LEADING HOSPITALS.
TRUSTED CARE.

ELEMENTS OF A RESEARCH PROTOCOL INVOLVING HUMAN SUBJECTS

I. Aim and Hypotheses

A. Begin with a brief introduction to describe the origin and importance of the study.

B. Clearly state the aim(s) and hypothesis(es), listing them by number if there is more than one.

II. Background and Rationale

A. Background:

1. Describe the facts, events, and thought processes leading to the currently proposed research project.
2. Summarize any pertinent studies supporting this proposed project. Human studies are preferred; include animal studies only if human studies data are lacking.

B. Rationale

1. Explain how the background information from the literature supports the current proposed hypothesis(es).
2. Explain how the performance of this proposed project will advance our knowledge in this field, and/or improve our understanding of the disease or physiological condition being studied.
3. Explain how this study, if the hypothesis(es) is (are) proven correct, might improve the diagnosis or treatment of the disease begin studied (if applicable), or advance knowledge in the field.

III. Research Plan

A. Experimental design

1. Indicate type of study (e.g. cross-sectional vs. longitudinal; multicenter, controlled, cross-over, randomized, etc) and describe how the study is to be conducted.

B. Sample size and statistical analysis(es)

1. Describe the analytic and statistical methods to be used, including the method of randomization and randomization ratio (1:1, 3:1; etc) if randomization is used.
2. If blinding (masking) is involved, describe the procedures, indicate who has the code to the blind, and the circumstances and procedures for breading the code.
3. State the maximum number of subjects to be enrolled in each group. Include power calculations to explain what can be studied with the proposed sample size and specify the statistical tests that will be used to test each hypothesis. If the research project needs to be pilot tested, state how many subjects will be enrolled in the pilot test and how the procedures for the pilot test will differ from those used in the research protocol.

C. Subject Characteristics

1. Subject criteria: Include age range, gender, disease, and stage of treatment. Justify excluding subjects based on race or gender (including child-bearing potential for women) or age (children).
    a) Inclusion criteria: State the criteria for inclusion in the study in a specific and detailed manner.
    b) Exclusion criteria: State the criteria for excluding potential subjects from the study in a specific and detailed manner.
    c) Withdrawal/Termination criteria: Include the specific circumstances in which the subject's participation will be terminated by the investigator. Include any necessary safety precautions to be applied to those who withdraw (tapering drug doses, evaluative x-ray, etc.)
    d) Clarity regarding whether a study subject may participate in another research study while participating in this research study.

D. Risk/benefit assessment: As appropriate, address the following parameters as each relates to the individual subject in the study. Be sure to include consideration of study assignment (Arm A, Arm B, placebo, active substance, etc):

1. Physical risk
2. Psychological risk
3. Social risk
4. Economic risk
5. Potential benefit of participating in the study
    a. to the individual subject and/or parent if any
    b. to the population from which the subject is drawn
    c. to science, society, and humanity in general

E. Specific methods and techniques used throughout the study

1. Laboratory tests: Indicate purpose, amount and timing of tests performed (e.g., blood tests, urine tests, CSF tests, EKGs, etc.).
2. Study Procedures: Describe imaging techniques including the instruments used, time required for each study, cognitive assessments)
3. Clearly indicate which procedures, tests, visits, etc., are part of usual standard therapy and which are performed solely for research purposes. Make it clear which tests are routinely performed for clinical care but are providing data for the research (and are billable to insurance companies), and which tests re only performed for research purposes (not billable to insurance companies).
4. Describe the fate of any body component (blood, CSF, bone marrow, etc.) used in the study, emphasizing confidentiality of labeling of the sample and the sample's destruction or storage.
5. Subject timeline: Consider attaching a study flow chart illustrating subject visits and tests or procedures to be performed at each visit.

F. Assessment of Subject Safety and Development of a Data and Safety Monitoring Plan

1. Describe how adverse events will be ascertained and handled. Explain exactly which adverse events will be considered serious and reported to the IRB. The reporting timeframe should also be detailed.
2. Describe how the severity of the adverse event and its relationship to the study protocol will be assessed and by whom.

3. Explain exactly what will happen if a patient experiences an adverse event (for example, will discontinue study drug).
4. Explain whether the study will be monitored by a Data and Safety Monitoring Board and if not, why a board is not necessary.
5. Describe Accountability procedures as they relate to drugs, devices, and data including who on the research team will be accountable (in addition to the Principal Investigator), who will interface with the pharmacy (drugs) or sponsor (devices).
6.

G. Subject Participation

1. Recruitment:
    a. Describe from where the subjects will be recruited and what arrangements have been made with other institutions (if applicable).
    b. Describe by whom and how the recruitment is performed.
    c. Attach copy of advertisements and/or flyers and state where they will be placed.
2. Registration: If subject registration is required (as in many multicenter trials), describe the procedure.
3. Screening Interview/questionnaire: If an interview or questionnaire will be used for screening, attach a copy and indicate where, how, and who will conduct the interviews and their qualification. Address how consent to participate in the screening process will be obtained.
4. Transportation: Describe subject transportation with emphasis on post-visit transportation.
5. Informed consent process and timing of obtaining of consent
    a. Indicate who will give subjects detailed and comprehensive information about the study and obtain their written consent.
    b. Indicate how the consenting process will be structured to ensure independent and thoughtful decision-making, and what steps will be taken to avoid coercion and guarantee confidentiality.
    c. Indicate how, and by whom, it will be determined whether the subject is able to give informed consent, or whether their legal guardian will give informed consent. For subjects whose ability to give informed consent may be compromised by cognitive and/or decisional impairment (examples may include individuals with a psychiatric disorder, an organic impairment, a developmental disorder, or those suffering from a terminal illness, degenerative disease, severe physical handicap or dependence on drugs or alcohol).
6. Study performance location: Indicate where all portions of the study will take place and where the research subject's records will be kept.
7. Personnel:
    a) Indicate, by title, who will be present during the study procedure(s) and their proximity during the study.
    b) Indicate who will have primary responsibility for the following activities:
        a. Obtaining informed consent

b. Providing on-going information to the study sponsor and the IRB
c. Maintaining participant's research records.

8. Subject fees: Indicate how much subjects will receive for each portion of the study and the reimbursement schedule to be used if the subject withdraws or is withdrawn during the study. Indicate if travel costs be reimbursed. Indicate what will happen if the subject's insurance company refuses to pay for costs of clinical are when those tests are also used for research purposes. Indicate what will happen if the study subject does not have insurance.
9. Study results: List any study results to be given to subjects and indicate how, when and why they will be given.
10. Identify any part of the study that may place subject confidentiality at risk. Describe study procedures to protect subject confidentiality.
11. Confidentiality:
    a) Certificate of Confidentiality: a Certificate of Confidentiality should be obtained for research involving collection of information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. For more information, go to: http://grants1.nih.gov/grants/policy/coc/index.htm
    b) Explain how data will be coded, recorded, and stored to protect confidentiality
    c) Identify all parties who will have access to the date, including the key to the identity code.
    d) Identify all parties who will have access to research records, such as research staff, sponsor, monitor(s), DSMB(s), IRB(s), etc.
12. Collaboration: If this is a collaborative effort with another institution, explain the collaboration and attach a copy of their current IRB protocol, consent form and approval.
13. A statement of alternatives to participation in this research study, if any.
14. Articulation of how new information will be conveyed to the study subject and how it will be documented.
15. Specifics regarding payment for participation, including a prorated plan for payment.
16. Information regarding payment for a research-related injury.

H. Outcome: Describe what results are expected, the criteria for success or failure and the end point of the study.

I. Tissue banking considerations.

VULNERABLE POPULATIONS

I. If the recruitment plan includes any of the groups noted below, explain how they will be protected and how consent will be obtained. In general, regulations allow subjects identified as part of vulnerable populations to be included if the research involves only minimal risk to them, or if they will directly benefit. Minimal risk is defined as the probability and magnitude of harm and discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

II. If the research involves greater than minimal risk and there is no prospect of direct benefit to individual subjects, but it is likely to valid generalizable knowledge about the subject's disorder or condition, the IRB will consider it based on the following:

a. The risk represents a minor increase over minimal risk;
b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of that disorder or condition; and
d. Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

III. **Cognitively or decisionally impaired:** Individuals with a psychiatric disorder, an organic impairment, a developmental disorder, and those suffering from a terminal illness, degenerative disease, severe physical handicap or dependence on drugs or alcohol.
a. Recruitment procedures
b. Consenting procedures and documents

IV. **Children:** Assent and consent forms must be submitted.
a. Recruitment procedures
b. Consenting procedures and documents
c. Consideration and procedures for re-consent if the minor will attain age 18 years while in the study.