**STUDY PROTOCOL**

|  |  |
| --- | --- |
| **PROTOCOL NUMBER:** | |
| <INSERT PROTOCOL NUMBER HERE> | |
|  | |
| **PROTOCOL TITLE:** | |
| <INSERT PROTOCOL TITLE HERE> | |
|  | |
| **VERSION:** | <Insert Version Number Here> |
| **DATE:** | <Insert Version Date Here> |
|  | |
| **CORRESPONDING PRINCIPAL INVESTIGATOR:** | |
| <Insert PI Name, Designation, Institution Here> | |
|  | |
| **SITE PRINCIPAL INVESTIGATOR:** | |
| <Insert PI Name, Designation, Institution Here> | |
| <Insert PI Name, Designation, Institution Here> | |
|  | |
| **SITE:** | |
| <Insert Site Name and Address Here> | |
| <Insert Site Name and Address Here> | |
| <Insert Site Name and Address Here> | |
|  | |
| **COLLABORATORS:** | |
| <Insert Collaborator Name, Designation, Institution > | |
| <Insert Collaborator Name, Designation, Institution > | |
| <Insert Collaborator Name, Designation, Institution > | |
| <Insert Collaborator Name, Designation, Institution > | |

**GENERAL INFORMATION**

|  |
| --- |
| **Name and address of the sponsor of the study:** |
| *If you are not seeking funding for this study, delete this section.* |
| **Name and address of the person authorized to sign the protocol and amendments:** |
| *Write the names of all the members of the study team who are authorized to sign protocol and amendments.* |
| **Name and address of study monitor:** |
| *If your study does not have a plan for monitoring, state that here.* |
| **Name, title, address and telephone number(s) of the medical expert for the trial** |
|  |
| **Name and title of the investigator(s) and sub-investigators responsible for the trial with address and phone number(s)** |
|  |
| **Name and addresses of the clinical laboratories and/or other institutions involved in the trial** |
|  |

**TABLE OF CONTENTS**

[1. BACKGROUND AND RATIONALE 5](#_Toc240699539)

[1.1. General Introduction 5](#_Toc240699540)

[1.2. Rationale and justification for the Study 5](#_Toc240699541)

[a. Rationale for the Study Purpose 5](#_Toc240699542)

[b. Rationale for Doses Selected 5](#_Toc240699543)

[c. Rationale for Study Population 5](#_Toc240699544)

[d. Rationale for Study Design 5](#_Toc240699545)

[2. HYPOTHESIS AND OBJECTIVES 5](#_Toc240699546)

[2.1. Hypothesis 5](#_Toc240699547)

[2.4. Potential Risks and benefits: 6](#_Toc240699548)

[a. End Points - Efficacy 6](#_Toc240699549)

[b. End Points - Safety 6](#_Toc240699550)

[3.1. List the number of subjects to be enrolled. 6](#_Toc240699551)

[3.2. Criteria for Recruitment 6](#_Toc240699552)

[3.3. Inclusion Criteria 6](#_Toc240699553)

[3.4. Exclusion Criteria 6](#_Toc240699554)

[3.5. Withdrawal Criteria 7](#_Toc240699555)

[3.6. Subject Replacement 7](#_Toc240699556)

[4. TRIAL SCHEDULE 7](#_Toc240699557)

[5. STUDY DESIGN 7](#_Toc240699558)

[5.1. Summary of Study Design 7](#_Toc240699559)

[6. METHODS AND ASSESSMENTS 7](#_Toc240699560)

[6.1. Randomization and Blinding 7](#_Toc240699561)

[6.2. Contraception and Pregnancy Testing 8](#_Toc240699562)

[6.3. Study Visits and Procedures 8](#_Toc240699563)

[7. TRIAL MATERIALS 9](#_Toc240699564)

[7.1. Trial Product (s) 9](#_Toc240699565)

[7.2. Storage and Drug Accountability 9](#_Toc240699566)

[8. TREATMENT 9](#_Toc240699567)

[8.1. Rationale for Selection of Dose 9](#_Toc240699568)

[8.2. Study Drug Formulations 9](#_Toc240699569)

[8.3. Study Drug Administration 9](#_Toc240699570)

[8.4. Specific Restrictions / Requirements 9](#_Toc240699571)

[8.5. Blinding 9](#_Toc240699572)

[8.6. Concomitant therapy 9](#_Toc240699573)

[9. SAFETY MEASUREMENTS 10](#_Toc240699574)

[9.1. Definitions 10](#_Toc240699575)

[9.2. Collecting, Recording and Reporting of Adverse Events 10](#_Toc240699576)

[9.3. Safety Monitoring Plan 10](#_Toc240699577)

[10. DATA ANALYSIS 10](#_Toc240699579)

[10.1. Data Quality Assurance 10](#_Toc240699580)

[10.2. Data Entry and Storage 10](#_Toc240699581)

[11. SAMPLE SIZE AND STATISTICAL METHODS 11](#_Toc240699582)

[11.1. Determination of Sample Size 11](#_Toc240699583)

[11.2. Statistical and Analytical Plans 11](#_Toc240699584)

[12. ETHICAL CONSIDERATIONS 11](#_Toc240699585)

[12.1. Informed Consent 11](#_Toc240699586)

[12.2. IRB review 11](#_Toc240699587)

[12.3. Confidentiality of Data and Patient Records 11](#_Toc240699588)

[13. PUBLICATIONS 12](#_Toc240699589)

[14. RETENTION OF TRIAL DOCUMENTS 12](#_Toc240699590)

STUDY PROTOCOL

|  |
| --- |
| **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. |
| Rationale for the Study Purpose |
| Briefly sketch the background to the current proposal, critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. |
| Rationale for Doses Selected |
| Briefly sketch the rationale for selection of the study dosage |
| Rationale for Study Population |
| Justify selection of target population. |
| Rationale for Study Design |
| State the rationale behind the proposed study design (e.g. two period cross over, case control etc.) |
|  |
| **HYPOTHESIS AND OBJECTIVES** |
| Study objectives are concise statements of the primary and secondary clinical and statistical questions that the study is designed to answer. Study hypothesis must relate to the hypothesis present in the rationale and should be consistent with the objectives described. Number objectives in order of priority. |
| Hypothesis |
| State concisely what hypothesis is to be tested |
| * 1. **Primary Objectives** |
| State primary protocol objective. This should always address a specific hypothesis |
| * 1. **Secondary Objectives** |
| State secondary protocol objective if pertinent. This may or may not be hypothesis driven, may include secondary outcomes, and may include more general non-experimental objectives e.g. to develop a registry etc. |
| Potential Risks and Benefits: |
| End Points - Efficacy |
| Include a discussion of anticipated benefits |
| End Points - Safety |
| Include a discussion of anticipated risks |
|  |
| 1. **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. |
| Criteria for Recruitment |
| 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.   * + - 1. The disease or disorder under study, and how it is to be documented i.e. diagnostic methods, criteria for classification etc.       2. For populations with cancer or pre cancer please include requirements for histological confirmation of diagnosis, time for diagnosis and disease status at entry.       3. Demographic characteristics (e.g. gender, age). Please explain age restrictions if any       4. Ability to provide informed consent       5. 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. |
| 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. |
|  |
| **TRIAL SCHEDULE** |
| Information outlined in this section should be consistent with the information in the schedule of study visits and procedures. |
|  |
| STUDY DESIGN |
| Discuss in detail the experimental design (e.g. two period crossover, case control, placebo control, blinding, randomization, number of study arms, phase of trial, approximate time to complete study recruitment, expected duration of subject participation, sequence and duration of all trial periods, including follow up, changes in scheduling, single or multi centre, healthy or sick population, in or outpatient etc.) to accomplish the specific aims of the project. Use diagrams to explain design complexities. |
| Summary of Study Design |
| Briefly describe the study design and indicate, in general terms, how the design will fulfil the intent of the study. |
|  |
| **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? |
| 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. |
| 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 |
| 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. |
| 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. |
|  |
| **TRIAL MATERIALS** |
| 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) |
| 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. |
| Storage and Drug Accountability |
| Describe product’s storage needs. Include storage requirements and stability (temperature, humidity, security and container). |
|  |
| **TREATMENT** |
| Rationale for Selection of Dose |
| Clearly explain the rationale for the dose used during the study. |
| 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. |
|  |
| **SAFETY MEASUREMENTS** |
| Definitions |
| Define terms (e.g. what would be regarded as serious adverse events etc.) |
| Collecting, Recording and Reporting of Adverse Events |
| Include details of the protocol specific reporting, procedures, including the individual responsible for each step (e.g. the Investigator, the medical monitor, etc.), how decisions will be made regarding determining relatedness and grading severity, how reports will be distributed and what follow up are required. Include specific details of reporting procedures for:   * Deaths and life threatening events * other SAEs * Other adverse events   Note: For reporting to IRB, please reference the UTHSC-Houston IRB policy. |
| Safety Monitoring Plan |
| Please include details on the Data Safety Monitoring Plan (DSMP) for the research study. Please discuss the plans in place to ensure the safety and well being of subjects, and integrity of data collected. |
|  |
|  |
|  |
| **DATA ANALYSIS** |
| Data Quality Assurance |
| Discuss the measures undertaken to ensure that the data obtained from this research is accurate, complete and reliable. |
| Data Entry and Storage |
| Briefly discuss where data will be entered (i.e. will these entries be on paper or electronically), stored and handled. |
|  |
| **SAMPLE SIZE AND STATISTICAL METHODS** |
| Determination of Sample Size |
| Details on sample size calculation and the means by which data will be analyzed and interpreted.  In particular, specify all of the following:   * Null and alternate hypothesis * Type I error rate * Type II error rate |
| Statistical and Analytical Plans |
| * + - 1. *General Considerations* |
| * + - 1. *Safety Analyses* |
| * + - 1. *Interim Analyses* |
| * + - 1. *Describe the types of statistical interim analyses and stopping guidelines (if any) that are proposed, including their timing.* |
|  |
| **ETHICAL CONSIDERATIONS** |
| Informed Consent |
| 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) |
| IRB review |
| This protocol and the associated informed consent documents must be submitted to the IRB for review and approval. |
| Confidentiality of Data and Patient Records |
| 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. |
|  |
| **RETENTION OF TRIAL DOCUMENTS** |
| 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. |

**List of Possible Attachments**

|  |  |
| --- | --- |
| Appendix 1 | Study Schedule |
| Appendix 2 | Blood Sampling Summary |
| Appendix 3 | Questionnaires used in the Trial |
| Appendix 4 | Laboratory Tests |
| Appendix 5 | Sample Patient Information Sheet and Informed Consent Form |