UCLA Health
Center for Nursing Excellence
Research and Evidence-Based Practice Program

Protocol Template: Non-Investigational Product Clinical Research Study

This protocol template is a tool to help facilitate the process of developing a human subjects' research protocol that does not involve an investigational product (drug, device, biologic, vaccine etc.). The study may be longitudinal in nature, prospectively following a population with a cohort or case control design, or involve an intervention, such as acupuncture, comparison of the efficacy of two surgical procedures, imaging, etc. This template can be used for construction of a UCLA Investigator initiated study conducted only at UCLA as well as at participating sites within a multi-site trial or collaborative network.

Directions for Using this Template:

- Language in blue italics and or brackets should be used as a guide for development of your protocol and should be replaced with language specific to your research study.
- Language outside of the blue/brackets can remain in the protocol as long as it makes sense within the context of your protocol. Remove this section with directions and any template language that is not being used prior to submitting to the IRB.
- The Appendix section also includes some references, and helpful links, which can be used when building portions of your protocol.

INSERT TITLE OF THE PROTOCOL

[Title should describe the design of the study randomized, longitudinal, feasibility and the target condition or outcome being studies in a specific population]

Principal Investigator	*Insert Name* *Insert Department* *Insert Address* *Insert Phone #* *Insert Email*
Regulatory Sponsor *[If applicable]*	*Insert the Name of the Sponsor* *Insert Department Name* *Insert Address* *Insert Phone Number*
Funding Sponsor *[If applicable include name of the entity funding the study.]*	*Insert the Name of Primary Funding Institution* *Insert Address* *Insert Phone Number*
Study Product *[If applicable]*	*Insert Study Product Name – For example acupuncture*
Protocol Number *[If applicable]*	*Insert Protocol Number Used by Regulatory Sponsor*
IRB Number	*Will not be available at the time of initial submission. Provided by the UCLA IRB*
NIH Grant Number *[If applicable]*	*Include NIH grant number*

Initial version [Date]
Amended [Date]
Amended [Date]

Table of Contents

BACKGROUND AND STUDY RATIONALE **6**

1 INTRODUCTION **6**

1.1 Background and Relevant Literature 6

2 STUDY AIMS **6**

2.1 Primary Aims 6
2.2 Secondary Aims (if applicable) 6
2.3 Hypotheses 6

3 INVESTIGATIONAL PLAN **7**

3.1 General Design 7
3.2 Allocation to Interventional Group [if applicable] 7
3.3 Study Measures 7
3.4 Study Endpoints 7
3.4.1 Primary Study Endpoint *7*
3.4.2 Secondary Study Endpoints *7*

4 STUDY POPULATION AND DURATION OF PARTICIPATION **8**

4.1 Duration of Study Participation 8
4.2 Total Number of Subjects and Sites 8
4.3 Inclusion Criteria 8
4.4 Exclusion Criteria 8
4.5 Subject Recruitment 8
4.6 Vulnerable Populations: 8

5 STUDY PROCEDURES **9**

5.1 Screening 9
5.2 Study Intervention or Observational Phase (Give this section a name that is relevant to the design of your study) 9
5.2.1 Visit 1 (sometimes referred to as the baseline visit) *9*
5.2.2 Visit 2 ..... *10*
5.2.3 Visit 3 ..... *10*
5.2.4 Visit X (If applicable for your study) *10*
5.2.5 End of Study Visit *10*
5.3 Unscheduled Visits 10
5.4 Subject Withdrawal 11
5.4.1 Data Collection and Follow-up for Withdrawn Subjects *11*
5.5 Early Termination Visits 11
5.6 Efficacy Evaluations (only if applicable) 11
5.7 Pharmacokinetic Evaluation (only if applicable) 11
5.8 Genetic Testing (only if applicable) 11
5.9 Safety Evaluation (only if applicable) 11

6 STATISTICAL PLAN **11**

6.1 Sample Size and Power Determination 11
6.2 Statistical Methods 12
6.3 Control of Bias and Confounding (if applicable, typically observational study or if randomization is not taking place) 12
6.3.1 Baseline Data *12*
6.3.2 Analysis of Primary Outcome of Interest *12*
6.3.3 Pharmacokinetic Analysis (only if applicable) *12*
6.3.4 Interim Analysis (only if applicable) *12*

7 SAFETY AND ADVERSE EVENTS **12**

7.1 DEFINITIONS 12
7.1.1 Adverse Event 12
7.1.2 Serious Adverse Event 13
7.2 RECORDING OF ADVERSE EVENTS 13
7.3 RELATIONSHIP OF AE TO STUDY 13
7.4 REPORTING OF ADVERSE EVENTS AND UNANTICIPATED PROBLEMS 14
7.4.1 Follow-up Report 14
7.4.2 Investigator reporting: notifying the study sponsor (if applicable) 14
7.4.3 Data and Safety Monitoring Plan 14

8 STUDY ADMINISTRATION, DATA HANDLING AND RECORD KEEPING 14

8.1 CONFIDENTIALITY 14
8.2 DATA COLLECTION AND MANAGEMENT 15
8.3 RECORDS RETENTION 16

9 STUDY MONITORING, AUDITING, AND INSPECTING 16

9.1 STUDY MONITORING PLAN 16
9.2 AUDITING AND INSPECTING 16

10 ETHICAL CONSIDERATIONS 16

10.1 RISKS 16
10.2 BENEFITS 16
10.3 RISK BENEFIT ASSESSMENT 17
10.4 INFORMED CONSENT PROCESS / HIPAA AUTHORIZATION 17
10.4.1 Alterations to Typical Consent Process (only include if applicable) 17

11 STUDY FINANCES 18

11.1 FUNDING SOURCE 18
11.2 CONFLICT OF INTEREST 18

12 PUBLICATION PLAN 18

13 REFERENCES 19

14 ATTACHMENTS 19

15 APPENDICES 19

15.1 EXAMPLE: TABLE 1: SCHEDULE OF STUDY PROCEDURES 19

Study Summary

Title	*Full title of protocol*
Short Title	*Shortened title, if one is typically used by you or your Center/Dept.*
IRB Number	*The standard protocol number used to identify this study by the UCLA IRB. Please note that this number will be assigned by the IRB and thus will not be in existence at the time of protocol development and initial review.*
Protocol Number	*May or may not exit for this particular type of study.*
Methodology	*Design attributes such as longitudinal cohort, feasibility, case control, etc.*
Study Duration	*Estimated duration for the main protocol (e.g. from start of screening to last subject processed and finished the study).*
Study Center(s)	*Single-center or multi-center. If multi-center, note number of projected centers to be involved.*
Objectives	*Brief statement of primary study objectives.* *Primary:* • *To determine (improvement, feasibility, etc.)* *Secondary:* • *To determine (obtain, evaluate, verify, etc.)*
Number of Subjects	*Number of subjects projected for the entire study not just for UCLA, if there are additional participating sites. (e.g. 100 subjects expected to be enrolled across 8 sites).*
Main Inclusion and Exclusion Criteria	*Include the key inclusion and exclusion criteria in this section.*
Intervention *[if applicable]*	*Include any interventional aspects of the study. For example if the study includes comparison of two surgical procedures or if there is an intervention involved such a acupuncture, cognitive behavioral therapy, diet, etc.*
Statistical Methodology	*A very brief description of the main elements of the statistical methodology to be used in the study. Limit this section to discussion of the analysis of the primary endpoint and perhaps the main secondary endpoint.*

Data and Safety Monitoring Plan	*Explain who will be responsible for the data quality management and the ongoing safety of subjects. This may be the PI, independent medical monitor, internal safety committee, data safety monitoring board (DSMB) or any combination of these reviewing entities.*

Background and Study Rationale

The introduction should open with remarks that this document is a research protocol and the described study will be conducted in compliance with the provisions set forth in the protocol as well as, Good Clinical Practice standards, associated federal regulations, and all applicable UCLA research requirements. The rest of the introduction is broken out into subsections. For example:

This study will be conducted in full accordance with all applicable UCLA Research Policies and Procedures and all applicable Federal and state laws and regulations including *[as applicable include the following regulations as they apply 45 CFR 46, 21 CFR Parts 50, 54, 56 All episodes of noncompliance will be documented.]*

1 Introduction

This should include a brief paragraph or two that describes the setting and rationale for this particular study.

1.1 Background and Relevant Literature

This section should contain a background discussion of the target disease, condition, research area of interest to which the study is designed.

This section should provide an overview of the literature and data relevant to the study, which help to support the rationale for the study. Also include the theoretical or conceptual framework used to guide this study. References should be listed in section 13.

2 Study Aims

Describe the overall objective(s) of the study. The primary objective is typically the main purpose of the study and may be to determine one of the following (feasibility, relative risk, association, comparative efficacy etc.) The primary objective should be both the most important and the objective upon which the study sample size is based.

Examples of primary and secondary objectives:

2.1 Primary Aims

- *To determine if there is a relationship between X and Y*
- *To compare the safety and/or efficacy of two available therapies (i.e. which is better, which is safer)*

2.2 Secondary Aims (if applicable)

- *To examine the effect of XX on Y*
- *Etc.*

2.3 Hypotheses

- *To examine the effect of XX on Y*
- *Etc.*

3 Investigational Plan

Section 3 will provide a brief overview of the study phases (screening, baseline, visits, follow-up period). More details on procedures will be included in subsequent sections of the protocol.

3.1 General Design

A description of study design should be included, e.g., randomized trial (for example randomizing subjects to exercise versus diet intervention for comparison or randomization to two standard of care therapies in order to compare efficacy or safety), concurrent or non-concurrent (retrospective) cohort study, case-control study, cross sectional study, descriptive study, natural history study, evaluation of a diagnostic, evaluation of an intervention, etc.

3.2 Allocation to Interventional Group [if applicable]

Describe the method that will be used to allocate study intervention if applicable for this study. If the study is randomized in nature describe how this process will take place. Include details as to who will be responsible for generating the randomization sequence. It may be a series of random numbers or a computer-generated algorithm. If there will be stratification or number blocking taking place in the randomization structure include information about this as well. Mention if there will be any blinding associated with the study. For example: Subjects will be randomized to either nutritional counseling or nutritional counseling and structured diet plan. Subjects will be randomized in a one to one fashion and the randomization will take place using a computer-generated algorithm.

3.3 Study Measures

Describe in detail the measures (questionnaires, scales, etc.) that will be used to collect information throughout the course of the study. Also include the relevant literature establishing the validity of any scales, evaluation tools, etc. which may be used in the study.
For example:

> *The International Index of Erectile Function Questionnaire (IIEF-5), also referred to as the Sexual Health inventory for Men (SHIM), will be used to assess ED and SD. Scores range from 0 to 25. Scores (>20) indicate normal degree of erectile function. Scores 10> indicate moderate to severe erectile dysfunction. The IIEF will be completed by patients at the following time points:*
>
> - *Screening visit for eligibility assessment*
> - *Baseline visit to establish a baseline measurement*
> - *4th week of intervention with exposure to either acupuncture or yoga regiment*

3.4 Study Endpoints

3.4.1 Primary Study Endpoint

Describe the primary endpoint to be analyzed in the study (e.g. could be safety or efficacy, depending on the main objective of the study). The primary endpoint is used as the justification for the sample size and represents the overall goal of the study. Section 2.1 Objectives provides the overall primary aim of the study, and this section 3.4.1 provides the detail on the specific endpoint(s) that will support the primary objective of the study (how it/they are to be measured, etc.)

For example the primary endpoint will be change in variable 1 between the baseline visit and visit 12.

3.4.2 Secondary Study Endpoints

Describe any secondary endpoints to be analyzed in the study. For example, if one of the study objectives noted above in section 2.2 includes "blood loss" as a measure of safety, this section should describe the specific parameters that would constitute important blood loss and how that will be measured for the purposes of the protocol and study analysis.

4 Study Population and Duration of Participation

The study population in every study is defined by the specific trial inclusion and exclusion criteria. This section will describe the inclusion/ exclusion criteria, duration of participation, number of subjects to be enrolled, etc.

4.1 Duration of Study Participation

This refers to the duration of study participation and not simply the duration of the study. This should include screening, study intervention phase and any follow up, if applicable, to this particular study.

4.2 Total Number of Subjects and Sites

Include the number of subjects that will be enrolled at UCLA and the number of subjects that will be enrolled elsewhere if applicable. Enrolled, for the intent and purpose of the UCLA IRB, means the consent form was signed. Consider writing the following: Recruitment will end when approximately XXX subjects are enrolled. It is expected that approximately XXXY subjects will be enrolled in order to produce XXX evaluable subjects.

Include details regarding if UCLA is the only site or if there are multiple sites.

4.3 Inclusion Criteria

Create a list of criteria subjects must meet to be eligible for study enrollment (e.g. age, gender, target disease, concomitant disease if required, etc.)
For example:

- *Males*
- *Over 65 years of age*
- *Patients must be able to read and understand English*
- *Participants must sign the informed consent form*

4.4 Exclusion Criteria

List of criteria that would exclude a subject from enrolling in the study
For example:

- *Prior diagnosis of breast cancer*
- *Active, regular cigarette smokers as defined as someone who smoke more than 10 cigarettes per day*
- *Alcohol consumption greater than 12 drinks per week*
- *Participation in another clinical trial within 3 months of the current study*

4.5 Subject Recruitment

Describe how subjects will be recruited for the study, e.g. from investigator or sub-investigator clinical practices, referring physicians, advertisement, etc. Include details as to whether or not the recruitment plan proposes to use outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.). Note: All recruitment materials, which will be seen by potential participants, need to be approved by the UCLA IRB.

4.6 Vulnerable Populations:

(HHS regulations 45CFR46 Subparts B, C, & D for, pregnant women, fetuses, neonates, prisoners; and FDA regulations 21CFR50 Subpart B for children).

Specify if the study involves any of the following populations:

- *Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus)*
- *Fetuses nor neonates*
- *Prisoners*

- *Children*
- *If none of the above populations are to be included into the study, write: "Children, pregnant women, fetuses, neonates, or prisoners are not included in this research study."*

Note: *This section is intended to elicit information regarding additional protections when specific populations are included in a research study. It is not intended to trigger an exclusion of these populations.*

Note: *Subjects who become imprisoned or are court-ordered to attend residential alcohol and other drug treatment facilities will be considered prisoners under Subpart C of the federal regulations 45CFR46. Such subjects cannot be continued in the research unless an amendment to the protocol is submitted and approved by the IRB and certification to the federal Office of Human Research Protections if the research is supported by the Department of Health and Human Services.*

Note: *Complete the supplemental form for each vulnerable population included in the study.*

5 Study Procedures

This section should list the procedures, observations, measures, etc. that will take place at each of the study visits. Every measure, procedure, observation, etc. that was listed in Section in Section 3.3 should be included in the study procedures section. A table can supplement this section. An example procedures table is included below in Appendix 15.1.

Below is a list of common procedures conducted within the context of research. Each of these procedures is associated with specific research support centers within the UCLA. As you click off procedures you will be using within the context of your research protocol, you will be taken to the appropriate language to include in your protocol and consent form. The procedures, and their appropriate protocol language, can be inserted into the visits within the procedures section during which they occur. For example 7TMRI at screening, baseline, Visit 4, etc.

Language from your Informed Consent Form (ICF) may be included, as applicable.

If you are unsure about any of the research procedures you are using, appropriate language to use, etc., it is suggested that you reach out to the Nurse Scientist in the Center for Nursing Excellence for consultation.

5.1 Screening

List the timing and the procedures to be performed at a screening visit. Include details as to what measurements exactly will be taken and how they will be retrieved.
For example:

- *Informed Consent*
- *Medical Record Review (describe what will be extracted form medical records and reviewed)*
- *Vital Signs (what vital signs will be taken and how they will be taken)*
- *Lab Tests (which lab tests will be conducted)*
- *Questionnaires (list questionnaires and measures which were described in Section 3.3)*
- *Physical Exam (describe which measures will be taken e.g. height, weight, etc.)*

5.2 Study Intervention or Observational Phase (Give this section a name that is relevant to the design of your study)

5.2.1 Visit 1 (sometimes referred to as the baseline visit)

This section should include all of the procedures, which take place during each of the study intervention or observational phase visits. All measures and procedures should be described in detail.
Standard of care procedures can be excluded from the study protocol. If there are research related procedures being conducted that can be replaced with standard of care procedures within a specific time

period, they can be included in the list of procedures and denoted as standard of care. For example: A physical exam must be conducted for screening purposes but if one was conducted within the past 30 days for standard of care purposes, this can be used for screening/eligibility.

Clearly identify which procedures are experimental (if applicable) or provide a statement that all procedures conducted are standard of care and the standard of care procedures are simply being compared.

If standard of care procedures are being conducted in a specific manner in conjunction with procedures conducted solely for research purposes, they may need to be included in the study procedures section but denoted as standard of care.

Include windows around study visits if applicable to the study so as to reduce the number of visits that may be considered out of window.

For Example:

- *Randomization (if applicable describe procedure to which subject may be randomized e.g. acupuncture, diet intervention, cognitive therapy, imaging, etc.)*
- *Physical Exam*
- *Vital Signs*
- *Laboratory Tests*
- *Quality of life assessments*

5.2.2 Visit 2

List all the procedures that will take place at study visit 2 and describe exactly what tests, lab values, etc. will be obtained and how. If the physical exam, for example, at visit 2 is completed in the same manner as the screening physical you can simply refer to that section as opposed to rewriting or copying all of the same information.
For example:

- *Physical Exam*
- *Laboratory Tests*
- *Medical Records Review*
- *Assess possible adverse events*
- *Review medication changes and updates*
- *Be certain to include details on any sort of genetic testing that may be taking place*

5.2.3 Visit 3

- *Etc.*

5.2.4 Visit X (If applicable for your study)

Include details of anything that will need to take place at follow up visits.

5.2.5 End of Study Visit

Describe the study visit including a list of all procedures to be conducted at this visit. Include details about any sort of subject debriefing, which will take place at this visit or any type of results that will be shared with the subject. If the study involves blinding and the subjects will be un-blinded at their final study visit include those details here.

5.3 Unscheduled Visits

Describe how unscheduled visits will be handled throughout the study.

5.4 Subject Withdrawal

Describe the scenarios under which a subject may be withdrawn from the study prior the expected completion of that subject (e.g. safety reasons, failure of subject to adhere to protocol requirements, subject consent withdrawal, disease progression, etc.) Also, if abrupt termination of study intervention could affect subject safety, describe procedure to transition subject off the study.

For example: Subjects may withdraw from the study at any time without impact to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to intervention or study procedures or visit schedules, AEs, or due to (list protocol specific reasons that could arise here). The Investigator or the Sponsor (if applicable) may also withdraw subjects who violate the study plan, to protect the subject for reasons related to safety or for administrative reasons. It will be documented whether or not each subject completes the study. Subjects who withdraw early will have one final visit to collect final evaluations and assess adverse events.

5.4.1 Data Collection and Follow-up for Withdrawn Subjects

Even though subjects may be withdrawn prematurely from the study, it is imperative to collect at least survival data on such subjects throughout the protocol defined follow-up period for that subject (though careful thought should be given to the full data set that should be collected on such subjects to fully support the analysis).
Include provisions within this section of the protocol that detail what attempts will be made to collect data from participants who have withdrawn consent. For example: Subjects who withdraw consent to participate in the study will be seen for one final study visit. During this visit they will be asked for permission to have the study team look into their survival status via publically available means.

5.5 Early Termination Visits

Include here the details and procedures that will take place if a subject decided to leave the study early or is asked by the investigator, sponsor, etc. to cease participation in the study.

5.6 Efficacy Evaluations (only if applicable)

These are the measures that will be used to assess the efficacy of the study intervention.

5.7 Pharmacokinetic Evaluation (only if applicable)

Sampling for pharmacokinetics will be done at X times. Include number of draws and what will be specifically analyzed.

5.8 Genetic Testing (only if applicable)

Include details about any sort of genetic testing that may be taking place in the study. Be sure to include if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and the provision for potential genetic counseling. (Consider in risks section as well).

5.9 Safety Evaluation (only if applicable)

Describe which procedures, labs, etc. within the study will be used to evaluate safety.

6 Statistical Plan

This section of the protocol should provide sufficient detail to assure that the sample size for the study is justified and that statistical methods are in place that are appropriate and adequate to answer the overall research question.

6.1 Sample Size and Power Determination

Describe the statistical methods for determining the sample size for the study and the power calculation (if appropriate for this particular study). All studies should include a sample size calculation even if a power calculation is not warranted (for example in a PK study).

6.2 Statistical Methods

Summarize the overall statistical approach to the analysis of the study. This section should contain the key elements of the analysis plan, but should not be a reiteration of a detailed study analysis plan. The full Statistical Analysis Plan can then be a "stand-alone" document that can undergo edits and versioning outside of the protocol and therefore not trigger an IRB re-review with every version or edit – as long as the key elements of the analysis plan do not change.

Be clear on primary as well as any applicable secondary analyses. Examples of common analyses are included below. Please note it is possible not all of this will be applicable to your study. Describe if any interim analysis, is planned, subject population for analysis (screened, randomized, per-protocol compliance, etc.)

6.3 Control of Bias and Confounding (if applicable, typically observational study or if randomization is not taking place)

Subjects in observational studies are not assigned by a process of randomization and are therefore these studies are particularly subject to bias. Briefly describe the measures to be taken to avoid bias. For example: psychological measurements can be made by an individual blinded to the subjects group assignment or outcome, charts can be reviewed without knowledge of outcome.

6.3.1 Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive statistics (including mean and standard deviation for continuous variables such as age and standard percentages for categorical variables such as gender).

6.3.2 Analysis of Primary Outcome of Interest

Describe the primary analysis.
For Example: The paired t-test will be used to compare differences in weight gain for the 2 months prior to surgery and the 2 months after surgery.

6.3.3 Pharmacokinetic Analysis (only if applicable)

Describe any pharmacokinetic parameters to be assessed. Note this could also be an ancillary study with a separate shortened protocol.

6.3.4 Interim Analysis (only if applicable)

Include details of any interim or safety analyses that are planned. Stopping rules for efficacy and/or safety should also be included here, if applicable.

7 Safety and Adverse Events

This section provides the safety management plans for the study. This section should be consistent with the UCLA IRB guidelines tailored to the requirements specific for each study. It should describe how safety reporting will be monitored and take place over the course of the trial.

7.1 Definitions

7.1.1 Adverse Event

Study definition of an adverse event (AE). Can include the UCLA IRB definition of an adverse event unless there are some differences in the adverse event definitions for this particular study. Standard definition of an adverse event as follows:
An adverse event (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event

- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

7.1.2 Serious Adverse Event

Study definition of serious adverse event. Potential definition that may be used if applicable:
Serious Adverse Event
Adverse events are classified as serious or non-serious. A serious adverse event is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- required intervention to prevent permanent impairment or damage
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as non-serious adverse events.

7.2 Recording of Adverse Events

The study investigator is ultimately responsible for the recording, and reporting, adverse events, which occur during the study. Define the time period of adverse event collection for the study (typically from study intervention start to end of the study), who will be collecting adverse events, how they will be recorded and tracked and who will review them. The plans with adverse event reporting should be consistent with the UCLA IRB guidelines.

For example: At each contact with the subject, the investigator will seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events will be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should be recorded in the source document, though should be grouped under one diagnosis.

All adverse events occurring during the study period will be recorded. The clinical course of each event will be followed until resolution, stabilization, or until it has been determined that the study intervention or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period will be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study intervention or study participation will be recorded and reported.

7.3 Relationship of AE to Study

The relationship of each adverse event to the study procedures should be characterized. This section should describe who will be making that determination (PI or medical monitor) and how relationship will be classified (definitely related, probably related, possibly related, unlikely or unrelated).

7.4 Reporting of Adverse Events and Unanticipated Problems

This section describes the requirements for reporting specific types of unanticipated problems, including adverse events. For UCLA reporting requirements and timelines refer to the following for UCLA IRB definition of reportable events and reporting timelines. https://ohrpp.research.ucla.edu

Include details in this section as to how and to whom adverse events will be reported.

For example:
The Investigator will promptly notify the UCLA IRB of all on-site unanticipated, Adverse Events that are related to the research activity. Other unanticipated problems related to the research involving risk to subjects or others will also be reported promptly. Written reports will be filed using the webIRB and in accordance with the UCLA IRB timeline of 10 working days.

7.4.1 Follow-up Report

Describe in this section how AEs will be followed up after initial report and which AEs will warrant a follow up report.

For example: If an AE has not resolved at the time of the initial report and new information arises that changes the investigator's assessment of the event, a follow-up report including all relevant new or reassessed information (e.g., concomitant medication, medical history) should be submitted to the IRB. The investigator is responsible for ensuring that all SAEs are followed until either resolved or stable.

7.4.2 Investigator reporting: notifying the study sponsor (if applicable)

Reporting to the study sponsor should be consistent with regulatory and or sponsor requirements for the study (if applicable). Include any details about requirements of reporting to funding agency, if applicable. Reporting to the UCLA IRB will follow UCLA IRB reporting timelines regardless of requirements to report to the sponsor.

7.4.3 Data and Safety Monitoring Plan

Describe the safety and monitoring plan for the study. Include the processes in place to identify any potential risks to research subjects and protect them during the execution of the trial. This plan should be tailored to the specific risk level of the study, study intervention and nature of the disease. The plan should provide oversight for emerging safety information and could include one or more of the following:

- *Principal Investigator Monitoring*
- *Medical monitor associated with the sponsor of the study (if applicable)*
- *Independent Safety Monitor (if applicable)*
- *Internal Steering Committee or Internal Data Monitoring Committee that is made up of representative from the sponsor and the study investigators (if applicable)*
- *Data Safety and Monitoring Board (DSMB) or a Data Monitoring Committee (DMC) made up of representative who are independent of the study sponsor and investigators (if applicable)*

7.4.3.1 Data Safety Monitoring Board (if applicable)

Certain studies (late Phase 2 and Phase 3 trials particularly for life-threatening diseases) require a DSMB or DMS. If a DSMB will be employed in the study use this section to include details about how the DSMB will operate, composition of its members, and how the interim analyses will be performed and when. This can also refer to an attached DSMB charter.

8 Study Administration, Data Handling and Record Keeping

8.1 Confidentiality

Potential language to include in this section included below. This section should be modified to fit your study.

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

Remember all PHI that is collected should be listed within the consent form. This includes the following

1. *Names*
2. *All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.*
3. *All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;*
4. *Phone numbers;*
5. *Fax numbers;*
6. *Electronic mail addresses;*
7. *Social Security numbers;*
8. *Medical record numbers;*
9. *Health plan beneficiary numbers;*
10. *Account numbers (CSN, HAR, Account, etc.);*
11. *Certificate/license numbers;*
12. *Vehicle identifiers and serial numbers, including license plate numbers;*
13. *Device identifiers and serial numbers;*
14. *Web Universal Resource Locators (URLs);*
15. *Internet Protocol (IP) address numbers;*
16. *Biometric identifiers, including finger and voice prints;*
17. *Full face photographic images and any comparable images; and*
18. *Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)*

8.2 Data Collection and Management

Describe the system for maintaining primary records and case report forms and the entering of the study data into computerized systems for analysis.

How will the confidentiality of the data be ensured, from abstraction through analysis? Describe this process in detail. Example 1: One method for this would be to keep a master list containing PHI and subject ID numbers separate from any data forms, whether they be paper or electronic. The master list should be on a separate computer, removable USB drive or locked filing cabinet. [Note: This type of data is considered to be coded and not de-identified. De-identified data no longer has any identifiers and cannot be linked back to the participant. Coded data can be linked back with a key.]
Another method is to use password protected files such as within Excel. Data files can also be encrypted.

Include details about the security of the data and how the data will be de-identified. Provide a specific plan for removing identifiers that meets the needs of the study and the potential future uses of the data. For example: The identifiers will be destroyed after publication. The other data will be retained for five years. This laboratory maintains a file drawer specifically for such archives, each folder labeled destroy by with a date.
Be sure that data retention procedures meet the requirements of the study sponsor, if applicable.

8.3 Records Retention

Summarize the record retention plan applicable to the study (taking into account any applicable UCLA Department, Division or Research Center requirements, or applicable funding sponsor requirements.)

9 Study Monitoring, Auditing, and Inspecting

9.1 Study Monitoring Plan

Describe what level of monitoring will take place for this particular study. May be sufficient to say the study PI will be responsible for ensuring the ongoing quality and integrity of the research study. It may be appropriate to attach an additional monitoring plan document along with the protocol when submitting to the IRB.

9.2 Auditing and Inspecting

For example: The investigator will permit study-related monitoring, audits, and inspections by the EC/IRB, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

10 Ethical Considerations

Describe relevant regulation which will be followed in this particular study (if applicable). Describe the process for review and approval of the protocol, amendments and continuing reviews through the UCLA IRB and other appropriate reviewing entities.

10.1 Risks

Describe the risks associated with participating in the research. Standard of care risks do not need to be discussed in this section unless the study product is combined/ used in conjunction with the standard of care in a way, which could elicit risks associated to this combination OR if forms of standard of care testing are being compared describe any foreseeable risks. For example, a standard of care that at least some of the individual subjects will be assigned to receive will be different from the standard of care they would receive if they were not participating in the study or different risks that might be associated with being assigned to one of two types of standard of care. This would not apply for observational studies of two types of standard of care.

Discuss the risks of each procedure or interaction in terms of magnitude or harm. Consider all risks: physical, emotional, economic, psychological or societal harms that may accrue to others not in the trial (e.g. a group in general or finding from genetic study that may have an impact on a family line).
Address how the study is designed to minimize the risk of harm to all subjects participating.

10.2 Benefits

Summarize the potential benefits, if any, from trial participation. Benefits should be broken down into those, which are direct benefits (to the subject directly from participating) and indirect benefits (benefits to individual or society as a hole in the future).

10.3 Risk Benefit Assessment

The Risk Benefit Assessment should include a justification for proceeding with the trial based on the perceived balance between the risks and benefits, i.e. the risks of participating in the study are outweighed by the potential benefits of participating in the study.

10.4 Informed Consent Process / HIPAA Authorization

Describe the procedures that will be used to obtain informed consent/ HIPAA Authorization. Include: who will obtain consent, where will consent process take place, how privacy will be assured, how much time subjects will be permitted to make a decision, how the investigators will assure that subjects comprehend the nature of the study, the study procedures and the risks and benefits of participation, steps that will be taken to avoid coercion and documentation of consent. Be sure to make the distinction between any consent process that may be different between prescreening, screening and the study intervention/ observational phase. Also, include whether a standalone HIPAA Authorization will be used or a combined consent-authorization document. It is recommended that the IRB template combined consent/HIPAA authorization be used click here

For example: All subjects for this study will be provided a consent form describing this study providing sufficient information for subjects to make an informed decision about their participation in this study. See Attachment [include attachment number here] for a copy of the Subject Informed Consent Form. This consent form will be submitted with the protocol for review and approval by the IRB for the study. The formal consent of a subject, using the IRB-approved consent form, must be obtained before that subject undergoes any study procedure. The subject, or legally acceptable surrogate, must sign the consent form, and the investigator-designated research professional obtaining the consent. Subjects will be consented by the study Principal Investigator, or appropriate designee, in a room we have selected in which to perform consent, which is located outside of the clinic. Potential subjects will review the consent form in detail with the person designated to consent (either PI or key study personnel) and have the ability to take the consent home for further review.

10.4.1 Alterations to Typical Consent Process (only include if applicable)

10.4.1.1 Waiver of Consent (In some cases for screening/portions of that study that qualify as minimal risk, a waiver of documentation of consent may be permissible IRB SOP)

Waiver or alteration of required elements of consent: According to HHS CFR 45.46.116(d): An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent. In order to qualify for a waiver or alteration to the informed consent process, please justify each of the following:

- *the research involves no more than minimal risk to the subjects;*
- *the waiver or alteration will not adversely affect the rights and welfare of the subjects;*
- *the research could not practicably be carried out without the waiver or alteration; and*
- *whenever appropriate, the subjects will be provided with additional pertinent information after participation.*

10.4.1.2 Waiver of Written Documentation of Consent

Waiver of written documentation of informed consent: According to HHS CFR 45.46.117(c)(1), an IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

10.4.1.3 Waiver of HIPAA Authorization

In order for the UCLA IRB to waive the HIPAA authorization the following criteria must be met pursuant to 45 CFR 164.512(i)(1)(i)
A statement that the IRB has determined that the alteration or waiver, in whole or in part, of authorization satisfies the following criteria:

- *The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:*
  (1) an adequate plan to protect the identifiers from improper use and disclosure;
  (2) an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
  (3) adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;
- *The research could not practicably be conducted without the waiver or alteration; and*
- *The research could not practicably be conducted without access to and use of the protected health information.*

11 Study Finances

11.1 Funding Source

This section should describe how the study will be financed, but should not contain specific dollar amounts (e.g. "This study is financed through a grant from the US National Institute of Health", or "… a grant from the American Heart Association", etc.)

11.2 Conflict of Interest

All UCLA Investigators will follow the university policy. https://rpc.research.ucla.edu/coi/

Subject Stipends or Payments
Describe any subject stipend or payment here. If there is no subject stipend/payment, either delete this section or state that there are no subject payments or stipends.
Examples of payments:

- *Reimbursement for time, travel, parking, meals, etc.*
- *Gifts- any tokens of appreciation given to a research subject, or their family, should be described here*
- *Payment to the subject for time, effort or inconvenience of being in the trial*
- *Payment to subject family for time effort to r inconvenience of being in the trial*

12 Publication Plan

This section should include the requirements of any publication policies of the University, Department, Division or Research Center. If this is a multi-site study or the UCLA investigator will not have full access to the data set include that information here in the context of how it will impact the publication and presentation plans.

13 References

This is the bibliography section for any information cited in the protocol. It should be organized as any standard bibliography.

1. Author, Title of work, periodical and associated information.
2. Author, Title of work, periodical and associated information.

14 Attachments

This section should contain all pertinent documents associated with the management of the study. The following lists a few examples of potential attachments but is in no way exhaustive:

- *Sample Consent Form*
- *Study Procedures Flowchart/Table*
- *Study Monitoring Plan*
- *Specimen Preparation And Handling (e.g. for any specialized procedures that study team must follow to process a study specimen, and/or prepare it for shipment)*
- *Recruitment Materials*
- *Screening Scripts*
- *Study questionnaires*

15 Appendices

15.1 EXAMPLE: Table 1: Schedule of Study Procedures

Study Phase	Screening	Observation Study Visits		
Visit Number		1	2	3
Study Days				
Informed Consent/Assent	X			
Review Inclusion/Exclusion Criteria	X			
Vital Signs: BP, HR, RR	X			
Height and Weight	X			
Pregnancy Test	X			
Prior/Concomitant Medications	X			
Clinical Laboratory Evaluation	X			
Adverse Event / Unanticipated Problems Assessment				

This table is an example of a schedule of procedures. The Investigator should construct a table based on the procedures in the protocol. If the study involves more than 1 or 2 visits, it is often preferable to include this table as an Appendix to the Consent Form. This simplifies the consent form.