**STUDY PROTOCOL TEMPLATE FOR**

**INVESTIGATOR INITIATED NON-INTERVENTIONAL STUDIES**

**PREFACE:**

Instructions: Protocols should be formatted according to the following outline and include all of the elements indicated, as applicable. Remove this preface before finalizing and distributing the clinical study protocol. Also remove the blue-colored writing which is only for guidance.

This IIT study protocol template is a suggested format for the investigator initiated studies at TJU that does not involve any interventions. Investigators for such studies are encouraged to use this template when developing protocols. The goal of this template is to assist investigators to write a comprehensive protocol that meets the standards outlined in the ICH-E6 guidance (GCP) and FDA regulations relating to clinical research. If the study is recruiting patients from a clinical setting, even though for observational purposes, then the study is clinical research. All clinical research must be run as per the GCP and FDA regulations. Clinical studies should be scientifically sound and described in a clear, detailed protocol and the study must be conducted in compliance with the protocol that has received IRB approval.

# THOMAS JEFFERSON UNIVERSITY

# Sidney Kimmel Cancer Center

<**Insert Protocol Title**>

|  |  |
| --- | --- |
| **Principal Investigator:** | Insert the name of the principal investigator  Insert department name  Insert address  Insert phone number |
| **Co-Investigator(s** | Insert the name of the co-investigator(s)  Insert department name  Insert address  Insert phone number |
| **Statistician:** | Insert the name of the statistician  Insert department name  Insert address  Insert phone number |
| **Funding Sponsor:** | Insert the name of primary funder (if applicable)  Insert address  Insert phone number |
| **Protocol IDs:** | Jeff Trial # pending (if applicable)  PRC # pending  IRB Control # pending |

**NOTICE: delete this text box before finalizing the protocol.**

Delete all instructions once protocol is finalized.

Delete all unused sample text once protocol is finalized.

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| **Version**  **Number** | **Version Date:** |
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# Signature Page

For multi-site studies, the protocol will be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site.

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator

Signed: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

<enter PI’s name here>

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

I’<<enter PI’s title here>

Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

# Statement of Compliance

This study will be conducted in accordance with the International Conference on Harmonisation guidelines for Good Clinical Practice (ICH E6), the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and Thomas Jefferson University research policies

List of Abbreviations(if any; please edit the following list as per your study specifications)

|  |  |
| --- | --- |
| CFR | Code of Federal Regulations |
| CIOMS | Council for International Organizations of Medical Sciences |
| CRF | Case Report Form |
| CRO | Clinical Research Organization |
| FDA | Food and Drug Administration |
| FWA | Federalwide Assurance |
| GCP | Good Clinical Practice |
| GWAS | Genome-Wide Association Studies |
| HIPAA | Health Insurance Portability and Accountability Act |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonisation |
| MOP | Manual of Procedures |
| N | Number (typically refers to participants) |
| NCI | National Cancer Institute |
| NIH | National Institutes of Health |
| OHRP | Office for Human Research Protections |
| PHI | Protected Health Information |
| PI | Principal Investigator |
| PRC | Protocol Review Committee |
| QA | Quality Assurance |
| QC | Quality Control |
| SKCC | Sidney Kimmel Cancer Center |
| SOP | Standard Operating Procedure |
| TJU | Thomas Jefferson University |
| UAP | Unanticipated Problem |

# STUDY SYNOPSIS

|  |  |
| --- | --- |
| Title: | |
| SUMMARY | **<A brief overview of the study design, including study groups, schedule of evaluations and/or schedule for specimen or data collection, and analysis to be performed.>** |
| Objectives | **<Insert objectives copied from the body of the protocol. Include the primary objective and secondary objectives and specify their outcome measures.>**  **Primary:**  **Secondary:** |
| Population | **<Population information, including sample size, gender, age, demographic group, general health status, geographic location.>** |
| Number of sites | **<Insert a list of sites>** |
| Methodology | **<a Brief description of the study – what hypothesis is being addressed and what’s being used to address it >** |
| Duration of the study | **<Estimated time (in months) from when the study opens to enrollment until completion of data analyses.>** |
| Participant Duration | **<Time it will take to conduct the study for each individual participant.>** |
| Estimated Time to complete enrollment | **<Estimated time from enrollment into study of the first participant to enrollment into the study of the last participant.>** |

# STUDY SCHEMA

The diagram below shows the preferred format and the level of detail needed to convey an overview of study design. Complete each text box with study-specific information and adapt the diagram to illustrate your study design (e.g., changing method of assignment to study group, adding study arms, visits, etc.). The time point(s) indicated in the schematic must correspond to the time point(s) in the protocol, Study Schedule, e.g., Visit 1, Day 0; Visit 2, Day 30 ± 7; etc.}

Prior to

Total N: Obtain informed consent. Screen potential subjects by inclusion and exclusion criteria; obtain history that’s applicable, document.

Enrollment

Randomize *(if applicable)*

Perform baseline assessments.

(*list specimens to be collected, examinations or imaging or laboratory assays to be performed, questionnaires to be completed*)

Administer initial study assessments.

Visit 1

Time Point

Visit 2 and

Repeat study assessments (*if applicable*).

other

Time Point

**Final Assessments if applicable**

*List analyses to be performed*

Visit X

Time Point

# 1. INTRODUCTION

## 1.1 BACKGROUND INFORMATION

This section is to include brief background information for this study. It will not be a copy of the background information from a grant application.

Include:

* A brief description of the health problem that the study will address
* A brief description of the study’s overall goal
* Applicable clinical, epidemiological, or public health background or context of the study

<Insert text>

## 1.2 RATIONALE FOR THE PROPOSED STUDY

Include a description of, and justification for, study assessments and/or procedures and selection of study population. Include a statement of the hypothesis.

<Insert text>

## 1.3 POTENTIAL RISKS AND BENEFITS

Include a discussion of known risks and benefits, if any, to human participants. Be sure that information in these sections is consistent with your consent document.

<Insert text>

## 1.3.1 Potential Risks

Describe in detail any physical, psychological, social, legal, economic, or any other anticipated risks to study participants. Include risks of study procedures.

One or more of the following may serve as the source of risk information:

{Begin sample text}

* *To protect patient information, we will minimize patient identifiers by assigning each participant with a unique code. All data generated in the study will be stored in RedCap with the unique code; the list of the unique codes will be maintained on secure servers, accessible to key research personnel only. However, there are no guarantees and there is always a risk that PHI could get released into public view.*

## 1.3.2 Potential Benefits

If the research is beneficial, describe any physical, psychological, social, legal, or any other anticipated benefits to participants. While it may not provide direct benefit to participants, the importance of the knowledge that may result from the study may be mentioned.

Note: Compensation to participants is not considered a “benefit.”

<Insert text>

## 1.3.3 Risk-Benefit Ratio

If possible, discuss the risk-benefit ratio of the study. 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.

**2.** STUDY OBJECTIVES & ENDPOINTS (SPECIFIC AIMS)

## 2.1 OBJECTIVES

Provide a detailed description of the one primary objective and any secondary objectives of the study. An objective is the reason for performing the study in terms of the scientific question to be answered (it is often written as the Aim in NIH grants). The primary objective is the main question. This objective generally drives statistical planning for the study (e.g., calculation of the sample size to provide the appropriate power for statistical testing). Secondary objectives are goals that will provide further information.   
Express each objective as a statement of purpose (e.g., to assess, to determine, to compare, to evaluate) and include the general purpose and/or specific purpose.

Add a subsection of hypothesis driving the objective, before or after the Objective statement. Alternatively, you can add a separate sub-section for Hypothesis.

<Insert text>

## 2.1.1 Hypothesis

## 2.1.2 Primary Objectives

<Insert text>

## 2.1.3 Secondary Objectives

<Insert text>

## 2.1.4 Exploratory Objectives

<Insert text>

## 2.2 ENDPOINTS/OUTCOME MEASURES

This section will include the methods for assessing how the objectives are met, i.e., the study outcome measures.

Outcome measures should be prioritized and will correspond to the study objectives and hypotheses being tested. Give succinct but precise definitions of the outcome measures used to address the study’s primary objective and key secondary objectives. Include the study visits or time points at which data will be recorded or samples will be obtained, if applicable.

<Insert text>

## 2.2.1 Primary Endpoints

Generally, there must be just one primary outcome measure that will provide a clinically relevant, valid, and reliable measure of the primary objective. Additional measures may require an adjustment to the sample size calculations and p-value threshold.

<Insert text>

## 2.2.2 Secondary Endpoints

Describe secondary outcome measures, whether they add information about the primary objective or address secondary objectives. Discuss their importance and role in the analysis and interpretation of study results.

<Insert text>

## 2.2.3 Exploratory Endpoints

<Insert text>

# 3. STUDY DESIGN

The scientific integrity of the study and the credibility of the data from the study depend substantially on the study design. Include a brief paragraph or bulleted text describing the study design. This section will include:

Present the Recruitment Plan and Study Design:

-Brief description of the study.

-Number of Subjects and brief description of the study population (– eg., healthy/sick, students, demographic groups, inpatient/outpatient etc)

-Number of study groups/arms and description thereof (include a table, if appropriate). Description of methods to be used to minimize bias (if any). How will arm assignment be done?

-Single or multisite

-Identification and specifics of the participants. Method of Contact and Consent (how will the subjects be approached and consented – will it be on telephone only, in person etc). How would participants be recruited?

-Method of Interaction/Procedure, randomization. Planned variation in schedule (eg. Visits can occur ±3days)

-Approximate time to complete study enrollment.

-How long will each subject participate including followup, if any.

-Describe the study methodology – the sequence of events and duration of all study periods, including participant’s followup, if applicable. Details of the study visits will be included in later **section 6**.

-Brief summary of methods for collecting data for assessment of the study objectives (details in **Section 6**).

-Survey Instruments – For each Instrument address the following: What are they? Under what conditions will they be administered (e.g. phone, face-to-face in private clinic area, self-administered at home or in clinic, when patient is visiting the doctor). How long will each instrument take/How much time the subjects have to complete and submit the questionnaires?

-End of study definition (Mostly, a study is considered closed when participants are no longer being examined or last participants last study visit is completed.)

# 4. STUDY ENROLLMENT AND WITHDRAWAL

In the following subsections, define the study population, describe participant recruitment, and discuss issues related to participant withdrawal. Address the following in these subsections as applicable:

-Provide the target sample size; identify anticipated number to be screened in order to reach the target enrollment.

-Specify approach(es) for conforming with NCI policy on inclusion of women and minorities. Include numbers of women and minorities expected to be recruited, or provide justification if women and/or minorities will not be recruited.

-Indicate from where the study population will be drawn (e.g., inpatient hospital setting, outpatient clinics, student health service, or general public). Where appropriate (single center studies), include names of hospitals, clinics, etc.

-If the study intends to enroll children, pregnant women, prisoners, or other vulnerable populations, refer to applicable section of 45 CFR Part 46 Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (45 CFR Part 46.201-46.207); Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (45 CFR Part 46.301-46.306); Subpart D – Additional Protections for Children Involved as Subjects in Research (45 CFR Part 46.401-46.409). Please refer to these regulations and Office for Human Research Protections (OHRP) guidelines when choosing the study population. Note that these regulations apply if any participants are members of the designated population even if it is not the target population (for example, if a participant becomes a prisoner during the study). Refer to: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html> <http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm>

If this is a multisite study, please specify all possible details for subsites as well – eg. how will enrollment at the subsites be recorded, must they report to TJU within 24hrs via phone or email and give a timeline of potential dates etc.

## 4.1 ELIGIBILITY CRITERIA

Use the following guidelines when developing participant eligibility criteria:

-The eligibility criteria must provide a definition of participant characteristics required for study entry.

-The same criterion should not be listed as both an inclusion and exclusion criterion (e.g., do not state age >32 years old as an inclusion criterion and age ≤32 years old as an exclusion criterion).

-Identify specific laboratory tests or clinical characteristics that will be used as criteria for enrollment.

-If reproductive status (i.e., pregnancy, lactation, reproductive potential) is an eligibility criterion, provide specific contraception requirements (e.g., licensed hormonal methods).}

## 4.1.1 INCLUSION CRITERIA

List each criterion.

Individuals must meet all of the following inclusion criteria in order to be eligible to participate in the study:

{Begin sample text}

* Provide signed and dated informed consent form
* Consider whether or not your study can enroll non-English speaking participants (eg. If questionnaires are in English only, then only English speaking participants can enroll).
* Willing to comply with all study procedures and be available for the duration of the study
* Any individual >18 years old
* In good general health as evidenced by medical history or Diagnosed with specific condition/disease or Exhibits specific clinical signs or symptoms or physical/oral examination findings
* Laboratory results within a specific range
* Women of reproductive potential must use highly effective contraception {specify methods of contraception acceptable for the study, e.g., licensed hormonal methods.}
* Men of reproductive potential must use condoms

{End sample text}

## 4.1.2 EXCLUSION CRITERIA

List each criterion.

An individual who meets any of the following criteria will be excluded from participation in this study:

{Begin sample text}

* Medical condition, laboratory finding, or physical exam finding {specify, e.g., vital signs outside of specific range} that precludes participation
* Use of disallowed concomitant medications {specify}
* Presence of <specific devices (e.g., pace maker)
* Recent febrile illness that precludes or delays participation {specify time frame}
* Pregnancy or lactation
* Known allergic reactions to components of the study product(s)
* History of or current tobacco, drug or alcohol use {define parameters for exclusion}
* Anything that would place the individual at increased risk or preclude the individual’s full compliance with or completion of the study.
* {End sample text}

## 4.2. PERMITTED MEDICATIONS/LIFESTYLE CONSIDERATIONS - if applicable

Describe any dietary or lifestyle restrictions participants must adhere to, during any parts of the study or for the entire duration of the study (e.g., food and drink restrictions, timing of meals relative to dosing, intake of caffeine, alcohol, or tobacco, or limits on activity). Describe what action will be taken if prohibited medications, treatments or procedures are indicated for care (e.g., early withdrawal). Include details about when the information will be collected.

Please make sure this section is consistent with the dietary/lifestyle/medication restrictions in inclusion-exclusion criteria. Describe the data that will be recorded – concomitant medications (eg. Herbal supplements, pain meds, dosage if applicable, start and end dates of the medications etc)

Describe how allowed concomitant therapy might affect the outcome (e.g., drug-drug interaction, direct effects on the study endpoints) and how the independent effects of concomitant and study procedures could be ascertained.

Example text provided as a guide, customize as needed:

*During this study, participants are asked to:*

* *Refrain from consumption of Seville oranges, grapefruit or grapefruit juice, from [X days] before the start of <study > until after the final dose.*
* *Abstain from caffeine- or xanthine-containing products (e.g., coffee, tea, cola drinks, and chocolate) for [x hours] before the start of each dosing session until after collection of the sample.*
* *Abstain from alcohol throughout the study period.*
* *Participants may participate in light recreational activities during studies (e.g., watching television, reading) but abstain from strenuous e rcise for [x hours] before each blood collection for clinical laboratory tests.*

## 4.3. STRATEGIES FOR RECRUITMENT AND RETENTION

Identify strategies for participant recruitment and retention. Briefly mention how subjects will be identified and approached. If subjects will be compensated for study participation, describe amount and schedule of payments.

Types of recruitment strategies planned (eg. Clinic itself, patient advocacy groups, local flyers, social media etc); specific names of advertising sites isn’t needed.

If the study requires long-term participation, describe procedures that will be used to enhance subject retention (e.g., multiple methods for contacting participants, visit reminders, incentives for visit attendance, etc.)

Include the number or approx. % of women and minorities expected to be recruited or provide justification for their exclusion.

<Insert text>

Eg. Potential research subjects will be identified by a member of the patient’s care treatment team, the investigator or a research team member. Investigators will then screen the patient’s medical records to determine the subject eligibility for study participation and discuss the study with the patient and their potential for enrolling in the research study. Consenting patients will be screened based on the inclusion/exclusion criteria above.

In addition, if applicable, this section should include justification for inclusion of vulnerable participants and recruitment and retention strategy. Vulnerable participants include, but are not limited to, pregnant women, those who lack consent capacity, including the mentally ill, prisoners, cognitively impaired participants, children, and employee volunteers. Include safeguards for protecting vulnerable populations. Please refer to OHRP guidelines when choosing the study population. Note that these regulations apply if any participants are members of the designated population, even if it is not the target population (e.g., if a participant becomes a prisoner during the study or woman becomes pregnant during the study).

## 4.4 SCREEN FAILURES/PARTICIPANT DISCONTINUATION/PARTICIPANT WITHDRAWAL

## Reasons for Withdrawal

Provide a list of reasons participants may be withdrawn from the study. It may be appropriate to provide distinct discontinuation criteria for participants and cohorts. If so, both sets of criteria will be listed separately and the distinction between the two must be stated clearly. Also note that participants may withdraw voluntarily from participation in the study at any time.

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may terminate a study participant’s participation in the study if:

* Any clinical event, laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant.
* The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.
* Study ends or is terminated.

## 4.5 PREMATURE TERMINATION OR SUSPENSION OF STUDY

List possible reasons for termination or suspension of the study, e.g., study closure based on principal investigator (PI) decision, or PRC decision. For any study that is prematurely terminated or suspended, the PI will promptly inform the IRB and provide the reason(s) for the termination or suspension.

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to <investigator, funding agency, sponsor and regulatory authorities>. If the study is prematurely terminated or suspended, the principal investigator will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination include, but are not limited to:

* Insufficient adherence to protocol requirements.
* Data that is not sufficiently complete and/or evaluable.
* Determination of futility.
* Withdrawal of funding

5. STUDY METHODOLOGY / ADMINISTRATION OF SURVEYS

This section describes the study methodology/evaluations and controls.

Describe procedures, evaluations and labs that will be needed as part of this study or as prerequisite.

Describe the study questionnaires that will be used. Describe the procedures for collection of all study data including clinical observations, lab results, biospecimen, images, and questionnaire responses.

Some procedures may be part of regular standard of care but required as part of study. Please specify the procedures that will be completed during the study and specify which will be standard of care and which will be part of research study. Describe the procedures/evaluations with reference to and consistent with the information in Schedule of Assessments in Appendix A.

For correlative studies, information about specimen preparation and handling and shipping needs to be specified; for questionnaires studies, information regarding how the questionnaires will be administered needs to be specified, their duration etc. needs to be specified. Also specify, who will handle (the specimen or questionnaires or other information obtained) and briefly describe how it will be done.

Mention if Patients will be compensated. Also address the following:

- Are subjects being paid? How much?

- If they do not complete the entire study, will they receive partial payment, at what timepoints and how is that determined?

- Will they be compensated for travel/parking?

## 5.1 STUDY PROCEDURES/EVALUATIONS

List and describe all study procedures and evaluations to be done as part of the study. Examples include:

- Medical history (describe what is included for history, e.g., time-frame considerations, whether from medical records using EPIC etc).

- Medications history (e.g., describe if a complete medications history is needed, or if only currently taken medications should be included; prescription medications only or also over-the-counter). Assessment of eligibility should include a review of permitted and prohibited medications.

- Physical examination (list the vital signs [including height and weight, temp, BP, pulse etc] and organ systems to be assessed. Address details in the MOP.); if appropriate, discuss what constitutes a targeted physical examination and at what visits it may occur.

- Radiographic or other imaging assessments.

- Biological specimen collection.

- Administration of questionnaires or interview and/or focus guides or other instruments. Eg. Paper-pencil or will an ipad be used to administer the questionnaire and it will take about 20 minutes to be completed…etc.

- Observation and coding of participant behaviors

<Insert text>

## 5.2 LABORATORY PROCEDURES (if applicable)

### **Special Assays or Procedures**

List special assays or procedures required to assess the effect (e.g., immunology assays, pharmacokinetic studies, images, flow cytometry assays, microarray, DNA sequencing). For research laboratory assays, include specific assays, estimated volume and type of specimen needed for each test. For procedures, provide special instructions or precautions or refer to the study’s MOP. If more than one laboratory will be used, specify which assays will be done by each laboratory.

<Insert text>

## 5.2.1 SPECIMEN PREPARATION, HANDLING, AND STORAGE (if applicable)

Special instructions for the preparation, handling, and storage of specimens must be explained clearly in this section (or refer to the study’s MOP), including specific time requirements for processing, required temperatures, aliquots of specimens, where they will be stored, and how they will be labeled. If possible, also include who will have access to the specimen.

<Insert text>

## 5.2.2 SPECIMEN SHIPMENT/ANALYSIS PLAN (if applicable)

If there is specimen to be obtained from other sites or investigators, please describe here what will be shared, how frequently, and to what address should samples be sent. In addition, note where approaches to decrease variability, such as centralized laboratory assessments, are being employed. Include details such as days, time, address, to be shipped on dry ice or wet if specimen is being transferred and provide a specimen log along with (create as one of the Appendices, if applicable). If specimen data is being shared, please describe how frequently and how it will be shared (deidentified data on secure server).

If specimens will be retained after the study is completed, include provisions for consent and the options that are available for the participant to agree to future use of his/her specimens, images or recordings. Specify who will have access, the location, duration of storage, and protections of confidentiality for any future studies (eg. Specimen will be coded, deidentified, identifying information will be redacted from the reports etc). Include statement whether or not genetic testing will be done. And mention if the specimen will be destroyed at the end of this study or retained for future research purposes.

See also Section 11 – Data Handling, Record keeping, Confidentiality and Privacy

Example text provided as a guide, customize as needed:

*With the participant’s approval and as approved by local Institutional Review Boards (IRBs), biological samples will be stored at the <specify name of Biosample Repository> with the same goal as the sharing of data with the <specify name of Data Repository>. These samples could be used to research the causes of <specify condition(s)>, its complications and other conditions for which individuals with < specify condition(s)> are at increased risk, and to improve treatment. The <specify name of Repository> will also be provided with a code-link that will allow linking the biological specimens with the phenotypic data from each participant, maintaining the blinding of the identity of the participant.*

*During the conduct of the study, an individual participant can choose to withdraw consent to have biological specimens stored for future research. However, withdrawal of consent with regard to biosample storage may not be possible after the study is completed.*

*All sites outside to TJU should send the specimen on <dry ice> to the below mentioned xyz address*

*ATTN: Observational research study*

*XYZ*

*Philadelphia PA 19107*

*Biologic specimens collected during the conduct of the study that are not used during the course of the study will be stored in the Department of XYZ at Jefferson until completion of the study.*

# 6. STUDY SCHEDULE OF ACTIVITIES:

Discuss the sequence of events that should occur during the screening process and any decision points regarding participant eligibility. Include the time frame prior to enrollment within which screening procedures/ evaluations, if any, must be performed (e.g., within 28 days prior to enrollment).

The specific timing of procedures/evaluations at corresponding study visits must also be captured in Appendix A, Schedule of Assessments (SoA). In addition, indicate where appropriate, that procedures/evaluations will be performed by qualified personnel.

## 6.1 SCREENING

Discuss evaluations/procedures necessary to assess or confirm whether an individual still meets the eligibility criteria and may be enrolled, and specify what will be recorded at baseline for later outcome measure comparison (e.g., baseline signs and symptoms prior to treatment, review of medical records). Discuss the sequence of events that will occur during enrollment and the decision points regarding eligibility. List any special conditions (e.g., results of the pregnancy test must be negative and available prior to and during the study). List the procedures/evaluations for the entire duration of the study (start-to-end). List the time frame prior to enrollment within which screening tests and evaluations must be done (eg., within 28 days prior to enrollment)

Confirm that the procedures listed are consistent with those included in the Schedule of Events (Appendix A).

This section must include instructions for obtaining signed informed consent. If screening procedures are required for eligibility (e.g., review of medical records, clinical examination, or laboratory tests), they may be performed under a separate screening consent form.

Confirm that the procedures listed are consistent with those included in the Schedule of Assessments (Appendix A).

<Insert text>

{Begin sample text}

**Screening Visit 0 (Day -28 to -1)** {include a window that is appropriate for the study}

* Obtain and document consent from potential participant on screening consent form.
* Review medical/dental history to determine eligibility based on inclusion/exclusion criteria.
* Review medications history to determine eligibility based on inclusion/exclusion criteria.
* Perform medical/dental examinations needed to determine eligibility.
* Collect blood/urine/saliva.
* Schedule study visits for individuals who are eligible and available for the duration of the study.
* Provide potential participants with instructions needed to prepare for first study visit {specify instructions to be provided}.

{End sample text}

If re-screening is allowed, please mention about it here, how many times and such details.

## 6.2 ON STUDY PERIOD

List each procedure or evaluation visit, including visit number and visit window. For each visit, list the procedures to be completed (in chronological order, if applicable).

Confirm that the procedures listed are consistent with those included in the Schedule of Assessments (Appendix A).

{Begin sample text}

***Visit 1, Day X ± Y***

{Repeat for each visit, providing a study-appropriate window for the visit.}

* *Record results of physical/dental, other applicable examinations.*
* *Collect blood/urine/saliva.*
* *Administer the <surveys, questionnaires, or interviews etc>.*

{End sample text}

## 6.3 END OF STUDY PROCEDURES

Define the conditions under which participants end of study visit can occur and then describe any special procedures/evaluations or instructions to the participant. If study results will be shared with participants, discuss when and how participants will receive this information.

Confirm that the procedures listed are consistent with those included in the Schedule of Assessments (Appendix A).

If participant withdraws early or investigator terminates participant participation, specify which of the procedures and evaluations required for the final study visit should be offered to the participant.

<Insert text>

{Begin sample text}

**Final Study Visit (Final Visit, Day X ± Y)**

* *Record results of physical or applicable examinations.*
* *Collect blood/urine/saliva.*
* *Administer final study <surveys, questionnaires, or interviews etc>*

{End sample text}

# 7. STATISTICAL CONSIDERATIONS

## 7.1 STUDY HYPOTHESES

If appropriate, state the formal, testable, null, and alternate hypotheses for the primary objective and key secondary objectives.

<Insert text>

## 7.2 ANALYSIS PLANS

Describe analyses for assessing the primary and secondary objectives.

Plans must clearly identify the analyses cohorts and methods to account for missing, unused or spurious data.

Discuss how outcome measures will be assessed and transformed, if relevant, before analysis. (Examples: Is the primary variable binary, categorical, or continuous? Will a series of measurements within a subject be summarized, such as by calculating the area under the curve?)

<Insert text>

## 7.3 SAMPLE SIZE CONSIDERATIONS

Provide all information needed to validate your calculations, and also to judge the feasibility of enrolling and following the necessary numbers of participants.

Consider applicable items from the following list when describing sample size determination:

* Statistical method used to calculate the sample size
* Outcome measure used for calculations (almost always the primary variable)
* Test statistic
* Type I error rate
* Type II error rate
* Method for adjusting calculations for planned interim analyses, if any
* Assumptions used in calculations:
  + Assumed event rate for dichotomous outcome (or mean or variance of continuous outcome) for each study arm, justified and referenced by historical data as much as possible
  + Assumed dropout rates, withdrawal, cross-over to other study arms, missing data, etc., also justified
  + Approach to handling withdrawals and protocol violations, i.e., to what extent data from withdrawn participants will be evaluable (e.g., whether participants will be included in the “intent-to-treat” population), whether withdrawn participants will be replaced

Present calculations from a suitable range of assumptions to gauge the robustness of the proposed sample size. Most assumptions are not accurate as point estimates.

Discuss whether the sample size also provides sufficient power for addressing secondary objectives or for secondary analyses in key subgroup populations.

<Insert text>

### **Accrual Estimates**

<Insert text>

## 7.4 EXPLORATORY ANALYSIS

<Insert text>

## 7.5 HANDLING SCREEN FAILURE/SUBJECT DISCONTINUATION

Describe how will premature withdrawal or screen failures of patients will be handled (statistics should be able to justify it too). Example text provided as a guide, customize as needed:

Example text provided as a guide, customize as needed:

*Patients, who prematurely withdraw before the end of the study, will be replaced by new patients to ensure an adequate number of patients completing the study, unless the reason for discontinuation is progression of disease.*

# 8. REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

## 8.1 ETHICAL STANDARD

If the study is conducted at international sites, the statement could be as above and/or could reference compliance with the Declaration of Helsinki, CIOMS, International Ethical Guidelines for Biomedical Research involving Human Subjects (2016), or another country’s ethical policy statement, whichever provides the most protection to human participants.

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45CFR Part 46 and/or the ICH-E6.

## 8.2 INSTITUTIONAL REVIEW BOARD

Each participating institution must provide for review and approval of this protocol and the associated informed consent documents and recruitment materials by an appropriate IRB registered with the OHRP. Any amendments to the protocol or consent materials must also be approved before they are placed into use. In the United States and in other countries, only institutions holding a current US Federalwide Assurance (FWA) issued by OHRP may participate. Refer to: <http://www.hhs.gov/ohrp/assurances> and modify as appropriate for a multi-site study.

The protocol, informed consent forms, recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both, the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

## 8.3 INFORMED CONSENT PROCESS

For some observational studies, no consents may be required. If there is no consent involved, please delete these instructions and move to next sub-section.

Identify different consent forms that are needed for the study (eg. Screening, study participation, future use of specimens, assent form minors).

When a study includes participants who may be enrolled in the study only with the consent of the participant’s legally authorized representative (eg. Minors or participants whose cognitive impairment is such that they are unable to give informed consent), the participant must be informed about the study to the extent compatible with the participant’s understanding. If capable, the participant will assent and sign and personally date in the written consent form. A separate IRB-approved assent form, describing (in simplified terms) the details of the study, study procedures, and risks may be used. Assent forms do not substitute for the consent form signed by the participants legally authorized representative.

If non-English speakers will be enrolled, state that a translated consent document will be available and an appropriate person will conduct the consent process. Consider other special circumstances such as low literacy, braille, or web-based consenting.

For multi-site study, each participating institution will be provided with a model informed consent form. Each institution may revise or add information to comply with the institution consent templates, but may not remove procedural or risk content from the model consent form. Adapt as needed for the specific study.

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to participants and their families, if applicable. A consent form describing in detail the study procedures and risks will be given to the participant. Consent forms will be IRB-approved, and the participant is required to read and review the document or have the document read to him or her. The investigator or designee will explain the research study to the participant and answer any questions that may arise. The participant will sign the informed consent document prior to any study-related assessments or procedures. Participants will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. The consent process will be documented in the clinical or research record.

## 8.4 EXCLUSION OF WOMEN, MINORITIES, AND CHILDREN (SPECIAL POPULATIONS)

Explain why any of these populations are excluded from the study participation, or state that individuals of any age, gender or racial/ethnic group may participate.

## 8.5 PARTICIPANT CONFIDENTIALITY

Include procedures for maintaining participant confidentiality and any special data security requirements. Describe who would have access to records, including the investigator and other study staff, the clinical monitor, representatives of the SKCC or other funding institutions, IRB representatives and regulatory representatives. For some studies, it may be necessary to obtain a Certificate of Confidentiality. A Certificate of Confidentiality protects researchers and research institutions from being forced to provide identifying information on study participants to any federal, state, or local authority. Authorization comes from NIH through section 301(d) of the Public Health Service Act [42 U.S.C. 241(d) which provides the Secretary of Health and Human Services the authority to protect the privacy of study participants. For additional information, see https://grants.nih.gov/policy/humansubjects/coc.htm

<Insert text>

{Begin sample text; include Certificate of Confidentiality and Data Sharing Policy text, only if applicable}

Participant confidentiality is strictly held in trust by the investigators, study staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to any study information relating to participants.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

The study monitor or other authorized representatives of the sponsor may inspect all study documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the study participants. The clinical study site will permit access to such records.

Certificate of Confidentiality (if applicable)

To further protect the privacy of study participants, a Certificate of Confidentiality will be obtained from the NIH. This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to participants.

NIH Data Sharing Policy for Genome-Wide Association Studies (GWAS) (if applicable)

This study is a genome-wide association study and will comply with the NIH Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, which calls for investigators funded by the NIH for GWAS to 1) share de-identified genetic (genotypic and phenotypic) data through a centralized NIH data repository; and 2) submit documentation that describes how the institutions have considered the interests of the research participants, such as privacy and confidentiality. Submission of data to the NIH GWAS repository will be consistent with the permissions and limitations delineated on the study consent signed by study participants.

{End sample text}

# 9. DATA HANDLING AND RECORD KEEPING

Source data are documents with all information, original records of findings, observations, or other activities in a study necessary for the reconstruction and evaluation of the study. Examples of these original documents and data includes, but are not limited to, questionnaires, surveys, interview notes, hospital records, clinical and office charts, lab results, memoranda, participants’ evaluation checklist, pharmacy dispensing records, recorded audio tapes of counseling sessions, recorded data from automated instruments, microfiches, photographic negatives, microfilm or magnetic media, x-rays, scans for the study. If it is acceptable to use CRFs as source documents, it should be stated in this section what data will be collected on CRFs and what data will be collected from other sources (and specify which other sources and each page of the CRF must be signed and dated by the investigator). If data is being obtained from EPIC, it should be specified here that data from EPIC will be printed and filed as source document for the particular visit.

Each participating site must maintain appropriate medical and research records for this study, in compliance with regulatory and institutional requirements for the protection of confidentiality of participants. For the purpose of quality assurance reviews, audits, and evaluation of the study safety, progress and data validity, regulatory agencies and authorized representatives must be permitted to examine the research records. Describe in this section who will have access to the records.

Include instructions for data handling or record-keeping procedures required for maintaining participant confidentiality (eg. data will be accessed by key research personnel only), any special data security or data transfer requirements, and record retention.

Briefly describe steps to be taken to ensure that the data collected are accurate, consistent, complete, reliable, and in accordance with ICH E6. The description will include reference to source documentation, CRFs, instructions for completing forms, data handling procedures, and procedures for data monitoring. Details may be provided in a MOP, a data management plan or other citable reference document.

<Insert text>

{Begin sample text – Edit as per your study}

Source data must be contained in designated source documents folders. Source data includes (but not limited to) all information, , observations, questionnaires, surveys, interview notes, original records of findings - hospital records, clinical and office charts, lab results, and, x-rays, scans for the study.

All entries should be printed legibly in black ink. The investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents must be completed in a neat, legible manner to ensure accurate interpretation of data.

All missing data must be explained. If any entry error has been made, to correct such as error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. Do not erase or white out errors.

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the regulatory bodies (eg. FDA), and University compliance and quality assurance groups of all study related documents (eg. Source documents, regulatory documents, data collection instruments, study data etc). The investigator will ensure the capability for inspections of applicable study-related facilities (eg. Pharmacy, diagnostic lab, etc).

The investigators will maintain adequate case histories of study participants, including accurate case report forms (CRFs), and source documentation.

{End sample text}

## 9.1 DATA MANAGEMENT RESPONSIBILITIES

Include a general description as in the sample text below and add study-specific details and information about the role of a data coordinating center, if applicable.

<Insert text>

{Begin sample text}

Data collection and accurate documentation are the responsibility of the study staff under the supervision of the investigator. All source documents and laboratory reports must be reviewed by the study team and data entry staff, who will ensure that they are accurate and complete. The investigator or designee must review unanticipated problems and deviations.

{End sample text}

## 9.2 DATA CAPTURE METHODS

Provide details regarding the type of data capture that will be used for the study. Specify whether it will be paper or electronic, distributed or central, batched or ongoing processing, and specify any related requirements (e.g., password protection and data quality checks for an electronic data system). Indicate expectations for time for submission of CRFs to a data coordinating center, if applicable.

<Insert text>

## 9.3 TYPES OF DATA

{Indicate the types of data that will be collected, such as safety, laboratory (clinical, immunology, other study specific), and outcome measure data (e.g., periodontal measurements, caries assessments, physical measurements, questionnaire responses). Specify if safety data are collected in a separate database.}

Describe any identifiable private information that will be collected. Describe if data to be collected contain any protected health information (PHI) and specify which PHI is to be collected and how the PHI will be protected.

Health information is considered PHI if it contains any of the following identifiers:

|  |  |  |
| --- | --- | --- |
| Name  Street address, city, county, precinct, zip code, and equivalent geocodes  All elements of dates (except year) for dates directly related to an individual and all ages over 89  Telephone numbers  Fax numbers  Electronic mail addresses | Social security numbers  Medical record numbers  Health plan ID numbers  Account numbers  Certificate/license numbers  Vehicle identifiers and serial numbers, including license plate numbers  Device identifiers/serial numbers | Web addresses (URLs)  Internet IP addresses  Biometric identifiers, including finger and voice prints  Full face photographic images and any comparable images  Any other unique identifying number, characteristic, or code |

Example of PHI language to be included provided as a guide, please customize as needed:

*[In order to contact patients and caregivers by telephone and by mail for the particular session activity purposes, it will be necessary to collect participants’ names, addresses, and telephone numbers. Sites must complete Contact order form and send via secure xxx system or hand it to the research study personnel. The contact and mailing addresses will be stored at a secure locked location accessible to key research personnel only and will be <destroyed/specify what will be done> upon completion of the study.*

*Each questionnaire takes about 10-15 minutes to be completed. The baseline questionnaires should be submitted within 15 days of screening visit; the first 6 months visit questionnaires must be submitted within ±21days]*

Schedule and Content of Reports: Indicate, as applicable, the schedule and content for data review and reports. Examples include reports to monitor enrollment, reports to study oversight committee, reports of study conduct, and reports for interim data analysis and study progress. Identify plans for data analysis and interim and final study reports, steps for locking the database prior to analysis, and precautions related to masked data. Indicate whether and when coding is to occur.

<Insert text>

## 9.4 STUDY RECORDS RETENTION

Specify the length of time for the investigator to maintain all records pertaining to this study. Consideration should be given to NIH grant and ICH guidance, federal and state and local regulations.

Data Retention and/or Data Destruction Plan – How long will you keep subject data? (generally 2 years on site and then 2-5 years after closing the study at Iron Mountain).

If study involves specimen – please describe what will be done with them at the end of study – will they be destroyed or will they be retained for future study beyond the scope of the protocol (this information will match the information in section 13). If specimen will be retained for future use, please describe what will be done of the data associated with the samples and how PHI will be protected.

<Insert text>

{Begin sample text}

Study records will be maintained for at least three years from the date that the grant federal financial report (FFR) is submitted to the NIH.

Study documents must be retained for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

{End sample text}

# 10. INVESTIGATOR OVERSIGHT

All protocols must have an investigator responsible for the overall study conduct.

It is the responsibility of the Principal Investigator to oversee the entire study; this oversight includes safety and study integrity. This oversight includes careful assessment and appropriate reporting of the study data.

# 11. COMPLIANCE WITH THE STUDY

Define how adherence to the protocol will be assessed, and verified (if applicable).

## 11.1 PROTOCOL DEVIATION AND UNANTICIPATED PROBLEMS

Example text provided as a guide, customize as needed. For multisite trials, please modify the language as needed (eg. Submit to the site’s IRB as per their IRB policy and send a copy of the submission to the TJU regulatory team).

There are 2 appendices - Appendix D and Appendix E – use Appendix D is the deviation log listing all deviations and Appendix E is site specific deviation log that can be used by the subsites and sent to the TJU regulatory team as well. Please specify Appendix E in case of multisite trials.

## UNANTICIPATED PROBLEMS

Unanticipated problems (UAPs) include, in general, any incident, experience, or outcome that meets the following criteria:

* unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
* UAPs are considered to pose risk to participants or others when they suggest that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

## PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the protocol, International Conference on Harmonization (ICH), Good Clinical Practice (GCP) and protocol-specific guidelines. The deviation (any activity conducted outside the parameters established by the protocol) may be either on the part of the participant, the investigator, or the study site staff and may or may not pose a risk to participants or others or may affect the integrity of the data obtained from the study.

The risk posed by the deviation, to the study or the study participant gives rise to an Unanticipated problem (UAP). It is crucial to document the deviation/unanticipated problem in the protocol deviation log (Appendix D) and submitted to the IRB as per the sites regulations. As a result of deviations, corrective actions are to be developed and implemented promptly.

UAPs and protocol deviations that pose risk to participants or others, and that are not AEs, or that affect study integrity will be submitted to the IRB via the <eazUP system> within 5 working days of the investigator becoming aware of the event.

UAPs and protocol deviations that do not pose risk to participants or others and do or do not affect study integrity must be entered in the deviation log (Appendix D) and submitted to the IRB at the next continuing review.

# 12. STUDY FINANCES

## 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.)

<Insert text>

## CONFLICT OF INTEREST

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All Jefferson University Investigators will follow the TJU Conflicts of Interest Policy for Employees (107.03).

# 13. FUTURE USE OF STORED SPECIMEN/DATA

Describe what specimen/data will be collected and how the specimen/data will be obtained and used. Describe what will be done with the left over samples after study completion. If residual specimen or data will be maintained after this study is completed, include provisions for consent and the options that are available for the participant to agree to the future use of his/her specimen, images, audio or video recordings. Refer to Human Subject Regulations Decision at: <http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html#c2>. to determine if the study is exempt and no consent needed.

Specify the location(s) where specimen/data will be maintained, how long specimen and other data will be stored, if the site’s IRB will review future studies, and protections of confidentiality for any future studies with the stored specimen or data (eg. Specimen will be coded, bar coded, deidentified, identifying information will be redacted from audio recording transcripts, who will have access to the de-coded list if any etc). Include information whether or not genetic testing will be performed. If genetic testing will be performed, mention the risks and how the information will be protected. A certificate of confidentiality may be obtained if genomic testing is planned.

Sometimes, the specimen may be needed for the participant’s future care as well. In such cases, using it for a research study purpose which may or maynot directly benefit the participant and will deplete the available tissue sample. In such cases, patients must be offered the opportunity to consent and in the consent form, it must be mentioned that the risk of depletion of the specimen leading to its unavailability for future care should be mentioned.

In case of multisite trials, please specify if the subsites will also be collecting the specimen or just be involved in data collection and analysis.

{Begin sample text}

Once the participant whose sample will be used has been identified, they are assigned a unique identification code. The key to the code will be maintained on a Jefferson secured server and will be accessible to key research personnel only. The specimen will be requested from the pathology in the form of whole blocks that will be then be masked for deidentification and hereon identified only by the unique identification code assigned to the participant. The research coordinator will download the study-relevant data from the patient charts, deidentify and save on the same TJU secured servers and the study will start analyzing the data. If for some reason, this is the only block for the participant that exists and pathology receives a request from the participant that the block is needed for further tests that may affect their future care, then the PI may consider returning the block early.

Once all the data has been collected, analyzed and published. After the analysis is complete, the leftover specimen will be returned to pathology.

{End sample text}

# 14. PUBLICATION AND DATA SHARING POLICY

The publication and authorship policies should be established and briefly outlined in this section. For example, for a study with multiple investigators, this section might state that an Executive Committee will be responsible for developing publication procedures and resolving authorship issues. If, in addition to the investigator, other investigators are involved with the study, identify who holds the primary responsibility for publication of the any results of the study. Also define the need to first obtain approval from the primary responsible party before any information can be used or passed on to a third party. If details of the publication policy will be described in the study’s MOP, refer to it here. Include applicable text and add study-specific information on publication and authorship policies, and compliance with NIH Data Sharing Policy, if applicable.

<Insert text>

{Begin sample text}

This study will comply with the [NIH Public Access Policy](http://publicaccess.nih.gov/policy.htm), which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive [PubMed Central](http://www.pubmedcentral.nih.gov/) upon acceptance for publication.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical studys registration policy as a condition for publication. The ICMJE defines a clinical study as any research project that prospectively assigns human participants to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE policy requires that all clinical studys be registered in a public studys registry such as [ClinicalStudys.gov](http://www.clinicaltrials.gov), which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. The ICMJE does not review specific studies to determine whether registration is necessary; instead, the committee recommends that researchers who have questions about the need to register err on the side of registration or consult the editorial office of the journal in which they wish to publish.

[U.S. Public Law 110-85](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf) (Food and Drug Administration Amendments Act of 2007 or FDAAA), Title VIII, Section 801 mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical studys:"

Studys of Drugs and Biologics: Controlled, clinical investigations, other than Phase I investigations, of a product subject to FDA regulation;

Studys of Devices: Controlled studys with health outcomes of a product subject to FDA regulation (other than small feasibility studies) and pediatric postmarket surveillance studies.

NIH grantees must take specific [steps to ensure compliance](http://grants.nih.gov/clinicaltrials_fdaaa/steps.htm) with NIH implementation of FDAAA.

{End sample text}

# 15. LITERATURE CITED

Include a list of relevant literature references in this section. Use a consistent, standard, modern format, which might be dependent upon the required format for the anticipated journal for publication (e.g., N Engl J Med, JAMA, etc). The preferred format is ICMJE.

{A full listing of ICMJE style guidelines can be found at:  
International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. JAMA. 1997;277:927-34.

You may also refer to:  
https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/write-your-application.htm#Important%20Writing%20Tips.}

<Insert text>

SUPPLEMENTAL MATERIALS

These are examples of documents that you may want to include as Supplemental Materials. If there are no supplemental materials to be referenced, this section should be deleted.

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

<Insert text>

{Begin sample text}

* Interview text and codes for interpretation
* Study questionnaires
* Repository Instructions (if applicable)
* Biosafety Precautions (if applicable)
* Laboratory Handling (if applicable)

{End sample text}

# APPENDIX - A

## Schedule of Activities (SoA)

**The schedule below is provided as an example and should be modified as appropriate.**

| **Procedures** | Screening  Day -7 to -1 | Study Visit 2  Day 7 ±3 day | Final Study  Visit 3 Day 30 ±3 day |
| --- | --- | --- | --- |
| Informed consent | X |  |  |
| Demographics | X |  |  |
| Medical history | X |  |  |
| Physical exam (including height and weight)\* | X |  | X |
| Vital signs\* | X |  | X |
| Performance status\* | X |  | X |
| Hematology a,b | X | X | X |
| Radiologic/Imaging assessment\* | X |  | X |
| Other assessments | X | X | X |
| Administer questionnaires | X | X | X |
| a: Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, AST, ALT, sodium.  b: Serum pregnancy test (women of childbearing potential).  \*: All with \* are part of Standard of Care. | | | |

The schedule of activities must capture the procedures that will be accomplished at each study visit, and all contact, with study participants e.g., telephone contacts. This includes any tests that are used for eligibility, participant randomization or stratification. Only include procedures that contribute to participant eligibility and study objectives and endpoints. Other procedures should be done sparingly and with consideration, as they may add unnecessary complexity and detract from recruitment. The tests/procedures that are part of standard of care should be specified using superscript, if needed.

Allowable windows should be stated for all visits. To determine the appropriate windows, consider feasibility and relevance of the visit time points to study endpoints (e.g., a 6-month follow-up visit might have a window of several weeks).

APPENDIX B – Study Questionnaires. Eg. Quality of life questionnaire

APPENDIX C – Study Questionnaires Eg. FACT-ES questionnaire

# APPENDIX D

# Protocol Deviation Tracking Log

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Protocol ID/Number:** | | |  | | **Site Name:** |  | | | |
| **Principal Investigator:** | | |  | |
| **Protocol Title:** | | |  | | | | | | |
| **Ref No.** | **Subject ID** | **Date of Deviation** | **Date Identified** | **Deviation Description** | **Was patient safety risked ?** | | **Did Subject Continue in Study?** | **Meets IRB Reporting Criteria?** | **IRB Reporting Date** |
| **1** |  |  |  |  |  | |  |  |  |
| **2** |  |  |  |  |  | |  |  |  |
| **3** |  |  |  |  |  | |  |  |  |
| **4** |  |  |  |  |  | |  |  |  |
| **5** |  |  |  |  |  | |  |  |  |
| **6** |  |  |  |  |  | |  |  |  |

# PI Signature: Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

# APPENDIX E

# UNANTICIPATED PROBLEM (DEVIATION) REPORT FORM

**For Site and Sub-site reporting (use another page as needed)**

Thomas Jefferson University Principal Investigator: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sub-site Principal Investigator:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

TJU IRB Control Number/Sub-site Identifier:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Protocol Title:

Subject ID:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Approximate Date of Problem: Date Aware:

Description of the Problem:

Is this Unanticipated Problem a Protocol Deviation? Yes No

Did the Unanticipated Problem affect subject safety? Yes No

Please explain your answer:

Has the problem resolved: Yes No

Does the consent/protocol require modification? Yes No

Is it being reported to the IRB immediately? Yes No

Corrective Action Plan?

Signature of the PI:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_