NON THERAPEUTIC PROTOCOL TEMPLATE

University of California, Los Angeles

**SPONSOR NAME**

**Research Protocol**

**PROTOCOL NAME**

|  |  |
| --- | --- |
| Protocol Number: |  |
| Version Date: |  |
| Investigational Product(remove if not applicable):: |  |
| IND Number(remove if not applicable):: |  |
| Development Phase: |  |
| Sponsor: | Name *(please note – for academic studies, the sponsor is the Investigator, not the funding agency.)*  Address  City, State |
| Funding Organization: |  |
| Principal Investigator: | Name:  Telephone:  Fax:  E-mail: |
| Medical Monitor (remove if not applicable): | Name:  Telephone:  Fax:  E-mail: |
| Coordinating Center(remove if not applicable): |  |

|  |  |  |
| --- | --- | --- |
| **Approval:** | | |
|  |  |  |
| *PI or Sponsor Signature (Name and Title)* |  | *Date* |
| **This confidential information about an investigational product is provided for the exclusive use of investigators of this product and is subject to recall at any time. The information in this document may not be disclosed unless federal or state law or regulations require such disclosure. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, with the obligation not to further disseminate this information.** | | |

**PROTOCOL AGREEMENT (for multisite studies)**

I have read the protocol specified below. In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision and providing [Sponsor Name or PI if no sponsor] with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site. Furthermore, on behalf of the study staff and myself, I agree to maintain the procedures required to carry out the study in accordance with accepted GCP principles and to abide by the terms of this protocol.

Protocol Number: Number

Protocol Title: Title

Protocol Date: TBD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | |  |  |
| *Site Investigator Signature* | | |  | *Date* |
|  | | | | |
| *Print Name and Title* | | | | |
| *Site #* |  |  | | |
| *Site Name* |  | | | |
| *Address* |  | | | |
| *Phone Number* |  | | | |

**LIST OF ABBREVIATIONS**

***Add all other abbreviations referenced in the protocol and delete any not referenced in the protocol.***

|  |  |
| --- | --- |
| **AE** | adverse event |
| **ALT** | alanine aminotransferase |
| **AST** | aspartate aminotransferase |
| **BUN** | blood urea nitrogen |
| **CFR** | Code of Federal Regulations |
| **CRF** | case report form |
| **CRP** | C-reactive protein |
| **DMC** | Data Monitoring Committee |
| **DSMB** | Data Safety Monitoring Board |
| **ESR** | erythrocyte sedimentation rate |
| **FDA** | Food and Drug Administration |
| **FEF25%-75%** | forced expiratory flow |
| **FEV1** | forced expiratory volume over one second |
| **FVC** | forced vital capacity |
| **GCP** | Good Clinical Practice |
| **GGT** | gamma-glutamyl transferase |
| **HIPAA** | Health Insurance Portability and Accountability Act of 1996 |
| **ICF** | informed consent form |
| **ICH** | International Conference on Harmonisation |
| **IEC** | Independent Ethics Committee |
| **IL-8** | Interleukin-8 |
| **IRB** | Institutional Review Board |
| **IV** | intravenous |
| **LDH** | lactate dehydrogenase |
| **mEq** | milliequivalent |
| **PI** | Principal Investigator |
| **PK** | pharmacokinetic |

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1.0 PROTOCOL SUMMARY AND/OR SCHEMA

A succinct summary: abstract of the research to be carried out (either in text and/or in a diagrammatic format) including the study title, objectives, patient population, design and treatment plan including agents if appropriate, and time to completion.

2.0 OBJECTIVES AND SCIENTIFIC AIMS

State the protocol objectives indicate all relevant objectives (primary, secondary, tertiary) in bullet form.

3.0 BACKGROUND AND RATIONALE

Give a full explanation of the necessary background information and detailed reasons for carrying out the study including references. Summarize the preclinical and/or animal data and relevant clinical data that are available. Include an explanation of benefit(s) than may be a result of the study for both the study participants and/or society.

4.0 OVERVIEW OF STUDY DESIGN/INTERVENTION

4.1 Design

Briefly describe the study design and how it will accomplish the aims set forth in section 2.0 (Objectives and Scientific Aims).

4.2 Intervention

Give a detailed explanation of the intervention to be conducted, the treatment plan and the rationale for its use.

5.0 CRITERIA FOR SUBJECT ELIGIBILITY

Describe the characteristics of the subject population.

5.1 Subject Inclusion Criteria

List detailed inclusion criteria in bullet form. Include all appropriate elements, e.g., disease status/history (if applicable), demographic characteristics, and descriptors for sub-populations that have been identified.

5.2 Subject Exclusion Criteria

List detailed exclusion criteria in bullet form, such as past medical history, present medical condition, physiological age, health status and other relevant subject demographic characteristics.

6.0 RECRUITMENT PLAN

Describe how subjects will be recruited to this trial and what efforts will be made to include women and minorities in the research study. This section should include the discussion process with the subject, informed consent procedures, registration procedures and any other relevant information. It is important to include any additional measures that may be used in accordance with the standard processes, for example advertisements, payments to participants, reimbursement plans, etc.

7.0 ASSESSMENT/EVALUATION PLAN

The Assessment/Evaluation Plan should be detailed in either a textual format (paragraphs) and/or bullet form. Describe all tests and measures (e.g., surveys, questionnaires, interviews, educational components, videotapes, counseling interventions, etc.) to be carried out prior to and throughout the intervention. Specify which will serve as baseline measures for the study. Please see Appendix 1.

8.0 TOXICITIES/SIDE EFFECTS

Give a detailed description of the anticipated side effects, their likelihood and expected frequency.

## 8.1 Adverse Events

(remove the portions of this section that do not apply)

An adverse event (AE) is any untoward medical occurrence in a clinical investigation of a patient administered a pharmaceutical product and that does not necessarily have a causal relationship with the treatment. An AE is therefore any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the administration of an investigational product, whether or not related to that investigational product. An unexpected AE is one of a type not identified in nature, severity, or frequency in the current Investigator’s Brochure or of greater severity or frequency than expected based on the information in the Investigator’s Brochure.

The Investigator will probe, via discussion with the subject, for the occurrence of AEs during each subject visit and record the information in the site’s source documents. Adverse events will be recorded in the patient CRF. Adverse events will be described by duration (start and stop dates and times), severity, outcome, treatment and relation to study drug, or if unrelated, the cause.

**Table 1. AE Severity Grading**

(remove this section if it does not apply)

|  |  |
| --- | --- |
| **Severity (Toxicity Grade)** | **Description** |
| Mild (1) | Transient or mild discomfort; no limitation in activity; no medical intervention or therapy required. The subject may be aware of the sign or symptom but tolerates it reasonably well. |
| Moderate (2) | Mild to moderate limitation in activity, no or minimal medical intervention/therapy required. |
| Severe (3) | Marked limitation in activity, medical intervention/therapy required, hospitalizations possible. |
| Life-threatening (4) | The subject is at risk of death due to the adverse experience as it occurred. This does not refer to an experience that hypothetically might have caused death if it were more severe. |

**Table 2. AE Relationship to Study Drug**

(remove this section if it does not apply)

|  |  |
| --- | --- |
| **Relationship to Drug** | **Comment** |
| Definitely | Previously known toxicity of agent; or an event that follows a reasonable temporal sequence from administration of the drug; that follows a known or expected response pattern to the suspected drug; that is confirmed by stopping or reducing the dosage of the drug; and that is not explained by any other reasonable hypothesis. |
| Probably | An event that follows a reasonable temporal sequence from administration of the drug; that follows a known or expected response pattern to the suspected drug; that is confirmed by stopping or reducing the dosage of the drug; and that is unlikely to be explained by the known characteristics of the subject’s clinical state or by other interventions. |
| Possibly | An event that follows a reasonable temporal sequence from administration of the drug; that follows a known or expected response pattern to that suspected drug; but that could readily have been produced by a number of other factors. |
| Unrelated | An event that can be determined with certainty to have no relationship to the study drug. |

## 

## 8.2 Serious Adverse Events

An SAE is defined as any AE occurring at any dose that results in any of the following outcomes:

* death
* a life-threatening adverse experience
* inpatient hospitalization or prolongation of existing hospitalization
* a persistent or significant disability/incapacity
* a congenital anomaly/birth defect

Other important medical events may also be considered an SAE when, based on appropriate medical judgment, they jeopardize the subject or require intervention to prevent one of the outcomes listed.

### 8.2.1 Serious Adverse Event Reporting

Study sites will document all SAEs that occur (whether or not related to study drug) per [UCLA OHRPP Guidelines](http://ora.research.ucla.edu/OHRPP/Pages/PoliciesandGuidance.aspx#authority). The collection period for all SAEs will begin after informed consent is obtained and end after procedures for the final study visit have been completed.

*Include appropriate wording here*

In accordance with the standard operating procedures and policies of the local Institutional Review Board (IRB)/Independent Ethics Committee (IEC), the site investigator will report SAEs to the IRB/IEC.

9.0 PRIMARY OUTCOMES

Describe the tests and/or measures to be carried out during the study, including the intervention and necessary follow-up time frames. Include the specific tests, time frame for each test and/or measure and a window of time that would be considered acceptable to eliminate protocol violations.  
  
It is recommended that this information also be displayed in tabular format in an appendix at the end of the protocol. Please see APPENDIX 1.

10.0 CRITERIA FOR REMOVAL FROM STUDY

Describe in detail any specification that could be utilized by the subject, attending physician or the Principal Investigator to remove the subject from study. This should include (if appropriate) but not limited to severe, unexpected toxicities/side effects, recurrent, progressive or new disease, subject non-compliance with the defined treatment plan, subject’s right to withdraw consent for continued participation, and /or death.

11.0 BIOSTATISTICS

This section can have multiple parts based on the complexity of the study; if there are multiple sections a bullet form can be used for each section.

Detailed explanation of the study design including rationale for the research; this may be a summary of information that has been described elsewhere in the protocol (e.g., Background and Rationale, Section 3.0). The plans for statistical analysis of the data should be described. The sample size should be discussed including the expected numbers of subjects and how the sample size was determined, the expected accrual rates and duration of the study. If applicable, randomization procedures and early stopping rules can be discussed. Please note, details on how to randomize a subject (steps) should be described in the next section 12.2.

12.0 RESEARCH PARTICIPANT REGISTRATION AND RANDOMIZATION PROCEDURES

12.1 Research Participant Registration

Confirm eligibility as defined in the section entitled Criteria for Patient/Subject Eligibility.

Obtain informed consent, by following procedures defined in section entitled Informed Consent Procedures.

During the registration process registering individuals will be required to complete a protocol specific Eligibility Checklist.

12.2 Randomization

If the research study requires randomization procedures, this section should be referenced in the Biostatistics section (11.0). Describe in detail the process of randomization, when it should occur, how it is being conducted and who is responsible for carrying it out.

# 13.0 DATA COLLECTION, RETENTION AND MONITORTING

## 13.1 Data Collection Instruments

The Investigator will prepare and maintain adequate and accurate source documents designed to record all observations and other pertinent data for each subject treated with the study drug.

Study personnel at each site will enter data from source documents corresponding to a subject’s visit into the protocol-specific electronic Case Report Form (eCRF) OR paper CRF, when the information corresponding to that visit is available. Subjects will not be identified by name in the study database or on any case report form to be collected by the Sponsor (or designee), but will be identified by a site number, subject number and initials.

*For eCRFs:* If a correction is required for an eCRF, the time and date stamps track the person entering or updating eCRF data and creates an electronic audit trail. *For paper CRFs:* If a correction is made on a CRF, the study staff member will line through the incorrect data, write in the correct data and initial and date the change.

The Investigator is responsible for all information collected on subjects enrolled in this study. All data collected during the course of this study must be reviewed and verified for completeness and accuracy by the Investigator. A copy of the CRF will remain at the Investigator’s site at the completion of the study.

## 13.2 Data Management Procedures

The data will be entered into a validated database. The Data Management group will be responsible for data processing, in accordance with procedural documentation. Database lock will occur once quality assurance procedures have been completed.

All procedures for the handling and analysis of data will be conducted using good computing practices meeting FDA guidelines for the handling and analysis of data for clinical trials.

## 13.3 Data Quality Control and Reporting

After data have been entered into the study database, a system of computerized data validation checks will be implemented and applied to the database on a regular basis. *For EDC studies:* Queries are entered, tracked, and resolved through the EDC system directly. *For paper studies:* Query reports (Data Clarification Requests) pertaining to data omissions and discrepancies will be forwarded to the Investigators and study monitors for resolution. The study database will be updated in accordance with the resolved queries. All changes to the study database will be documented.

## 13.4 Archival of Data

The database is safeguarded against unauthorized access by established security procedures; appropriate backup copies of the database and related software files will be maintained.  Databases are backed up by the database administrator in conjunction with any updates or changes to the database.

At critical junctures of the protocol (e.g., production of interim reports and final reports), data for analysis is locked and cleaned per established procedures.

## 13.5 Availability and Retention of Investigational Records

The Investigator must make study data accessible to the monitor, other authorized representatives of the Sponsor (or designee), IRB/IEC, and Regulatory Agency (e.g., FDA) inspectors upon request. A file for each subject must be maintained that includes the signed Informed Consent, HIPAA Authorization and Assent Form and copies of all source documentation related to that subject. The Investigator must ensure the reliability and availability of source documents from which the information on the CRF was derived.

All study documents (patient files, signed informed consent forms, copies of CRFs, Study File Notebook, etc.) must be kept secured for a period of two years following marketing of the investigational product or for two years after centers have been notified that the IND has been discontinued. There may be other circumstances for which the Sponsor is required to maintain study records and, therefore, the Sponsor should be contacted prior to removing study records for any reason.

## 13.6 Monitoring

Monitoring visits will be conducted by representatives of the Sponsor according to the U.S. CFR Title 21 Parts 50, 56, and 312 and ICH Guidelines for GCP (E6). By signing this protocol, the Investigator grants permission to the Sponsor (or designee), and appropriate regulatory authorities to conduct on-site monitoring and/or auditing of all

appropriate study documentation.

## 13.7 Subject Confidentiality

In order to maintain subject confidentiality, only a site number, subject number and subject initials will identify all study subjects on CRFs and other documentation submitted to the Sponsor. Additional subject confidentiality issues (if applicable) are covered in the Clinical Study Agreement.

# 14.0 ADMINISTRATIVE, ETHICAL, REGULATORY CONSIDERATIONS

The study will be conducted according to the Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), Institutional Review Boards (21 CFR 56), and Obligations of Clinical Investigators (21 CFR 312).

To maintain confidentiality, all laboratory specimens, evaluation forms, reports and other records will be identified by a coded number and initials only. All study records will be kept in a locked file cabinet and code sheets linking a patient’s name to a patient identification number will be stored separately in another locked file cabinet. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by the FDA. The Investigator must also comply with all applicable privacy regulations (e.g., Health Insurance Portability and Accountability Act of 1996, EU Data Protection Directive 95/46/EC).

## 14.1 Protocol Amendments

Any amendment to the protocol will be written by the Sponsor. Protocol amendments cannot be implemented without prior written IRB/IEC approval except as necessary to eliminate immediate safety hazards to patients. A protocol amendment intended to eliminate an apparent immediate hazard to patients may be implemented immediately, provided the IRBs are notified within five working days.

## 14.2 Institutional Review Boards and Independent Ethics Committees

The protocol and consent form will be reviewed and approved by the IRB/IEC of each participating center prior to study initiation. Serious adverse experiences regardless of causality will be reported to the IRB/IEC in accordance with the standard operating procedures and policies of the IRB/IEC, and the Investigator will keep the IRB/IEC informed as to the progress of the study. The Investigator will obtain assurance of IRB/IEC compliance with regulations.

Any documents that the IRB/IEC may need to fulfill its responsibilities (such as protocol, protocol amendments, Investigator’s Brochure, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB/IEC. The IRB/IECs written unconditional approval of the study protocol and the informed consent form will be in the possession of the Investigator before the study is initiated. The IRB/IECs unconditional approval statement will be transmitted by the Investigator to the Sponsor or designee prior to the shipment of study supplies to the site. This approval must refer to the study by exact protocol title and number and should identify the documents reviewed and the date of review.

Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB/IEC approval except when necessary to eliminate immediate hazards to the patients or when the change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB/IEC and written verification that the modification was submitted and subsequently approved should be obtained.

The IRB/IEC must be informed of revisions to other documents originally submitted for review; serious and/or unexpected adverse experiences occurring during the study in accordance with the standard operating procedures and policies of the IRB; new information that may affect adversely the safety of the patients of the conduct of the study; an annual update and/or request for re-approval; and when the study has been completed.

## 14.3 Informed Consent Form

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH GCP, US Code of Federal Regulations for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA, if applicable), and local regulations.

The Investigator will prepare the informed consent form, assent and HIPAA authorization and provide the documents to the Sponsor or designee for approval prior to submission to the IRB/IEC. The consent form generated by the Investigator must be acceptable to the Sponsor and be approved by the IRB/IEC. The written consent document will embody the elements of informed consent as described in the International Conference on Harmonisation and will also comply with local regulations. The Investigator will send an IRB/IEC-approved copy of the Informed Consent Form to the Sponsor (or designee) for the study file.

A properly executed, written, informed consent will be obtained from each subject prior to entering the subject into the trial. Information should be given in both oral and written form and subjects (or their legal representatives) must be given ample opportunity to inquire about details of the study. If appropriate and required by the local IRB/IEC, assent from the subject will also be obtained. If a subject is unable to sign the informed consent form (ICF) and the HIPAA authorization, a legal representative may sign for the subject. A copy of the signed consent form (and assent) will be given to the subject or legal representative of the subject and the original will be maintained with the subject’s records.

## 14.4 ClinicalTrials.gov

*ClinicalTrials.gov* is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](http://www.clinicaltrials.gov/), as required by U.S. Law. This website will not include information that can identify the subject. At most, the website will include a summary of the results.

# 15.0 PUBLICATIONS

The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a process determined by mutual written agreement among the study Sponsor and participating institutions. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996.

# 16.0 INVESTIGATOR RESPONSIBLITIES

By signing the Agreement of Investigator form, the Investigator agrees to:

1. Conduct the study in accordance with the protocol and only make changes after notifying the Sponsor (or designee), except when to protect the safety, rights or welfare of subjects.
2. Personally conduct or supervise the study (or investigation).
3. Ensure that the requirements relating to obtaining informed consent and IRB review and approval meet federal guidelines, as stated in § 21 CFR, parts 50 and 56.
4. Report to the Sponsor or designee any AEs that occur in the course of the study, in accordance with §21 CFR 312.64.
5. Ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations in meeting the above commitments.
6. Maintain adequate and accurate records in accordance with §21 CFR 312.62 and to make those records available for inspection with the Sponsor (or designee).
7. Ensure that an IRB that complies with the requirements of §21 CFR part 56 will be responsible for initial and continuing review and approval of the clinical study.
8. Promptly report to the IRB and the Sponsor (or designee) all changes in the research activity and all unanticipated problems involving risks to subjects or others (to include amendments and IND safety reports).
9. Seek IRB approval before any changes are made in the research study, except when necessary to eliminate hazards to the patients/subjects.
10. Comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements listed in § 21 CFR part 312.

17.0 REFERENCES

SAMPLE FORMAT:  
Author(s) Last Name, Initial (s). Title of Reference Article, Year Journal, Volume, Page(s)  
Ashbaugh DG, Petty TL, Bigelow DB, Harris TM. Continuous positive-pressure breathing (CPPB) in adult respiratory disease syndrome. 1990 J Thoracic Cardiovasc Surg 57:31-41

18.0 APPENDICES

List appendices here. Appendices will be stored in a separate file and will be submitted in electronic and/or paper format. If electronic format, please submit on file per appendix.

## APPENDIX 1. EXAMPLE OF SCHEDULE OF STUDY VISITS

|  |  |  |
| --- | --- | --- |
|  | **Visit 1 (Day/Week/Month #)a** | **Visit X (Day/Week/Month #)** |
| Informed Consent | **X** |  |
| Medical History | **X** |  |
| Complete Physical Exam | **X** | **X** |
| Abbreviated Physical Exam |  |  |
| Height | **X** | **X** |
| Weight | **X** | **X** |
| Vital Signs | **X** | **X** |
| Oximetry | **X** | **X** |
| Spirometry | **X** | **X** |
| Pharmacokinetics |  |  |
| Chemistry | **X** | **X** |
| Pregnancy Test (Urine or Serum) | **X** | **X** |
| Hematology | **X** | **X** |
| ESR | **X** | **X** |
| C-Reactive Protein | **X** | **X** |
| Urinalysis | **X** | **X** |
| Randomization | **X** |  |
| Dispensing or Administration of Study Drug | **X** |  |
| Counting of Returned Study Drug |  | **X** |
| Initiate Subject Diary | **X** |  |
| Subject Diary Review |  | **X** |
| Concomitant Medication Review | **X** | **X** |
| Adverse Experiences |  |  |

a ±2 days