets*.*]

<Locations to enter study-specific text is indicated by black font and within angle brackets. Delete any instructional text and enter study-specific language.>

**Delete all language in blue/brackets [ ]/angle brackets < >/italics, and enter language specific to your research study.**

Version control is important to track protocol development, revisions, and amendments. It is also necessary to ensure that the most recently updated and IRB approved version of a protocol is used by all staff conducting the study. **With each revision, the version number and date located in the header of each page should be updated**. When making changes to an approved and “final” protocol, the protocol amendment history should be maintained.

If you would like to number the headings – click on Design on the Word tool bar and choose the design with numbers.

Do not forget to update the table of contents – when you have completed all the sections- click on the Table of Contents and click on Update Table, Update Entire Table.

Contact clinicaltrials@uth.tmc.edu if you have any questions about this template.

**PROTOCOL TITLE**

Short Title: <short title>

Protocol Number: <protocol number >

Protocol Version: <Insert Version Number Here>

Protocol Version Date: <Insert Version Date Here>

Funded by: <funding agency name>

<IND/IDE> Sponsor: <Sponsor name, if applicable>

IND/IDE Number: <IND/IDE number>

NCT Number: <NCT number>

Principal Investigator: <Name, Title, Institution>

Collaborators: <Name, Title, Institution >

< Name, Title, Institution >

Study Statistician: <Name, Title, Institution>

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# BACKGROUND AND RATIONALE

Briefly sketch the background to the current proposal, critically evaluating the existing knowledge and specifically identify the gaps that the project is intended to fill.General Introduction

Give a brief description of the drug/device to be studied. Their mechanism of action, whether currently in use and approved for use.

## Rationale and justification for the Study

Include a description and justification for the route of administration, dosage, dosage regimen, intervention periods, and selection of study population. Include a statement of hypothesis.

## Background

Include summary of findings from summary of relevant clinical research and any history of human use or exposure to the study intervention, including use in other countries, and clinical pharmacology studies. Include nonclinical in vitro or in vivo studies that have potential clinical significance. Discussion of important literature and data that are relevant to the trial and that provide background for the trial (list references at the end)

Applicable clinical, epidemiological, or public health background or context of the clinical trial/ Importance of the clinical trial and any relevant treatment issues or controversies.

## Risk Benefit Assessment

#### Potential Risks

Include a discussion of known potential risks from either clinical or nonclinical studies. If a package insert or device labeling from a licensed or approved product is available, it should be used as the primary source of risk information. If the product is investigational, the IB should be the primary source of the risk information. In addition, relevant published literature can also provide relevant risk information. If the risk profile cannot be described from the package insert, device labeling, or the IB, the risk information discussion will result from published literature and should be included and referenced appropriately.

Describe any physical, psychological, social, legal, economic, or any other risks to participants by participating in the study that the Principal Investigator (PI) foresees, addressing immediate risks, and long-range risks.

If risk is related to proposed procedures included in the protocol, describe alternative procedures that have been considered and explain why alternative procedures are not included

#### Potential Benefits

Include a discussion of known potential benefits from either clinical or nonclinical studies. If a package insert or device labeling from a licensed or approved product is available, it should be used as the primary source of potential benefit information. If the product is investigational, the IB should be the primary source of the potential benefit information. In addition, relevant published literature can also provide potential relevant benefit information. If the potential benefit cannot be described from the package insert, device labeling, or the IB, the potential benefit information discussion will result from published literature and should be included and referenced appropriately.

Describe any physical, psychological, social, legal, or any other potential benefits to individual participants or society in general, as a result of participating in the study, addressing immediate potential benefits and long-range potential benefits.

# HYPOTHESIS, OBJECTIVES, and OUTCOME MEASURES

## Hypothesis

Concisely state the hypothesis to be tested. The study hypothesis must relate to the rationale and should be consistent with the objectives described.

## Objectives and Outcome Measures

Note that objectives are distinct from outcome measures, definitions below.

*In the table below, state Objectives. Study objectives are concise statements of the scientific questions that the study is designed to answer. Express each objective as a statement of purpose (e.g., to assess, to determine, to compare, to evaluate) and include the general purpose (e.g., efficacy, effectiveness, safety) and/or specific purpose (e.g., dose-response, superiority to placebo, effect of an intervention on disease incidence, disease severity, or health behavior).*

*Also, in the table below state Outcome Measures (also known as “Endpoints”), listing a timepoint for each outcome measure. An outcome measure should be clearly linked to achieving the corresponding objective. Outcome measures are specific measurements or observations used to assess the effect of the study intervention (for example, specific laboratory tests that define safety or efficacy, clinical assessments of disease status, assessments of psychological characteristics, patient reported outcomes, etc.). A general formula for an outcome measure is: [thing being measured] as assessed by [type of assessment] at [timepoint(s)], and see this link for examples of outcome measures.>*

| **OBJECTIVES** | **OUTCOME MEASURES (a.k.a. ENDPOINTS)Include TIMEPOINTS for each Outcome Measure** |
| --- | --- |
| **Primary** |  |
| The primary objective is the main question. This objective generally drives statistical planning for the trial (e.g., calculation of the sample size to provide the appropriate power for statistical testing).[EXAMPLE: To compare the efficacy of drug A and drug B for treatment of pain] | The primary outcome measure(s) should be clearly specified, and a timepoint should be listed for each primary outcome measure.The primary outcome measure(s) is the basis for concluding that the study met its objective (e.g., “the study wins”), and the outcome measure(s)’s role in the analysis and interpretation of study results should be defined in the statistical analysis section.In a trial designed to establish efficacy, a primary outcome measure should measure a clinically meaningful therapeutic effect or should have demonstrated ability to predict clinical benefit.[EXAMPLE: Pain as assessed by a Visual Analogue Scale (VAS) at baseline and day 30] |
| **Secondary** |  |
| The secondary objective(s) are goals that will provide further information on the use of the intervention. | Secondary outcome measure(s) should be clearly specified, and a timepoint should be listed for each secondary outcome measure).Secondary outcome measure(s) are those that may provide supportive information about the study intervention’s effect on the primary outcome measure or demonstrate additional effects on the disease or condition.  |
| **Tertiary/Exploratory**  |  |
| Tertiary/exploratory objective(s) serve as a basis for explaining or supporting findings of primary analyses and for suggesting further hypotheses for later research. | If applicable, specify exploratory outcome measure(s). Exploratory outcome measure(s) may include clinically important events that are expected to occur too infrequently to show a treatment effect or endpoints that for other reasons are thought to be less likely to show an effect but are included to explore new hypotheses. |

# STUDY DESIGN

## Overall Study Design.

A description of the type/design of trial to be conducted (e.g., randomized, placebo-controlled, double-blinded, parallel design, open-label, dose escalation, dose-ranging, adaptive, cluster randomized, group sequential, multi-regional, superiority or non-inferiority design).

A description of the measures taken to minimize/avoid bias, such as randomization and blinding.

A description of the trial treatment(s). The number of study groups/arms and study intervention duration. 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” and “dose adjustment” or “dose interruption” for individual participants, parts of trial and entire trial.

## Scientific Rationale for Study Design

Describe the rationale for the type and selection of control (e.g. placebo, active drug, dose-response, historical) and study design (e.g., non-inferiority as opposed to superiority). Discuss known or potential problems associated with the control group chosen in light of the specific disease and intervention(s) being studied.

## Rationale for Dose (for drug studies)

Provide a justification for the route of administration, planned maximum dosage, and dosing regimen, including starting dose, of the study intervention(s) and control product(s).

# STUDY POPULATION

## List the number of subjects to be enrolled.

Indicate from where the study population will be drawn from. State if there are any subject restrictions based on race of the subject. Justify the exclusion of women, children or minorities if the study tends to exclude them in context of the study design.

## Eligibility Criteria

Discuss evaluations/procedures necessary to assess or confirm whether a subject meets the eligibility criteria and may be enrolled. Discuss the sequence of events that should occur during recruitment.

## Inclusion Criteria

Provide a statement that subject must meet all of the inclusion criteria to participate in this study and list each criterion.

* The disease or disorder under study, and how it is to be documented i.e. diagnostic methods, criteria for classification etc.
* For populations with cancer or pre cancer please include requirements for histological confirmation of diagnosis, time for diagnosis and disease status at entry.
* Demographic characteristics (e.g. gender, age). Please explain age restrictions if any
* Ability to provide informed consent
* If men and women of reproducible age are enrolled, provide details of allowable contraception methods for the trial.

## Exclusion Criteria

Provide a statement that all subjects meeting any of the exclusion criteria at baseline will be excluded from participation and then list the criterion.

Examples include the following: medical condition or laboratory finding that precludes participation, recent (with time frame) illness that precludes or delays participation, pregnancy or lactation, characteristics of household or close contacts (e.g. household contacts who are immunocompromised), known allergic reactions to components of study product(s), treatment with another investigational drug (with time frame), history of drug/alcohol abuse, disallowed concomitant medications etc.

## Screening

Participants who are consented to participate in the clinical trial, who do not meet one or more criteria required for participation in the trial during the screening procedures, are considered screen failures. Indicate how screen failures will be handled in the trial, including conditions and criteria upon which re-screening is acceptable, when applicable. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, including demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

## Withdrawal Criteria

List possible reasons for discontinuation of study intervention/product in this section, e.g. development of laboratory toxicities, study closure due to DSMB review etc.

## Subject Replacement

State whether subjects who drop out will be replaced.

## Recruitment Plan

Identify general strategies for participant recruitment and retention. This section may refer to a separate detailed recruitment and retention plan.

# METHODS AND ASSESSMENTS

Discuss the procedures to be used to accomplish the specific aims of the project. Will any of the procedures be placed on an electronic medium (to include audiotape, film / video, etc?) If yes, what is the medium? Explain how the recorded information will be used? How long will it be retained and/or disposed of?

Information outlined in this section should be consistent with the information in the schedule of study visits and procedures.

## Randomization and Blinding

This section should describe randomization and blinding procedures (if applicable to the study design). Include a description or a table that describes how study subjects will be assigned to the study groups. The timing and procedures for planned and unplanned breaking of randomization codes should be included. Include statement when unmasking may occur and who may unmask.

## Contraception and Pregnancy Testing

For females of childbearing age included in the trial describe methods of pregnancy testing and contraception if pregnancy is to be avoided during the trial.

## Study Visits and Procedures

Provide a brief outline of the all the study visits, procedures to be done during the study, follow up after the study and discontinuation visit. Include discussion of evaluations/procedures required to assess or confirm study outcome measures and study evaluations. Discuss the sequence of events that should occur during the visit, if applicable. Include, as applicable, counselling, medications, assessment of adverse events etc.

Screening Visits and Procedures - Include only those evaluations necessary to assess whether a subject meets recruitment criteria. Discuss the sequence of events that should occur during screening and the decision points regarding eligibility. List the timeframe prior to recruitment within which screening tests and evaluations must be done (e.g. within 28 days prior to recruitment). Describe all procedures that must be completed before the study begins

Study Visits and Procedures- Describe all the visits and procedures that must be performed during the study intervention phase.

Final Study Visit***:*** Define when the final study visit should occur and any special procedures / evaluations or instructions to the subject.

Post Study Follow up and Procedures (if applicable) - Describe any follow up procedures that may occur after end of study.

Discontinuation Visit and Procedures - Specify which of the evaluations required for the final study visit should be done if withdrawal occurs. Subjects may withdraw voluntarily from participation in the study at any time. Subjects may also withdraw voluntarily from receiving the study intervention for any reason. Clearly differentiate between what evaluations are to be done in each of these circumstances.

If voluntary withdrawal occurs, the subject should be asked to continue scheduled evaluations, complete an end of study evaluation, and be given appropriate care under medical supervision until the symptoms of any adverse event resolve or the subject’s condition becomes stable. Describe efforts to continue follow - up, especially for safety outcome measures.

# STUDY INTERVENTION

If multiple products are to be evaluated in the study, the following sections should be repeated for each product and the sections should be renumbered accordingly. Describe placebo or control product.

## Trial Product (s) or Intervention(s)

Please provide background information on the trial product, its safety issues and duration of exposure. For drugs, also include information on dosage.

Information about the drugs could also be obtained from the I.B or the package insert. Please include I.B or package insert.

## Trial Product Storage and Accountability

Describe product’s storage needs. Include storage requirements and stability (temperature, humidity, security and container).

## Treatment

Study Drug Formulations- Describe in what form the study drug will be dispensed to the subjects.

Study Drug Administration - Describe the drug regimen to be used. State any special precautions or warnings relevant for the study drug administration.

Specific Restrictions / Requirements - Indicate any limitations on medications, herbs, vitamins and mineral supplements (other than study agents) while participating in the study. Include time periods if applicable.

Blinding - If applicable describe the measures that will be undertaken to blind the study participants and/or study staff from participant treatment assignments. State when unblinding is expected and if/when participants will be told their assignments. [Note plans to handle early unblinding to protect participant safety, if any.]

Concomitant therapy - All medications (prescription and over the counter), vitamin and mineral supplements, and / or herbs taken by the participant should be documented.

# STUDY ASSESSMENTS AND PROCEDURES

## Efficacy Assessments

List and describe all study procedures and evaluations to be done as part of the study to support the determination of efficacy, as per the primary and secondary objectives outlined in this protocol. Discuss the sequence of events that should occur during the screening process and any decision points regarding participant eligibility. Include the time frame prior to enrolment within which screening procedures/ evaluations must be performed (e.g., within 28 days prior to enrolment). If a separate screening protocol is developed, describe how the screening protocol will be used to identify participants for this study. In addition, discuss any special conditions that must be achieved during the enrolment and/or initial administration of study intervention. Include the procedures for administering the study intervention and follow-up procedures after administration (e.g., assessment of vital signs), as well as any specifics about subsequent follow-up visits, and unscheduled visits. Also, note if a specifically qualified person (e.g., physician, psychologist) should be performing any of the assessments. Include any definitions used to characterize outcomes (e.g., criteria for determining occurrence of acute myocardial infarction, characterization of a stroke as thrombotic or hemorrhagic, distinction between transient ischemic attack and stroke), should be explained fully.

## Safety and Other Assessments

List and describe all study procedures and evaluations to be done as part of the study to monitor safety and support the understanding of the study intervention’s safety or that are done for other purposes (e.g., screening, eligibility, enrollment).

Discuss the sequence of events that should occur during the screening process and any decision points regarding participant eligibility. Include the time frame prior to enrollment within which screening procedures/ evaluations must be performed (e.g., within 28 days prior to enrollment). If a separate screening protocol is developed, describe how the screening protocol will be used to identify participants for this study. In addition, discuss any special conditions that must be achieved during the enrollment and/or initial administration of study intervention.

Note that the protocol should provide a high-level discussion of all procedures. In addition, note where approaches to decrease variability, such as centralized laboratory assessments, are being employed. The specific timing of procedures/evaluations to be done at each study visit are captured in **Schedule of Activities** and the time points of these procedures do not need to be included here. In addition, indicate where appropriate, that procedures/evaluations will be performed by qualified personnel.

## Adverse Events and Serious Adverse Events

#### Definitions:

***Adverse Event*** *-* Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related.

***Serious Adverse Event*** – An adverse event (AE) or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

#### Classification of Adverse Events

***Severity of Event*** - The following guidelines will be used to describe severity.

* + - Mild – Events require minimal or no treatment and do not interfere with the participant’s daily activities.
		- Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
		- Severe – Events interrupt a participant’s usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term “severe” does not necessarily equate to “serious”.

***Relationship to Study Intervention***

* Related – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
* Not Related – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

***Expectedness***

* Expected - An AE or suspected adverse reaction is considered "unexpected" if it is not listed in the IB, package insert, or device labeling or is not listed at the specificity or severity that has been observed; or, if an IB is not required or available, is not consistent with the risk information described in the protocol, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the IB or package insert referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the IB or package insert listed only cerebral vascular accidents.
* Unexpected – Refers to AEs that are not specifically mentioned as occurring with the particular study intervention under investigation.

#### Reporting of Adverse Events and Serious Adverse Events

The PI will immediately assess whether each adverse event or serious adverse event meets the criteria for reporting to the IRB. The PI will immediately report to the sponsor any serious adverse events whether or not considered study intervention related, including those listed in the protocol or investigator brochure and must include an assessment of whether there is a reasonable possibility that the study intervention caused the event. Study endpoints that are serious adverse events (e.g., all-cause mortality) must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the study intervention and the event (e.g., death from anaphylaxis). In that case, the investigator must immediately report the event to the sponsor.

## Data and Safety Monitoring

Include details on the Data Safety Monitoring Plan (DSMP) for the research study. Discuss the plans in place to ensure the safety and well being of subjects, and integrity of data collected or reference a separate data and safety monitoring charter.

# STATISTICAL ANALYSIS

Provide details on sample size calculations.

For descriptive statistics, describe how categorical and continuous data will be presented (e.g., percentages, means with standard deviations, median, range).

For inferential tests, indicate the p-value and confidence intervals for statistical significance (Type I error) and whether one or two-tailed.

Indicate whether covariates will be pre-specified in the sections below or in a Statistical Analysis Plan.

State whether checks of assumptions (e.g., normality) underlying statistical procedures will be performed and whether any corrective procedures will be applied (e.g., transformation or nonparametric tests).

Efficacy analysis - For each primary efficacy and secondary efficacy endpoint define the measurement or observation and describe how it is calculated, describe the statistical procedure that will be used.

Safety analysis – For each safety end point describe how safety endpoints will be analysed (e.g., as summary statistics during treatment and/or as change scores from baselines such as shift tables).

Describe the types of statistical interim analyses and stopping guidelines (if any) that are proposed, including their timing.

# ETHICAL CONSIDERATIONS

Describe the procedures for obtaining and documenting informed consent of study subjects. Make provision for special populations e.g. non English speakers, children, illiterate or non-writing individuals, and vulnerable populations. In obtaining and documenting informed consent, the investigator should comply with GCP guidelines and to the ethical principals that have their origin in the Declaration of Helsinki. Please specify when consent will be taken and who will take consent.

Identify different consent forms that are needed for the study(e.g. screening, study participation, HIV screening, future use specimens, assent from minors)

This protocol and the associated informed consent documents must be submitted to the IRB for review and approval.

Include procedures for maintaining subject confidentiality, any special data security requirements, and record retention. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to the participating subjects.

# PUBLICATIONS

State publication policy for study findings.

# DOCUMENT RETENTION

Records for all participants, including CRFs, all source documentation (containing evidence to study eligibility, history and physical findings, laboratory data, results of consultations, etc.) as well as IRB records and other regulatory documentation should be retained by the PI in a secure storage facility. The records should be accessible for inspection and copying by authorized authorities. Describe the retention plans for study documents.

# REFERENCES

List references.