10.1 SUBJECT SELECTION AND RECRUITMENT

A. Equitable Selection of Subjects

The selection of subjects for a research project should be equitable, ensuring that the burdens and benefits of research are fairly distributed. Federal regulations state that, when assessing methods of subject selection and recruitment, "*the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.*" 45 CFR 46.111(3) and 21 CFR 56.111(3)

In addition, social justice requires that there be a hierarchy of preference in the selection of subjects when the research involves more than minimal risk. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) recommends that studies that involve more than minimal risk be conducted in animals and adults before children, competent individuals before incompetent individuals, and non-institutionalized persons before institutionalized. In order to assess the appropriateness of the subject population for a particular research protocol, the IRB will evaluate the characteristics of the chosen subject population - considering age, gender, and population diversity - and the methods and materials that investigators propose to use to recruit subjects.

i. Inclusion of Women and Minorities

The NIH requires that its grantees include women and minorities in study populations "*so that the research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study.*" Women and minorities should be appropriately represented (in proportion to the demographic makeup of the eligible community) unless there is sound medical or scientific justification for their exclusion.

ii. Inclusion of Minors

The NIH requires that its grantees include children in study populations with the goal "*to increase the participation of children in research so that adequate data will be developed to support the treatment modalities for disorders and conditions that affect adults and may also affect children.*" Children should be included in a research protocol unless there is compelling medical or scientific reason for their exclusion.

B. Recruitment Principles

The IRB reviews an investigator's proposed recruitment methods in order to ensure that the procedure for recruiting subjects to a study is not unduly coercive. In addition, the IRB must review all recruitment materials, including electronic materials, to ensure that advertising for the study does not promise or imply a certainty of favorable outcome (e.g., cure) or other benefits beyond what is outlined in the consent document and the protocol. This review is especially critical when a study involves subjects who are likely to be vulnerable to undue influence.

i. Minimizing Coercion and Undue Influence During Recruitment

Patients may be hesitant to opt out of participation for fear of disappointing the doctor who presents the research. In order to minimize coercion or undue influence (if not

avoid it altogether), the IRB suggests that investigators make information about the study available and let interested patients contact the research team. Recruitment flyers describing the research (and includes contact information of the research staff) can be distributed by outside physicians or posted in offices. Where appropriate, other members of the research team can inform patients about the study and direct them to talk with their physician if interested.

ii. Protecting Privacy During Recruitment

In the process of recruiting for a research study, investigators must uphold the privacy of potential subjects and the confidentiality of their medical records. The Privacy Rule applies to such activities and sets limits and conditions on the uses and disclosures of protected health information (PHI) that may be made without patient authorization. Typically, employees of the covered entity (i.e., the Institution) may access PHI needed in order to contact patients in order to obtain HIPAA authorization. However, no PHI may be used for research without HIPAA authorization or a waiver (full or partial) from the IRB. Recruiting Subjects by Telephone

In studies involving a telephone interview to determine basic eligibility for a study, the IRB requires that investigators submit the telephone script for review. The script must indicate that participation in the research is voluntary and that the telephone interview can cease at any time the subject feels uncomfortable, or wishes to end the interview for any reason. Additionally, the IRB reviews the investigator's plans for protecting the confidentiality of the collected data and privacy during this telephone interview.

C. Special Circumstances in Recruitment

The IRB recognizes that some populations are more vulnerable to coercion and undue influence than others are. Accordingly, special consideration is given to studies that involve any of the following circumstances.

i. Recruitment of Children

Since the majority of children are in a dependent relationship to adult caregivers, they are particularly vulnerable to undue influence. When recruiting children, an investigator must take extra steps to ensure that the child's decision to participate in research is voluntary. Children should always be engaged in the assent process, to the level of their understanding. Written assent is required for children between the ages of 12 and 17.

The investigator is expected to minimize the possibility that a child's parent(s) or legal guardian(s) will pressure him or her to participate. Children should not be made to feel that refusal to participate will bear negative consequences, but likewise should not be offered incentives to participate that could cloud their ability to assent (incentives may differ substantially from those which influence adults).

ii. Recruitment of an Investigator's Patients

As there may be the potential for conflict of interest, a recruiting investigator who is also the treating physician of potential subjects must take special precautions to present the study information without undue influence or pressure. Ways to minimize undue influence include waiting to introduce the possibility of research participation until

after standard care options have been presented to a patient; offering patients the opportunity to discuss the research option with an uninvolved physician or staff member; and giving patients an appropriate amount of time to consider their participation. Investigators must detail the steps that will be taken to emphasize the voluntary nature of research participation in the clinical setting.

iii. Recruitment of Family Members

The identification and recruitment of family members of subjects for participation in research can be particularly sensitive, such as studies of genetics that require the participation of multiple family members. In many cases, a single subject is first identified and if that individual is a good candidate for the study, they can be provided with written informational materials to share with family members. The relatives may initiate contact with the research team, or let the study subject know that they would be willing to be contacted by the research team.

In addition to concerns about the privacy of individuals, investigators and the IRB should consider that the nature of family studies inherently exerts pressure on family members to take part. The investigator should be aware of potential for invasions of privacy and the appearance of coercion, both from the subject and from the investigator.

iv. Recruitment of Employees or Colleagues

When employees, colleagues and/or their families are recruited for participation in a research study, they may be vulnerable to perceived but unintentional pressures to appear cooperative and motivated. In extreme cases, they may feel that their participation is necessary in order to avoid jeopardizing their job or relationship with the investigator. Employees and colleagues must not be pressured to participate in research due to fear of job loss, delayed promotion or other influence of an investigator. It is particularly important to be sensitive to coercion when an individual is in a direct reporting relationship to an investigator.

Therefore, investigators requesting to directly recruit employees or colleagues as research subjects will be carefully reviewed by the IRB and the investigators' plan to minimize coercion must take into account these considerations. Investigators are encouraged to post flyers in the hospital or advertise using IRB approved global e-mails in lieu of direct solicitation so that any employee who is interested may initiate contact with the research team (if applicable).

v. Recruitment of Patients for Research at External Institutions

Recruitment of subjects for a study taking place at an outside institution is allowable when permission has been obtained from the department/division in which recruitment materials will be distributed/posted. The person authorizing the distribution of the materials is responsible for ensuring that the study/recruitment materials were reviewed and approved by an external IRB.

When Lurie Children's is not engaged in the research, our IRB does not need to perform an additional review of the recruitment materials for such studies. Lurie Children's is not considered engaged in a study, if the activity of our employees is limited to the following:

- informing prospective subjects about the availability of the research;
- providing prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but the Institution's employee(s) does directly not obtain the subjects' consent for the research or act as representatives of the investigators from the external institution;
- providing prospective subjects with information about contacting external investigators for information or enrollment; and/or
- seeking or obtaining permission from prospective subjects for external investigators to contact them.

vi. Investigator Self-Experimentation

All research involving human subjects must undergo IRB review to protect the rights and welfare of participants and the integrity of the research. Faculty and staff members who wish to act as participants in their own research protocols should consider themselves human subjects. Federal regulations do not allow for an exception when the investigators or staff elect to participate in their own research. Alternatives to self-experimentation are encouraged when available (i.e., use of discarded, deidentified clinical specimens, specimens from biobanks, etc.). Prior to commencing any research activity that involves self-experimentation (i.e., blood draws, sample collection) the investigator must obtain IRB approval.

The IRB will review the protocol and determine the appropriateness of the research, the type and level of self-experimentation, and the potential risks and benefits to the investigator/staff as research participants. The primary purpose of IRB review for studies involving self-experimentation is to: 1) protect investigators and staff from taking unwarranted risks, and 2) ensure junior investigators/staff do not feel undue influence or coerced to participate. The IRB will review each protocol and request additional safeguards for the research participants if necessary (e.g., specify who can obtain informed consent, type and frequency of testing, etc.). A standard consent form must be developed that includes all required elements of consent as outlined in 45 CFR 46.116 and/or 21 CFR 50.25.

D. Compensation and Reimbursement

Investigators may offer compensation for participation in research or reimbursement of expenses incurred. Study compensation is intended to offset the inconvenience of participation, but should not be at a level that would be perceived as coercive or exert undue influence on participation. The amount offered should be appropriate to the length and nature of the subject's participation, and must be clearly outlined in the informed consent form. In evaluating the appropriateness of the compensation or other incentives, the IRB will consider factors likely to affect the decision of the eligible population. In addition, compensation should not be contingent upon the subject completing the study. Any subject who withdraws from the study or is withdrawn from the study should receive payment for the portion of the study (i.e., visits) completed in a manner described at the time of enrollment and in the informed consent document. Reimbursement is payment to cover expenses incurred by the participant because of clinical trial participation (most often travel related).

The Institution's preferred method of payment of study compensation is via gift/debit cards. Payment by cash and/or check is discouraged (due to costs, etc.), but may be allowed when pre-approved on an individual basis. The investigator/study team is responsible for keeping a record of all study payments regardless of the method of payment made to each research participant.

Please note that the IRS requires study compensation payments of $600 or more in a calendar year be reported as taxable income. It is the responsibility of the investigator to obtain a complete W-9 form (including social security or tax id number) from the participant when study compensation meets this level regardless of the method of payment. The W-9 form can be found at https://www.irs.gov/pub/irs-pdf/fw9.pdf. The completed W-9 should be forwarded via e-mail to Accounts Payable at ap@luriechildrens.org. The Institution will generate a form 1099-MISC and send a copy to the IRS and the participant.

Reimbursement of expenses is typically made by check based on receipts/costs incurred and is not considered taxable income. The Institution's Accounts Payable Department requires that a W-9 form accompany any check request (for reimbursement and/or compensation) regardless of the amount. However, the participant's social security or tax ID number does not need to be completed on the W-9 when: 1) the check request is for reimbursement of expenses, or 2) the cumulative study compensation is less than $600 in a calendar year.

NOTE: The Ensuring Access to Clinical Trials Act of 2015 (S. 139/H.R. 209) (EACT) is a law which allows individuals who participate in rare disease clinical trials to receive up to $2,000 of compensation, without those funds counting against their income eligibility for Medicaid and SSI.

E. Advertisement for Research Subjects

i. General Guidelines

As a general rule, anything that is intended to be directly seen or heard by prospective subjects and/or parent, should be reviewed/approved by the IRB.

Direct advertisements for research subjects, regardless of the medium, (e.g., flyers, global e-mails, solicitations by e-mail, social media, etc.) are an extension of the informed consent and subject selection processes. Advertisements for the recruitment of research subjects require IRB approval. The IRB will review the advertisement and the mode of its communication to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. Only IRB approved documents may be used for recruitment.

Note that "Dear Doctor" or doctor-to-doctor letters (even when soliciting for study subjects) are **not** considered advertising and do not require approval by the IRB. Information that is available to the general public (i.e., news stories, press releases, public websites such as clinicaltrials.gov, etc.) that are not created specifically for the study are not considered advertising.

The IRB reviews advertising and recruitment materials with Initial applications or as Modifications in Cayuse IRB any time during the study. The IRB will take into consideration the procedures, amounts, population, time commitments, location where ads will be placed, and determine what is most appropriate for all recruitment methods. Advertisements that are to appear on television or other predominately public locations

may be subject to review by the hospital's media relations department. The IRB does not consider "cold calling" an acceptable recruitment practice (e.g., calling subjects with whom no previous in person contact was made and no mailing of study information was sent).

ii. Content of Recruitment Materials

Any proposed notice or advertisement for subject recruitment must contain the following information:

a. The condition under study and/or the purpose of the study
b. Who can participate in the study, i.e. summary of eligibility criteria
c. Brief description of what study participation will entail (i.e., number of visits, length of participation, general study procedures)
d. If reimbursement for expenses or payment for time and effort will be provided, these may be included as long as the dollar amount is not overemphasized
e. The location of the research and the person or office to contact for further information
f. Required approval verbiage (this is to appear on all approved recruitment, and may be modified with explicit approval from the IRB): "This study is Lurie Children's IRB #, TITLE, Principal Investigator Name. The content of this flier/brochure/e-mail/etc. has been approved by the Lurie Children's IRB."

The IRB will approve a recruitment document only if the following conditions are met:

a. The form and method of advertising are not unduly coercive and do not imply the certainty of a favorable outcome or benefit.
b. The use of investigational drugs or devices is explicitly stated, when applicable. Claims are not to be made about the safety or effectiveness of the investigational product.
c. The advertisement does not make claims that that the test article or therapy is known to be equivalent or superior to other articles and therapies
d. The advertisement is to be professional in appearance
e. The advertisement does not include exculpatory language

Advertisements should **not:**

a. Include the terms "new treatment," "new medication" or "new drug" to describe into investigational drugs, biologics, or devices without explaining that the test article is investigational. Such terms leads study subjects to believe they will be receiving newly improved products of proven worth.
b. Promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation. Do not use terms such as "free care" or "free assessments"

iii. Submission and Approval Procedures after Protocol Approval

If the original Initial application/protocol did not include advertising for the research subjects, the research investigator must submit a Modification in Cayuse IRB and provide for review all recruitment materials and methods for dissemination of the materials. The use of the recruitment materials/methods may not begin until IRB review and approval is provided.

iv. Recruitment Utilizing Clinical Trial Websites

Clinical trial websites provide a significant opportunity not only to recruit subjects, but also to foster informed consent by increasing the amount of information that is available to an individual interested in a clinical trial. The websites, such as the National Cancer Institute or CancerNet, can often generate a large number of site visits by individuals wanting to learn more about clinical trials. In some cases, the information provided on these websites may constitute the earliest components of the informed consent process.

When information posted on a clinical trial website goes beyond directory listings with basic descriptive information, such information is subject recruitment therefore requires IRB review and approval. The basic descriptive information includes title, purpose, protocol summary, basic eligibility criteria, location(s), and contact information. Information included beyond these basic listings will require review and approval by the IRB. For complete guidance, please see the OHRP guidance at http://www.hhs.gov/ohrp/policy/clinicaltrials.html. FDA guidance mirrors these principals and can be found at http://www.fda.gov/oc/ohrt/irbs/toc4.html#recruiting.

IRB review and approval of listings of clinical trials on the internet is not required for listing services such as the National Cancer Institute listing, the government-sponsored AIDS Clinical Trials Information Service, Clinicaltrials.gov, etc. However, if you plan to add additional descriptive information that is beyond the listing, IRB review and approval is required.

F. Payment Arrangement among Sponsors/Organizations, Investigators and Others

Payment in exchange for referrals of potential subjects (finder's fees) and payments designed to accelerate recruitment tied to the rate or timing of enrollment (bonus payments) is generally unacceptable. It is impermissible to accept bonus payments. The Institution's physicians and employees cannot accept personal payments from sponsors or other researchers in exchange for accelerated recruitment or referrals of patients.

10.2 INTERNET AND SOCIAL MEDIA

A. Using Internet and Social Media to Conduct Research Activities

The internet has become an increasingly popular tool for conducting research and recruiting subjects. Computer- and internet-based methods of collecting, storing, utilizing, and transmitting data in research involving human subjects are developing at a rapid rate. As these new methods become more widespread in research, they present new opportunities for potential enhancement of the dissemination of surveys, obtaining informed consent, subject tracking, and direct participation, while also presenting new compliance challenges to the protection of research subjects. The purpose of this chapter is to guide investigators in addressing the ethical and practical considerations needed for protecting human subjects when