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Elements of A Research Protocol Involving Human Subjects For Experimental Studies

The following is a guideline to be used when preparing a research protocol for submission to the Presbyterian Healthcare Services (PHS) Institutional Review Board (IRB). There are different types of research studies being conducted at PHS by physicians, residents, and staff. This guideline is for studies that are experimental in nature (i.e., clinical or non-clinical interventions, randomized placebo controlled trial, etc.). For experimental studies, the IRB will be looking for a research protocol containing the following elements. Please also include additional information that you consider to be important for review by the IRB.

I. Protocol Title and Study Information: Include principal and sub-investigators name(s). Also include the protocol version number, date, and page numbers on the footer of each page of the protocol.

II. Specific Aims and Hypothesis: Provide a brief introduction to describe the origin and importance of the study. Clearly state the specific aims(s) and hypothesis(es), listing them by number if there is more than one.

III. Background & Significance:

a. Background – Describe the facts, events, and thought processes leading to the currently proposed research project. Summarize and cite any relevant studies supporting this proposed project. Human studies are preferred; include animal studies only if human studies data are lacking.

b. Significance – Explain how the background information from the literature supports the current proposed hypothesis(es). 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. Explain how this study, if the hypothesis(es) is(are) proven correct, might improve the diagnosis or treatment of the disease being studied (if applicable), or advance knowledge in the field.

IV. Design & Procedures:

a. Experimental Design – Indicate type of experimental design (e.g., two-group parallel design; more than two study groups, comparison of different dosages, multicenter, controlled, cross-over), and describe how the study is to be conducted.

b. Procedures – Describe the study, providing detail regarding

- Randomization method, randomization ratio (1:1; 3:1; etc.);
- The study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.);

- If blinding (masking) is involved, describe the procedures, indicate who has the code to the blind and the circumstances and procedures for breaking the code;
- Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods, if applicable;
- Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk/ benefit ratio, and use of tissue/specimens. Indicate purpose, amount, and timing of tests performed (e.g., blood tests, urine tests, CSF tests, EKGs, etc.). Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any. Consider adding a timeline.

c. Measures – Describe what the primary outcome measure(s) are and the method for collecting the outcomes (e.g., medical record, phone survey, etc.).
   - Describe any other measures that will be collected, the purpose (i.e., to adjust for possible confounding), and method of collecting the information.

V. Selection of Subjects: List inclusion/exclusion criteria and how subjects will be identified. Include age range, gender, disease, stage of treatment, and if Spanish-speaking or other non-English-speaking populations will be considered. Justify excluding subjects based on race or gender (including child-bearing potential for women) or age (children). Government funded studies (i.e., NIH, AHRQ) do not allow for non-English speaking participants and minorities and women to be excluded unless it is justified and approved by them.

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.). Include a description of what would happen if a woman became pregnant while in the study.

VI. Subject Participation:

a. Recruitment – Describe from where the subjects will be recruited and what arrangements have been made with other institutions (if applicable). Describe by whom and how the recruitment is performed. Attach a copy of advertisement and/or flyers and state where they will be placed.
b. 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 qualifications. Address how consent to participate in the screening process will be obtained. If pregnancy test is part of the screening process, this should also be described.

c. Informed Consent Process/ Timing of Obtaining Consent – Indicate who will give subjects detailed and comprehensive information about the study and obtain their written consent. Indicate how the consenting process will be structured to ensure independent and thoughtful decision-making, what steps will be taken to avoid coercion and guarantee privacy[1] and confidentiality[2], how much time will likely be allocated for conducting the consent process, and how much time the potential subject (or surrogate) will have to consider whether or not to participate. 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).

d. Subject Fees: Indicate if and 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 care when those tests are also used for research purposes. Indicate what will happen if the study subject does not have insurance.

VII. Risk/Benefit Assessment: Include a thorough description of how risks and discomforts will be minimized. Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant women, prisoners or cognitively impaired adults – see section on vulnerable populations), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject, science, society, and humanity in general. What is the importance of the knowledge expected to result from the research? Do not overstate possible benefits.

VIII. Data Analysis & Statistical Considerations: Describe endpoints and power calculations.

a. Data Analysis – Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis.

b. Sample Size Estimation – Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

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[1] Privacy means having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

[2] Confidentiality means methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

If you need assistance in designing this section, statistical support may be available from PHS. Please contact the Office of Human Research Protections (OHRP) at 505-841-1436 or PHSResearch@phs.org for more information.

IX. Data & Safety Monitoring: Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor. All studies that are greater than minimal risk[3] require a data and safety monitoring plan.

X. Data Storage & Confidentiality: Identify any part of the study that my place subject confidentiality at risk. Describe study procedures to protect subject 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 data, 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.
e. If data is being moved/shared outside of PHS, explain how it will be transferred (paper form, electronically, etc.). When preparing this section, please consider that only the minimum necessary[4] data for the conduct of the study should be collected and of that only the minimum necessary transferred to any outside party or organization. If data is being stored off site on a specific network or server, please provide a description of the network or server including its protections.

XI. Other:

a. 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.
b. Articulation of how new information will be conveyed to the study subject and how it will be documented.
c. Outcome: Describe what results are expected, the criteria for success or failure and the end point of the study.
d. Tissue banking considerations.

[3] Minimal risk means the probability and magnitude of harm or 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 (45 CFR 46.102(1)).

[4] Minimum necessary means the data with the least amount of protected health information (PHI) necessary for the analysis of the data. The data can be stripped of identifiers and coded with a unique identifier.

If subject Social Security Numbers (SSNs) are being transmitted electronically or in paper outside of PHS as part of Case Report Forms or other study data, you must include (1) a rationale as to why SSNs are required by the sponsor or collaborator; and (2) a statement that the information containing SSNs will be transmitted in encrypted form.

Vulnerable Populations

The following are additional considerations for vulnerable populations. Vulnerable populations include, but are not limited to: Pregnant Women, Human Fetuses and Neonates (Subpart B); Prisoners (Subpart C); Children (under the age of 18) (Subpart D); and Cognitively or Decisionally Impaired Individuals (45 CFR 46.111(b)).

I. If the recruitment plan includes any of the groups noted above or any other group that may be considered vulnerable, 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 riskto them, or if they will directly benefit.

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 yield 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. Pregnant Women – To reduce the risks associated with research studies among pregnant women and their unborn child, the protocol should

a. recruitment procedures; and
b. consenting procedures and documents.

IV. Cognitively or Decisionally Impaired – To reduce the risks associated with research studies among cognitively or decisionally impaired individuals (defined as individuals with a psychiatric disorder, an organic impairment, a developmental disorder, those temporarily incapacitated due to an injury or medical condition, and those suffering from a terminal illness, degenerative disease, severe physical handicap or dependence on drugs or alcohol), the protocol should include

a. recruitment procedures; and
b. consenting procedures and documents.

V. Children – To reduce the risks associated with research studies among children, assent and consent forms must be submitted, and the protocol should include

a. recruitment procedures; and
b. consenting procedures and documents; and
c. consideration and procedures for re-consent if the minor will attain age 18 years while in the study; and
d. consideration and procedures in the event children are determined to be wards of the state (45 CFR 46.409).