Research Proposal for Interventional Studies

Title:	The complete title of the protocol
Short Title	myIRB will request a short title of up to 5 words for tracking purposes
Funding Information:	
myIRB Number	
Protocol Date:	
Amendment 1 Date: None	Amendment 4 Date: None
Amendment 2 Date: None	Amendment 5 Date: None
Amendment 3 Date: None	Amendment 6 Date: None
Principal Investigator	Name
Contact Information	Office Address Phone: XXX-XXX-XXXX email: XXXXX@jax.ufl.edu

Sponsor (IND or IDE holder, if applicable)
Sponsor Name
Address
City, State, Zip
Country

Study Principal Investigator

(if multicenter study with UF-Jax PI responsible)
Office Address
City, ST, ZIP
Phone XXX-XXX-XXXX
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Site Principal Investigator
UF Investigator (if PI different from the above)

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Jacksonville, FL 32209

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INSTRUCTIONS:

The highlighted text is instructional and should be deleted before finalizing the document and submitting it to the IRB.

This protocol template may be used for interventional studies.

Sections that are not applicable can be marked "not applicable."

For the descriptive studies, use the "Descriptive Studies Protocol Template."

For non-drug or non-device interventional studies, delete areas related to study drug or devices (**Section 9**)

NOTE: The investigator must demonstrate that the study is consistent with "sound scientific design" and that the design is sufficient to achieve the study objectives. The investigational plan, study procedures, and analysis plan must provide sufficient details to provide the IRB with a basis for its decisions. Even though the risks of the research may be minimal, the IRB will not approve studies that offer insufficient information.

TABLE OF CONTENTS

Be sure to update the "Table of Contents" after the protocol is finalized. If using MS Word 2016 or later, right-click anywhere in the "Table of Content" and click "Update Field" then select "Update Entire Table."

ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Description
°C	Degrees centigrade
AE	Adverse event

1 ABSTRACT

Use JAMA format (http://jama.ama-assn.org/misc/ifora.dtl#Abstracts). Limit to 150 – 200 word abstract, written for lay members. This abstract is used in the IRB database and in the minutes of meetings.

Context: (Background)

Include 1 - 3 sentences about the clinical importance of the condition and the importance of the research question.

Objectives: (primary and important secondary objectives).

State the precise objective or study question.

If more than 1 objective, limit to only the key secondary objectives.

Study Design:

Basic design: Randomized controlled trial, cohort study, case-control study, cross-sectional study, etc.

Setting/Participants:

The setting including location (referral or community center) and level of care (inpatient or outpatient).

The number of sites.

The number and description of participants including key eligibility criteria.

Study Interventions and Measures:

The study drug, or other intervention and main monitoring procedures

Main study outcome measures (assessments of primary and key secondary endpoints)

2 PROTOCOL SYNOPSIS

(Do NOT include a Synopsis if submitting a protocol for expedited review)

Study Title	LIMIT SYNOPSIS to no more than 2 - 3 pages. The synopsis should provide a rapid overview of the study for lay members and for members who are not the primary reviewers. Keep the synopsis BRIEF. Use bullet points.
Funder	Grant Agency, Pharmaceutical company, or Departmental funds
Clinical Phase	(Phase I, II, III or IV - if applicable)
Study Rationale	No more than ½ page
Study Objective(s)	Primary • To determine (obtain, evaluate, verify, etc.) … Secondary • To determine (obtain, evaluate, verify, etc.) … • .....
Test Article(s) (If Applicable)	Describe the study drug, device, diagnostic, diet or other intervention
Study Design	Overview of design. Explain the basic design such as parallel-group randomized controlled trial, open-label single-arm PK study, diagnostic test evaluation, etc.
Subject Population key criteria for Inclusion and Exclusion:	Inclusion Criteria 1. Subjects age X – X 2. Include the main criteria but does not need to be complete, etc. Exclusion Criteria 1. Subjects with X or Y, etc. 2.
Number Of Subjects	Total Number of Subjects, Total Number at UF-Jax, Total Number of Sites
Study Duration	Each subject's participation will last … The entire study is expected to last….
Study Phases Screening Study Treatment Follow-Up	The study phases listed at the left are **examples only**. Intervention studies have at least 2 phases: (1) Screening: screening for eligibility and obtaining consent and (2) Intervention: study intervention/experimental treatment.
Efficacy Evaluations	Primary evaluation measurements that will be used to assess the efficacy of the intervention
Pharmacokinetic Evaluations	(include only if applicable)
Safety Evaluations	Primary measurements that will be used to assess the safety
Statistical And Analytic Plan	Limit the discussion of analysis to primary endpoint and possibly main secondary endpoint
Data And Safety Monitoring Plan	Describe how is responsible for data quality management and ongoing assessment of safety: PI, independent medical monitor, internal safety committee, or DSMB

EXAMPLE: TABLE 1: SCHEDULE OF STUDY PROCEDURES

Study Phase	Screening	Treatment/Intervention			Open-Label Treatment		Follow-up		
Visit Number		1	2	3	4	5	6	7	8
Study Days									
Informed Consent/Assent	X								
Review Inclusion/Exclusion Criteria	X								
Demographics/Medical History	X								
Physical Examination	X								
Vital Signs: BP, HR, RR	X								
Height and Weight	X								
Pregnancy Test	X								
Prior/Concomitant Medications	X								
Clinical Laboratory Evaluation	X								
Randomization									
Dispense Study Drug									
Drug Compliance									
Adverse Event 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.

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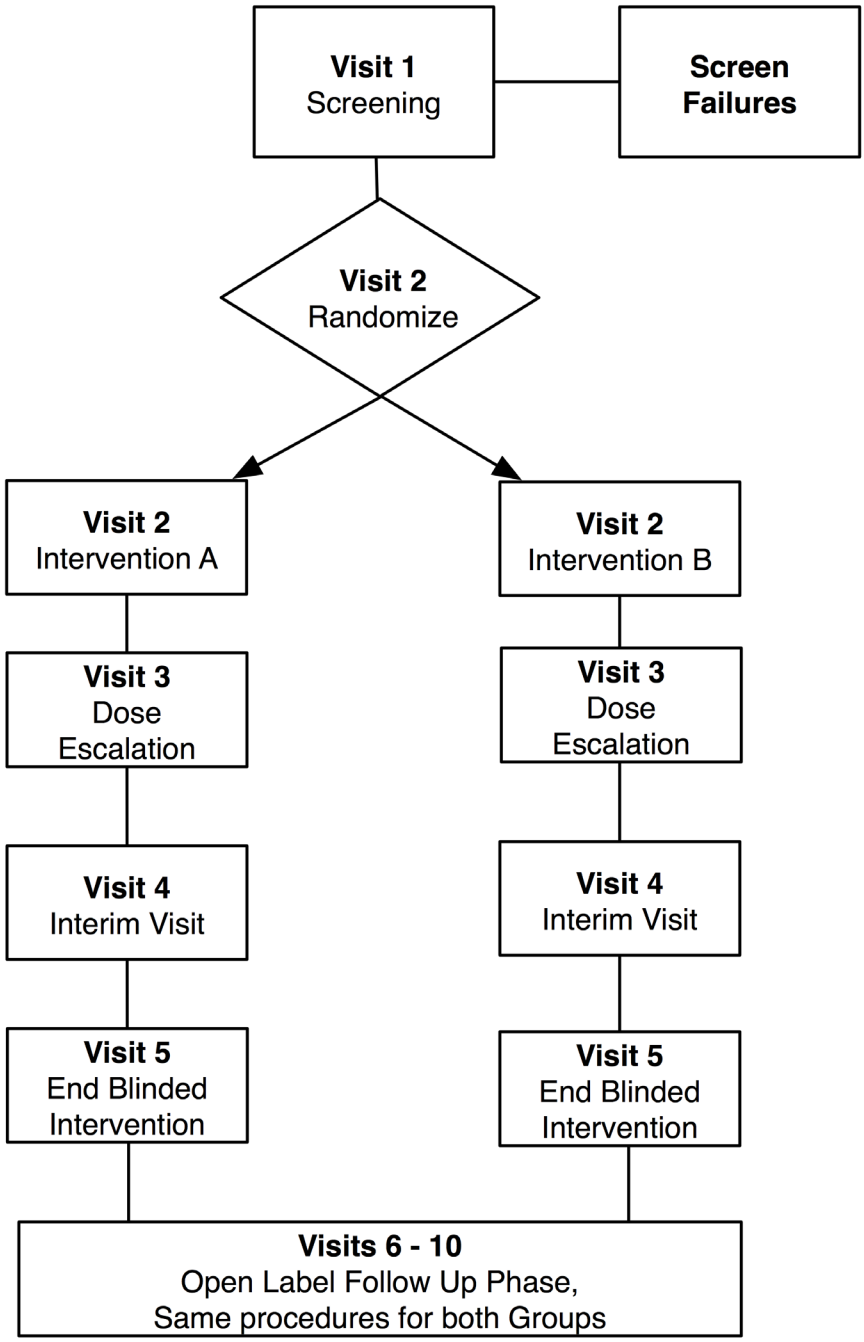
EXAMPLE: FIGURE 1: STUDY DIAGRAM

A flow diagram of the study may be relevant to explain the flow of subjects in the trial. An example flow diagram for randomized, controlled clinical trial design is included as an example below.



3 BACKGROUND INFORMATION AND RATIONALE

Section 1 should be no more than 3 – 5 pages. Refer the reader to the applicable grant, or attached literature references for more detailed information. If referring to the grant it is helpful to include page citations.

3.1 Introduction

Brief paragraph or two to describe the setting and rationale for the study. The details of the background go into Section 1.6

3.2 Name and Description of Investigational Product or Intervention

Name and description of the study intervention (drug, device, diagnostic, diet, experimental psychological therapy, etc.). If a drug, device, or biologic, the specific description, packaging, control systems will go in Section 7.

Important information regarding use of a drug or device not approved by the FDA for the disease that is being treated in the current proposed study.

An IND is required when a drug is involved in a clinical investigation that is not exempt from the regulations. The new guidance gives greater clarity to what is a 'drug', what is a 'clinical investigation,' and which clinical investigations are exempt for the IND process.

A clinical investigation of a drug is exempt from the IND requirements if all (emphasis is author of this document and not FDA's) of the criteria for an exemption in § 312.2(b) are met:

1. The drug product is lawfully marketed in the United States.
2. There is no intent to report the investigation to the FDA as a well-controlled study in support of a new indication and no intent to use it to support any other significant change in the labeling of the drug.
3. In the case of a prescription drug, the investigation is not intended to support a significant change in the advertising for the drug.
4. The investigation does not involve a route of administration, dose, patient population, or other factors that significantly increase the risk (or decreases the acceptability of the risk) associated with the use of the drug product (21 CFR 312.2(b)(1)(iii)).
5. The investigation is conducted in compliance with the requirements for review by an IRB (21 CFR part 56) and with the requirements for informed consent (21 CFR part 50).
6. The investigation is conducted in compliance with the requirements of § 312.7 (i.e., the investigation is not intended to promote or commercialize the drug product).

In most case of commercial development there is intent to report the study as part of an FDA filing. However, exploratory studies might be within the exemption if all of the other factors are met.

There may be other examples where an IND may not be required. However, the UF IRB requires documentation from the FDA whether or not the study is Exempt from the IND/IDE.

How to ask the FDA: Please contact Dr. Wajeeh Bajwa (wajeeh.bajwa@jax.ufl.edu) to get additional information/guidance/assistance and to obtain templates for an IND/IDE or submit a request to the FDA for IND-Exemption.

3.3 Findings from Non-Clinical and Clinical Studies

(This section is only applicable for drugs, biologics, and devices)

3.3.1 Non-Clinical Studies

3.3.2 Clinical Studies

3.3.2.1 Human Pharmacokinetics

3.3.2.2 Clinical Studies in Adults

3.3.2.3 Clinical Studies in Children

3.4 Selection of Drugs and Dosages

Description of dosage forms available and those to be used in the study

3.5 Relevant Literature and Data

Overview of the literature and data relevant to the trial and provide background for the trial. Also, the relevant literature establishing the validity for scales, evaluation tools, etc. The reference citations should be listed at the end in Section 11. It is usual to limit this to 10 (at most 20) key references.

3.6 Compliance Statement

This study will be conducted in full accordance all applicable Policies and Procedures of University of Florida, Federal, and state laws and regulations including 45 CFR 46, 21 CFR Parts 50, 54, 56, 312, 314 and 812 and the Good Clinical Practice: Consolidated Guideline approved by the International Conference on Harmonization (ICH). Note: Only include the sections of Title 21 if the study is regulated by the FDA. Only include ICH compliance if the study will actually comply with these requirements. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, and will report unanticipated problems involving risks to subjects or others in accordance with the UF IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

4 STUDY OBJECTIVES

State the overall objectives of the study.

The purpose of the study is to determine the (efficacy, pharmacokinetics, safety etc.) of ….

4.1 Primary Objective (or Aim)

The primary objective of this study is to determine whether the XXX (intervention) reduces, increases, etc. outcome measure XXX in children X to X years. This should be specific, for example: "to determine if enalapril decreases systolic blood pressure after 4 weeks compared to placebo."

The primary objective should be both the most important and the objective on which the study sample size is based. Objectives (aims) are usually phrased in some variant of "…to determine…". Protocols differ from grants in that they do not usually enumerate specific hypotheses. If included, these belong in the Analysis section.

4.2 Secondary Objectives (or Aim)

The secondary objectives are to:

- Determine if there is a relationship between X to Y.
- Determine the pharmacokinetics of drug X.
- Evaluate the tolerability and safety of XXXX for short-term administration in the stated population.
- .....

5 INVESTIGATIONAL PLAN

5.1 General Schema of Study Design

Section 5 is a brief overview of the study design. In Sections 5.1.1– 5.1.2, include a brief overview of the study phases (Screening, Baseline assessment, Treatment Phase, Follow-Up, etc.).

Section 3.1 is intended to be a brief overview. Do not put the details of the entire study into this Section. Section 4 is where the details of the study and its procedures belong. A description of the study design should be included, e.g., randomized controlled trial, concurrent or non-concurrent (retrospective) cohort study, case-control study, cross-

sectional study, pharmocokinetic-pharmacodynamic study, descriptive study, natural history study, evaluation of a diagnostic, etc. Provide a general description here and a general description of the various phases in Sections 5.1.1, 5.1.2, etc.

Reference to Figure of Study Schema and to Table of Procedures as applicable.

5.1.1 Screening Phase

How will subjects be identified, screened, and how will they be approached for informed consent and subject assent.

For example, "Potential subjects will be screened using the protocol inclusion and exclusion criteria. Subjects will be recruited into two strata: children 6-12 years of age, and children 13-16 years of age with a goal of 50% of subjects per age strata.

Parental/guardian permission (informed consent) and, if applicable, child assent, will be obtained prior to any study-related procedures being performed, including discontinuation of current therapy. Blood samples will be drawn to confirm eligibility based on clinical laboratory parameters. Females ≥ 11 years of age will have a urine pregnancy test."

5.1.2 Study Treatment Phase (start of the study intervention)

Avoid using Phase I and Phase II etc. for your project unless these phases meet the FDA description of the clinical trials. Phase I and Phase II apply to specific study phases according to the FDA Guidelines. Use Stage I and Stage II or similar terminology for different phases of your project.

See https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research or https://www.nccn.org/patients/resources/clinical_trials/phases.aspx

Description of Part 1 of the study.

5.1.3 Phase 2 (Use an appropriate descriptor such as "Open-label Treatment")

(*If applicable*) Description of Part 2 of the study.

5.1.4 Follow-up Part

(*If applicable*) To be eligible for the follow-up part, subjects must either have (1) ……

The follow-up part will continue for up to XXXX days.

5.2 Allocation to Treatment Groups and Blinding

Describe the method for treatment allocation. If the study is randomized, provide an overview of the process - who will generate the randomization sequence, how will the sequence be generated (table of random numbers, computer, etc.), where will the schedule be maintained, how will the assignment be concealed from the investigators. If there will be stratification, describe the groups. If blocking is used, do NOT include the block size(s). Describe how blinding (if any) will be maintained.

5.3 Study Duration, Enrollment, and Number of Sites

5.3.1 Duration of Study Participation

This section refers to the duration of the subject's participation, not the duration of the study. The study duration per subject will be up to XXX days, with up to XXX days screening, up to XXX days Phase 1, up to XXX days Phase 2, and XXX days follow-up.

5.3.2 Total Number of Study Sites/Total Number of Subjects Projected

The study will be conducted at approximately XX investigative sites in the United States and XXXX.

Recruitment will stop when approximately XXX subjects are ….. It is expected that approximately XXX subjects will be enrolled to produce XXXX evaluable subjects.

5.4 Study Population

The study population for every type of study design is defined by Inclusion and Exclusion criteria. A few examples are included below.

5.4.1 Inclusion Criteria

1) Males or females age X to XX years.
2) Weight ≥ XX kg.
3) Girls ≥ 11 years of age must have a negative urine/serum pregnancy test and must use an acceptable method of contraception, including abstinence, a barrier method (diaphragm or condom), Depo-Provera, or an oral contraceptive, for the duration of the study.
4) Additional criteria as required
5) Parental/guardian permission (informed consent) and if appropriate, child assent.

5.4.2 Exclusion Criteria

1) Exclusion 1
2) Exclusion 2
3) Laboratory abnormalities that indicate clinically significant hematologic, hepatobiliary, or renal disease (EXAMPLE below):

AST/SGOT	> 2.0 times the upper limit of normal
ALT/SGPT	> 2.0 times the upper limit of normal
Total bilirubin	> 2.0 times the upper limit of normal
Hemoglobin	< 9 gm/dL
White blood cell count	< 3,000/ mm^3
Platelet count	< 100,000/mm^3

4) Any investigational drug use within 30 days prior to enrollment.
5) Pregnant or lactating females.
6) Parents/guardians or subjects who, in the opinion of the Investigator, may be non-compliant with study schedules or procedures.

Subjects that do not meet all of the enrollment criteria may not be enrolled. Any violations of these criteria must be reported in accordance with IRB Policies and Procedures.

6 STUDY PROCEDURES

This section should list the procedures, observations, measures, etc. at each study visit, including history, examination, study drug administration, or other interventions. Section 4 lists what will be done. Section 5 describes how it will be done. For complicated studies with several visits, it is recommended that the investigator create a Table of Procedures (Page xx).

6.1 Screening Visit

List the timing and all of the procedures to be performed at the screening visit. This can be a simple bullet list.

- Informed Consent
- Physical Exam
- Vital Signs
- Laboratory tests
- Medical Record Review

6.2 Study Treatment Stage

General overview of this phase/stage.

6.2.1 Visit 1

A detailed description of the study visit, including all procedures. This is usually included as a simple bullet list of all of the interventions, monitoring procedures and measurements that will take place. The study coordinator should be able to quickly review the list of procedures at each visit in order to correctly execute the study.

- Physical Exam
- Vital Signs
- Laboratory tests
- Start study intervention
- Dispense study diary
- Medical Record Review

6.2.2 Visit 2

Detailed description of study visit including all procedures.

- Physical Exam
- Vital Signs
- Laboratory tests
- Collect unused study drug
- Dispense study drug
- Assess possible adverse events
- Medical Record Review

6.2.3 Visit 3

- …….

6.3 Stage 2 of the Study (e.g., Open-Label Treatment)

(Only include if applicable) General description of the phase.

6.3.1 Visit 4

A detailed description of study visit including all procedures – listed like the above examples.

6.3.2 Visit 5

Detailed description of study visit – listed like above examples.

6.4 Follow-up Phase (only if applicable)

A general overview of this stage.

6.4.1 Visit 6

A detailed description of study visit including all procedures – listed like the above examples.

6.4.2 Visit 6: End of Study

A detailed description of study visit including all procedures – listed like the above examples.

6.5 Unscheduled Visits

Description of how unscheduled visits will be handled.

6.6 Concomitant Medication

(Include if appropriate) Example: All prior and concomitant medications used within XX days before the screening visit and through the end of the study will be recorded. The dates of administration, dosage, and reason for use will be included.

6.7 Rescue Medication Administration

If subjects may receive rescue medication for adverse reactions or inadequate response to study medication, the options, and how the decision will be made to permit such treatment should be included here.

6.8 Subject Completion/Withdrawal

Criteria for withdrawal of subjects and plans for the provision of care after withdrawal. Example: Subjects may withdraw from the study at any time without prejudice to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to study treatment or visit schedules, AEs, or due to REASON (list). The Investigator or the Sponsor (if applicable) may also withdraw subjects who violate the study plan or to protect the subject for reasons of safety or administrative reasons. It will be documented whether or not each subject completes the clinical study. If the Investigator becomes aware of any serious, related adverse events after the subject completes or withdraws from the study, they will be recorded in the source documents and on the CRF.

6.8.1 Early Termination Study Visit

List the procedures that will be performed for each subject that withdraws prior to completing the study. Example: Subjects who withdraw from the study will have all procedures enumerated for Visit XXX as the early termination visit.

7 STUDY EVALUATIONS AND MEASUREMENTS

Every monitoring procedure, measurement, and intervention listed in Section 4 should have a corresponding description of exactly how the measurement will be made. Each evaluation, BP, QOL questionnaire, etc. should be listed with a description here. A copy of any non-standard measurement tool should be attached as an appendix. The IRB website contains a list of validated measurement tools that do not need to be appended to the protocol or application.

Examples of evaluations are included below. Inclusion of data collection forms or case report forms is not required but every data element that is collected should be described along with how it will be measured. Standard, validated tests and test instruments do not have to be included in the Appendix but non-standard and non-validated instruments should be included.

7.1 Screening and Monitoring Evaluations and Measurements

7.1.1 Medical Record Review

Include a listing of the variables that will be abstracted from the medical chart (paper or electronic).

- Date of birth
- Weight
- .....

7.1.2 Physical Examination

Describe the baseline evaluations, including the medical history, physical examination, demographic characteristics (age, gender, race), and other information that will be collected.

7.1.3 Vital Signs

Describe which measures will be made and how they will be made. Example: will BP be measured with an automated device or with an aneroid sphygmomanometer? Which arm will be used? Sitting or lying down? Will more than one BP measurement be made and averaged?

7.1.4 Laboratory Evaluations

Example: Blood sampling will be performed for the following laboratory evaluations

- Hematology
- .....

7.1.4.1 Hematology

Details as appropriate for each test. Example: Hematology testing will be performed at the laboratory at the University of Florida, Jacksonville Campus. Hemoglobin, hematocrit, RBC count, WBC with differential, etc. will be ….

Alternate format for Laboratory Evaluations

7.1.4.2 Table: Clinical Laboratory Tests

Category	Tests
Hematology	RBC, hemoglobin, hematocrit, platelet count, WBC with differential
Liver function tests	SGOT/AST, SGPT/ALT, total Bilirubin
Renal function tests	BUN, creatinine

7.1.4.3 Pregnancy Testing

(If appropriate) A urine pregnancy test will be performed for female subjects ≥ 11 years of age and girls <11 years who are physically capable of becoming pregnant.

7.1.5 Other Evaluations, Measures

Describe other rating scales, tests, psychological tools, laboratory evaluations, etc.

7.2 Efficacy Evaluations

These are the measures that will be used to assess the efficacy of the study intervention. The discussion of these evaluations is usually more detailed.

7.2.1 Diagnostic Tests, Scales, Measures, etc.

Methods and timing the measures that will be used to assess the efficacy

7.3 Pharmacokinetic Evaluation

(only if applicable) Sampling for pharmacokinetics will be …. The parameters determined will be … Both model-independent and model-dependent methods will be used. Etc.

7.4 Safety Evaluation

Example: Subject safety will be monitored by adverse events, vital signs, physical examinations, laboratory data (QQQQ rating scales (AAA, BBB, and CCC). It will also include YYYY and ZZZZ examinations/evaluations/scales, etc.

8 STATISTICAL CONSIDERATIONS

This section should provide sufficient detail to permit assurance that the sample size is justified and the statistical methods sufficient and appropriate for the research question(s).

8.1 Primary Endpoint

The primary endpoint is the variable that relates back to the Primary Objective and serves as the basis for the justification for the Sample Size.

Example: The primary endpoint will be the change in Variable1 between Screening and Visit X.

8.2 Secondary Endpoints

Secondary endpoints will include the following:

- The change in ……
- The change in …..
- Safety and tolerability of DRUG based on Adverse Events. Measurements and evaluations

- ……

8.3 Statistical Methods

8.3.1 Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender).

8.3.2 Efficacy Analysis

The primary analysis will be based on an intention to treat approach and will include all subjects randomized at Visit 1.

The primary efficacy endpoint will be the change in XXX between Visit X and Visit Y.

Secondary endpoints will include the change in

8.3.3 Pharmacokinetic Analysis

Description of pharmacokinetic parameters to be assessed and methods to be employed to calculate those parameters:

8.3.4 Safety Analysis

Example: All subjects entered into the study at Visit 1 will be included in the safety analysis. The frequencies of AEs by type, body system, severity, and relationship to study drug will be summarized. SAEs (if any) will be described in detail.

AE incidence will be summarized along with the corresponding exact binomial 95% two-sided confidence intervals.

8.4 Sample Size and Power

Sample size justification and power analysis *(if appropriate)*. All studies must include a justification for the chosen sample size, even if a power analysis isn't appropriate (for example, a PK study). The basis for how the size was chosen should be explained. Any assumptions made (mean and SD), clinically important differences, and the details of the calculation should all be included.

8.5 Interim Analysis

Interim efficacy or safety analyses if planned and include a description of stopping rules for efficacy and stopping rules for safety. Stopping rules for efficacy should generally be limited to life-threatening and serious diseases.

9 STUDY MEDICATION (STUDY DEVICE OR OTHER STUDY INTERVENTION)

9.1 Description

A description of the study drug, device, or other intervention should be included here. Omit sections that do not apply.

9.1.1 Packaging

Clinical supply description

9.1.2 Labeling

Description of the product label

9.1.3 Dosing

XXX can be taken as a \…. Directions for use

9.1.4 Treatment Compliance and Adherence

Assessment of compliance and requirements for continuation in the trial

9.1.5 Drug Accountability

Who will maintain the receipt and disposition records for study medications? For example Adequate records of study drug receipt and disposition will be maintained by the UF-Jax Pharmacy Records of receipts, investigational drug orders, dispensing records, and disposition forms will be examined during the course of the study. The purpose of these records is to ensure regulatory authorities and the sponsor that the investigational new drug will not be distributed to any person who is not a study subject under the terms and conditions set forth in this protocol. The study medication is to be prescribed by the Investigator or designee and may not be used for any purpose other than that described in this protocol. At study completion, all drug supplies, including partially used and empty containers, must be returned to the sponsor or designee.

10 SAFETY MANAGEMENT

This section provides two generic safety management plans. One is if minimal risk studies (in red). This section should be consistent with UF IRB Guidelines tailored to the requirements for each study. For example, it may be appropriate to exclude scheduled hospitalizations from inclusion as an SAE or if the study is observational and does not involve an intervention, to propose limiting SAE reporting to those AEs directly related to the study and not to the underlying illness.

10.1 Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study.

10.2 Adverse Event Reporting

The Investigator is responsible for recording and reporting unanticipated problems related to research that occur during and after study treatment. The plan for Adverse Event reporting should be consistent with the UF IRB Guidelines. Two examples are included below, one for greater than minimal risk and one for minimal risk studies.

Unanticipated problems related to the research involving risks to subjects or others that occur during the course of this study (including SAEs) will be reported to the IRB in accordance with UF IRB (see: http://irb.ufl.edu/index/irb-policies-guidelines-and-guidances.html). AEs that are not serious but that is notable and could involve risks to subjects will be summarized in narrative or other format and submitted to the IRB at the time of continuing review.

For Minimal Risk Studies use the following paragraph instead of the one above.

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with UF IRB (see: http://irb.ufl.edu/index/irb-policies-guidelines-and-guidances.html). AEs that are not serious but that are notable and could involve risks to subjects will be summarized in narrative or other format and submitted to the IRB at the time of continuing review.

For minimal risk studies, the remainder of Section 8 may be deleted.

10.3 Definition of an Adverse Event

An adverse event is any untoward medical occurrence in a subject who has received an intervention (drug, biologic, or other intervention). The occurrence does not necessarily have to have a causal relationship with the treatment. An AE can, therefore, be any unfavorable or unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

All AEs (including serious AEs) will be noted in the study records and on the case report form with a full description including the nature, date and time of onset, determination of non-serious versus serious, intensity (mild, moderate, severe), duration, causality, and outcome of the event.

10.4 Definition of a Serious Adverse Event (SAE)

An SAE is any adverse drug experience occurring at any dose that results in any of the following outcomes:

- death,
- a life-threatening event (at risk of death at the time of the event),
- requires inpatient hospitalization or prolongation of existing hospitalization,
- a persistent or significant disability/incapacity, or
- a congenital anomaly/birth defect in the offspring of a subject.

Important medical events that may not result in death be life-threatening, or require hospitalization may be considered a serious adverse drug event when based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

A distinction should be drawn between serious and severe AEs. A severe AE is a major event of its type. A severe AE does not necessarily need to be considered serious. For example, nausea, which persists for several hours, maybe considered severe nausea, but would not be an SAE. On the other hand, a stroke that results in only a limited degree of disability may be considered a mild stroke but would be an SAE.

10.4.1 Relationship of SAE to study drug or other intervention

The relationship of each SAE to the study intervention should be characterized using one of the following terms in accordance with UF IRB Guidelines: definitely, probably, possibly, unlikely or unrelated.

10.5 IRB/IEC Notification of SAEs and Other Unanticipated Problems

The Investigator will promptly notify the IRB of all on-site unanticipated, serious 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 eIRB system and in accordance with the timeline below. External SAEs that are both unexpected and related to the study intervention will be reported promptly after the investigator receives the report. (External events that don't change the risks to subjects or result in a change to the research protocol or consent form usually do not require reporting to the IRB. See the IRB website for SAE reporting requirements.)

Type of Unanticipated Problem	Initial Notification (Phone, Email, Fax)	Written Report
Internal (on-site) SAEs Death or Life-Threatening	24 hours	Within 2 calendar days
Internal (on-site) SAEs All other SAEs	7 days	Within 7 business days
Unanticipated Problems Related to Research	7 days	Within 7 business days
All other AEs	N/A	Brief Summary of important AEs may be reported at the time of continuing review

10.5.1 Follow-up report

If an SAE 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 SAE are followed until either resolved or stable.

10.6 Investigator Reporting of a Serious Adverse Event to Sponsor

Reporting must be consistent with regulatory, sponsor or GCRC requirements (if applicable)

10.7 Medical Emergencies

(If applicable) Describe any plans or procedures for taking care of medical emergencies that might develop during the course of the study.

11 STUDY ADMINISTRATION

11.1 Treatment Assignment Methods

11.1.1 Randomization

Procedures for generation, maintenance and execution of the randomization schedule.

11.1.2 Blinding

Describe the procedure for maintaining the study blind (if any) for subjects, investigators, and trial personnel.

11.1.3 Unblinding

Procedures, if any, for unblinding of study personnel during the conduct of the study.

11.2 Data Collection and Management

Describe the system for maintaining primary records (source documents) and case report forms and for entering the data into any computerized systems. The plan should be consistent with UF IRB (see: http://irb.ufl.edu/index/irb-policies-guidelines-and-guidances.html). Address the following:

1. Confidentiality. How will the confidentiality of the data be ensured, from abstraction through analysis?

- One method is to keep a master list containing PHI and subject ID number separate from data forms (paper and electronic) that have only a study ID number. The master list should be on a separate computer, removable disk drive, or in a locked file cabinet. This form of data is considered "coded" not de-identified. As long as the data can be re-linked to identifiers, the data is coded. Only when the key to the code or the Master List is destroyed are the data considered de-identified.

- Another method is to use password-protected files; in Excel, type "password" in the Help box for instructions. NOTE: if any of the investigators who access identifiable data are not in the UF workforce, there are important HIPAA rules on disclosure. The investigators and IRB may also need to consider whether the external investigator(s) is engaged in the research.

- Data files can be encrypted

2. Security. Have a plan for backing up or otherwise recovering data. This can be as simple as a copy of the password-protected file on your office computer, with the original in one of the Hospital's secure servers.
3. Anonymization, de-identification, or destruction. Provide a specific plan for removing identifiers that meets the needs of the study and potential future uses of the data. For example, "The identifiers will be destroyed after publication. The other data will be retained for three years. This laboratory maintains a file drawer specifically for such archives, each folder labeled "Destroy by…," with the earliest

dates at the front." Be sure that data retention procedures meet the requirements of the study sponsor.

11.3 Confidentiality

Include a statement that all data and records generated during this study will be kept confidential in accordance with Institutional policies and HIPAA on subject privacy and that the Investigator and other site personnel will not use such data and records for any purpose other than conducting the study. Describe the safeguards to maintain subject confidentiality.

No identifiable data will be used for future studies without first obtaining IRB approval. The investigator will obtain a data use agreement between the provider (the PI) of the data and any recipient researchers (including others at UF-Jax) before sharing a limited dataset (PHI limited to dates and zip codes).

11.4 Regulatory and Ethical Considerations

11.4.1 Data and Safety Monitoring Plan

Describe the safety and monitoring plan. Include the processes and safeguards that will be in place to identify risks to research subjects and to protect subjects during the execution of the trial. See IRB SOP 803 for additional details. The plan should be tailored to the risks of the study intervention and the nature of the disease process and should provide oversight for the emerging safety information could include one or more of the following:

- Principal Investigator
- Medical Monitor associated with the sponsor or the study
- Independent Safety Officer,
- Internal Steering Committee or Internal Data Monitoring Committee made up of representatives of the sponsor and study investigators;
- Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) made up of representatives who are independent of the study sponsor and investigators.

Certain studies (late Phase 2 and Phase 3 trials, particularly for life-threatening diseases) may be required to include an independent Data and Safety Monitoring Board (DSMB) that will be in place to monitor the safety events associated with the study. If a DSMB is employed, the full details of the composition of the DSMB, how it will operate, and how the interim analyses are to be performed should be provided.

11.4.2 Risk Assessment

Risks are either not greater than minimal, a minor increase above minimal or greater than minimal. Describe the risks of each research intervention or procedure in terms of magnitude and probability of harm. Consider all physical, psychological, economic, or societal harms that might accrue to subjects or others.

Distinguish between risks associated with routine clinical care from those that will occur as a result of research. Summarize the overall anticipated risks from the study intervention and study-related procedures.

Address how the study design and execution will minimize the risks of harm.

11.4.3 Potential Benefits of Trial Participation

Summarize all potential benefits, if any, from trial participation. Benefits should be broken down into direct benefits (accrue to the study subject as a result of participation) and indirect benefits (benefits that accrue to the individual or society in the future).

11.4.4 Risk-Benefit Assessment

The Risk-Benefit assessment should include justification for proceeding with the trial based on the balance between risks and benefits.

11.5 Recruitment Strategy

Describe the approach to recruiting subjects. Where will they come from? How will the investigator identify prospective subjects? Will the subjects come from the investigator's patients, or will they be patients of other care providers? If the prospective subjects are not patients of the investigator, who will first approach the subjects and by what method (in person, via mail, via telephone contact?) Will advertising be used (note: all recruitment materials that subjects will see and/or hear must be reviewed and approved by the IRB before they are used to recruit subjects)? Will there be sufficient subjects to achieve the study goals?

If eligibility screening requires the collection of data about prospective subjects (via medical record review, direct query or other procedures), and this screening will take place before subjects consent to participation in the study, describe the plan for obtaining consent/assent and authorization for the screening (unless the screening qualifies for a waiver of consent/assent/authorization).

For more information, see the IRB's webpage on the differences between recruitment and screening: UF IRB (see: http://irb.ufl.edu/index/irb-policies-guidelines-and-guidances.html).

11.6 Informed Consent/Assent and HIPAA Authorization

Describe the procedures that will be used to obtain informed consent/ HIPAA Authorization and assent. Include: who will obtain consent and assent, where will consent/assent process take place, how privacy will be assured, how much time will subject 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. Also, include whether a stand-alone HIPAA Authorization will be used or a combined consent-authorization document.

11.6.1 Waiver of Consent

If the study appears to qualify for a waiver of consent (studies limited to existing data), the protocol must provide sufficient information explaining why the research meets the criteria

of 45 CFR 46.116(d) so that the IRB can grant the request. The myIRB application will request this same information.

45 CFR 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 set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) the research involves no more than minimal risk to the subjects;

(2) the waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) the research could not practicably be carried out without the waiver or alteration; and

(4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

11.6.2 Waiver of Assent

When the subjects of the research are children, a wavier of consent means a waiver of parental permission and assent (the IRB must waive both). The criteria of §116(d) listed above must be met to obtain a waiver of assent.

Assent could also be waived (with or without a waiver of parental permission) under 45 CFR 46.408, if the capability of some or all of the children is so limited that they cannot reasonably be consulted or if the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

In either case, the request to waive assent must be justified and appropriate for the study being proposed.

11.6.3 Waiver of HIPAA Authorization

The criteria for waiver of HIPAA Authorization are similar to, but different than those for waiver of consent.

45 CFR 164.512(i.)(2)(ii) A statement that the IRB or privacy board has determined that the alteration or waiver, in whole or in part, of authorization, satisfies the following criteria:

(A) The use or disclosure of protected health information involves no more than 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 the 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;

(B) The research could not practicably be conducted without the waiver or alteration; and

(C) The research could not practicably be conducted without access to and use of the protected health information.

See the IRB website for more information about Waivers of Consent, Assent, and HIPAA. UF IRB (see: http://irb.ufl.edu/index/irb-policies-guidelines-and-guidances.html).

11.7 Payment to Subjects/Families

If subjects or parents/guardians are to be paid for the inconvenience of participating in the study, the amount of payment(s) must be stated in the protocol. The amount paid to parents/guardians should be separated from the amount paid to subjects. The IRB must review both the amount and method of payment to subjects to ensure that neither presents an undue influence on the trial subjects. Subjects not completing the study, for whatever reason, must be paid on a pro-rata basis.

See the UF IRB SOPs at website: http://irb.ufl.edu/index/irb-policies-guidelines-and-guidances.html.

11.7.1 Reimbursement for travel, parking, and meals

Amount per visit, justification, and form of reimbursement.

11.7.2 Payments to parent for time and inconvenience (i.e., compensation)

Amount per visit, justification, and form of payment.

11.7.3 Payments to the subject for time, effort and inconvenience (i.e., compensation)

Amount per visit, justification, and form of payment.

11.7.4 Gifts

If any tokens of appreciation will be given to subjects or families, these should be described here.

12 PUBLICATION

Describe the plans for publication. If the UF-Jax investigator does not have access to the complete trial data, describe how the publication will proceed.

13 REFERENCES

References …..

APPENDIX

Append relevant information.