Recruitment and Screening of Potential Participants for Research Reviewed by the NIH IRB

Recruitment activities and materials are intended to provide prospective study participants with their first introduction to the research study and are considered part of the process of informed consent. Investigators must describe plans for recruitment in the protocol so that the IRB can determine whether the proposed process respects potential participants' autonomy, is not coercive, and does not subject the potential participant to undue influence. The IRB will also evaluate if the recruitment plan includes provisions to protect the privacy and confidentiality of the prospective participants. Additionally, the IRB must determine that the process and materials used for participant recruitment promote fair and equitable participant selection based on the scientific question that the study will address, and that it avoids unfairly targeting any specific groups especially those considered to be vulnerable. The plan and proposed recruitment materials should be submitted at the time of the protocol's initial review or, if such materials are added later, as a protocol amendment.

Definitions

Recruitment materials: The term "recruitment materials" encompasses information potential subjects will see or hear that is used as part of the research recruitment process including, but not limited to, the following which are described in greater detail below:[1]

- Flyers and posters
- Newspaper advertisements
- Television and/or radio advertisements (PI should submit a script of ad content for IRB review)
- Brochures
- Recruitment letters
- Doctor-to-patient or Investigator-to-participant letters
- Social networking advertisements (e.g. Facebook)[2]
- Scripts or guides to be used for in-person or telephone recruitment interviews
- Website postings (some website postings may not require IRB review if the they meet specific criteria noted below)

Recruitment Methods: The means used to identify potential research subjects, or to draw a potential research subject's attention to participation in research, including but not limited to identification through records review, in-person discussion, and use of recruitment materials.

[1] Additional information is available in NIH Policy 302 *Subject Recruitment and Compensation*

[2] NIH investigators who plan to use social media for recruitment purposes should be familiar with the NIH Social Media Guidelines

Recruitment plan

When preparing the recruitment plan for the research, the following information should be considered and included, as applicable, in the protocol:

- What method of recruitment is planned? Describe the where, when and how details of the recruitment plan.
  - What is the source and location for recruitment of participants? How are participants identified? (e.g., inpatient setting, clinic, community center, general public)
  - Are the potential participants given enough time to consider enrolling without undue pressure?
  - NIH investigators, or their supporting ICs, are not permitted to provide, or receive, finder's fees (e.g., payment in exchange for referrals of individual prospective research participants, which are sometimes referred to as "recruitment incentives"), from any source in connection with research at NIH.
  - The IRB prohibits "cold-calling" of potential research subjects unless specifically approved by the IRB. "Cold-calling" is the practice of investigators or research staff, unknown to the potential research participant, initiating contact with the potential participant based on the investigator's prior knowledge of private health information. (E.g. through review of the potential participant's private health records as discussed further below.)
- Who will be conducting recruitment activities?
  - If a specific individual is performing recruitment activities, the plan should indicate why the individual is qualified and appropriate. The person to whom the potential participant is directed for information must be knowledgeable and able to answer relevant questions.
  - In cases where family members will be considered potential participants, how will the privacy of the family member be protected? Often the researcher can ask the proband to discuss possible study participation with the family member, or the investigator might create an information sheet that the participant (proband) can provide to the family member who is not yet known by the investigator.
- Does the proposed recruitment plan promote fair and equitable selection of participants?
  - The plan should promote equitable, appropriate participant selection based on the protocol's scientific question(s).
  - The recruitment plan should reflect populations burdened by the disease under study.
  - No specific group of people should be unfairly targeted nor unfairly excluded from the research.

- Are there special considerations that should be addressed if the cohort(s) will include individuals from vulnerable populations?
  - If the study permits enrollment of NIH staff, additional protections are required per NIH policy.
  - Depending on the cohorts being studied, recruitment information regarding eligibility may need to be revised based on regulations in specific 45 CFR 46 Subparts A-D respectively, if pregnant women, human fetuses, neonates, prisoners or children are being recruited.
- Do recruitment plans take cultural and social practices into consideration (e.g., group or family recruitment before individual recruitment), if applicable? If recruitment materials are translated to a non-English language, a certified translation or a back translation must be approved by the IRB prior to use of the materials.
- What materials will be used for recruitment? Examples include:
  - Publicly posted recruitment material: For example, advertisements, posters or flyers, or directed advertising such as posting study recruitment materials in a location where it will be seen by those possibly eligible for participation (e.g. flyer/poster placed in clinics where patients receive care specifically for the disease being studied in the research)
  - Direct recruitment (e.g. physicians talk to their own patients about the study): In this case, it is preferable that a knowledgeable investigator from the study team who is not providing direct care for the patient approach the potential participant to discuss the study in order to prevent undue influence or pressure on the potential participant.
  - Recruitment letters: Communications sent to prospective participants should indicate how the individual was identified and include study information and a contact person who can provide additional details.
  - Referrals: Clinicians who are not part of the research can provide their patients who are potentially eligible for the protocol with IRB approved recruitment materials or letters that describe the study. The potential participant, if interested, can then contact the investigator directly. Alternatively, after obtaining any required authorization,[3] the clinician who initiated the discussion may share the potential participant's contact and relevant health information with investigators so that they can contact the individual

[3] HIPAA regulations may apply if the non-NIH local clinician is part of a HIPAA covered entity. In such cases, required authorization (or a waiver of authorization issued by a privacy board) from the potential participant would be required prior to the local clinician providing medical records with Protected Health Information to the investigator. This includes the non-NIH local clinician disclosing to the research team patient demographics and a diagnosis suggesting potential study eligibility. Information regarding HIPAA and research can be found here: Clinical Research and the HIPAA Privacy Rule and a Department of HHS webpage regarding Health Information Privacy as it relates to Research. See References section for additional links

directly. For multi-site research with non-NIH investigators, requirements related to circumstances necessitating that Protected Health Information (PHI) be provided by a HIPAA covered entity are further discussed below.

- Websites: Informed consent must be obtained for the collection of any information about the respondent unless the IRB has determined that the informed consent requirement can be waived. A mockup of the proposed website should be submitted for prospective IRB review. OHRP in its guidance on IRB review of clinical trial websites noted the following: "*Some clinical trial websites ask viewers to answer questions regarding eligibility for a specific clinical trial. If identifiable private information is collected via the clinical trial website, the IRB should review plans for protecting the confidentiality of that information. The IRB should ensure that the website clearly explains how identifiable private information might be used. Informed consent must be obtained for the collection of any information about the respondent unless the IRB has determined that the informed consent requirement can be waived*."[4] Conditions when IRB review of clinical trial websites is not required are discussed below.
- Review of medical records: This is discussed further below.

Information to be included in recruitment materials

- The protocol and recruitment materials must be consistent. For example, for a Phase 1 study, does the recruitment material(s) make it clear that the research is only intended to evaluate the safety and not the efficacy of the investigational product?
- Recruitment materials should be balanced and fair. These materials should include information that prospective participants need to determine interest and eligibility and should include all of the following:
  - A clear statement that the study is a research study
  - Name of the investigator conducting the research and their affiliation such as the specific NIH IC (e.g. NIH National Cancer Institute)
  - The purpose of the research and/or condition under study
  - Summary of eligibility criteria
  - A brief discussion of what study participation involves (duration of the study, number of study visits/time commitment, study procedures)
  - Research location
  - Person or office to contact for further information

[4] See OHRP Guidance: IRB Review of Clinical Trial Websites (2005)

- Materials may also include:
  - Brief list of significant risks, if any
  - Brief list of possible benefits, if any
  - Payment information, if applicable
- Recruitment materials may not:
  - State or imply benefits or outcomes beyond what is stated in the consent and the protocol
  - Include exculpatory language (language that suggests that the participant could be made to waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution, or its agents from liability for negligence)
  - Overemphasize payment (e.g. list payment information in a larger font) or characterize payment as a benefit
- Additionally, for clinical trials:[5]
  - Recruitment materials must state that the test article (drug, biologic or device) is investigational (as applicable).
  - Do not make claims either explicitly or implicitly that the test article is safe or effective for the purposes under investigation, or that it is equivalent or superior to currently available treatment.
  - Do not use the terms "new treatment," "new drug," or "new medication" without explaining that the test article is investigational.
  - Do not promise "free medical treatment or care," when the intent is only to inform participants that they will not be charged for participating in the study.

Conditions when IRB review of clinical trial websites is not required include the following:[6]

- If the website provides only direct listings with basic information about clinical trials in general (e.g. clinicaltrials.gov) AND
- Posting includes only basic descriptive information limited to the following:
  - study title
  - purpose of the study
  - protocol summary
  - basic eligibility criteria

[5] For additional information, see FDA Information Sheet *Recruiting Study Subjects: Guidance for Institutional Review Boards.*

[6] See OHRP Guidance IRB Review of Clinical Trial Websites

- study site location(s), and
- how to contact the study site for further information

Identification of potentially eligible participants via prospective review of private medical information

When a protocol will target individuals with specific health concerns/diseases, review of medical records, patient registries, clinical databases and referrals from local treating physicians may be helpful resources for recruiting. Under the pre-2018 Common Rule regulation(45 CFR 46), unless the research qualified for specific exemptions, consent from the potential participant for recording their identifiable private information being obtained for recruitment was required unless waived by the IRB. Under the revised 2018 Common Rule (45 CFR 46, effective January 21, 2019), there is an exception to informed consent for certain recruitment activities. For those protocols subject to the 2018 Common Rule, the IRB may approve research "*in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met*

(1) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

(2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens." [7]

The current regulation means that collection of private medical information for the purpose of participant recruitment can occur without informed consent or an IRB waiver of consent. **However**, the solicited information should be limited to the minimum necessary for screening or to determine study eligibility. The process needs to be clearly described in the protocol, so that the IRB can determine whether sufficient privacy and confidentiality protections are in place regarding these activities. Collection of private health information from a HIPAA covered entity may require authorization by the potential participant as further discussed below.

Implications of HIPAA on recruitment activities at non-NIH recruitment sites

NIH is not considered a covered entity and is thus not subject to the HIPAA Privacy Rule but is, instead, subject to the Privacy Act of 1974. However, NIH researchers should be aware of the HIPAA Privacy Rule because it establishes the conditions under which covered entities can use or disclose PHI for many purposes, including for research. The Privacy Rule Health Insurance Portability and Accountability Act of 1996 (also known as HIPAA, the HIPAA Privacy Rule or the

[7] 45 CFR 46.116 (g)

Privacy Rule) regulates the way certain health care groups or organizations called covered entities[8] under the Rule (such as health care providers in local medical practices, hospitals, academic medical centers etc.), handle individually identifiable protected health information (PHI). The Privacy Rule may impact various areas of research, including clinical research, repositories and databases, and health services research as it establishes conditions under which covered entities can provide researchers access to and use of PHI when necessary to conduct research. As it relates to recruitment of potential research participants, the HIPAA Privacy Rule permits a covered entity to disclose PHI if it has obtained an individual's written permission in the form of an Authorization. The Rule also permits covered entities to use and disclose PHI without Authorization for certain types of research activities if a covered entity obtains documentation that an Institutional Review Board (IRB) or Privacy Board has waived the requirement for Authorization or allowed an alteration. Since NIH is not subject to HIPAA, the NIH IRB does not provide such waivers. However, in the case of multisite research overseen by the NIH IRB, review by the local sites that are subject to HIPAA can be undertaken by that site's Privacy Board. There are other research related regulations under the HIPAA Privacy Rule (e.g. use of PHI under a waiver of HIPAA authorization such as for limited data sets, review of PHI preparatory to research or research on decedent's information) that are not directly related to recruitment. For additional information, see the HIPPAA related documents in the References and Links section.

NIH researchers should be aware that even though NIH is not a HIPAA covered entity, it is essential that we are aware of and respect the restrictions placed by HIPAA on those entities that are subject to the rule. The use or disclosure of information in violation of HIPAA can result in substantial penalties to the covered entity.

Screening activities

If an investigator wishes to initiate a clinical procedure that will be performed solely for determining research eligibility, informed consent must be obtained. Clinical screening procedures for research eligibility are considered part of the subject selection and recruitment process and, therefore, require IRB oversight and must be described in the protocol. Screening should include the fewest and least risky tests/interventions necessary to determine study eligibility and should minimize participant exposure to potential harm for those who fail screening. The IRB should receive a written outline of the screening procedure(s) to be

[8] Non-NIH "Covered entities" are defined in the HIPAA rules as (1) health plans, (2) health care clearinghouses, and (3) health care providers who electronically transmit any health information in connection with transactions for which HHS has adopted standards. Generally, these transactions concern billing and payment for services or insurance coverage. (HHS Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule Health Services Research and the HIPAA Privacy Rule (NIH Publication Number 03-5388))

followed and how consent for screening will be obtained. If a separate consent for the screening portion of the protocol is used, the IRB may find it appropriate to limit the scope of the screening consent to a description of the screening tests and reasons for performing the tests including a brief summary description of the study in which the individual may be asked to participate. Unless the screening tests involve more than minimal risk or involve a procedure for which written consent is normally required outside the research context, the IRB may decide that prospective study subjects need not sign a screening consent document.

References and Links

1. NIH Policy 302 Subject Recruitment and Compensation
2. NIH Social Media Guidelines
3. FDA information sheet: *Recruiting Study Subjects- Guidance for Institutional Review Boards and Clinical Investigators* (January 1998)
4. FDA Information sheet: *Screening Tests Prior to Study Enrollment* (January 1998)
5. OHRP *Guidance on Institutional Review Board Review of Clinical Trial Websites* (Sept. 2005)
6. HHS *Clinical Research and the HIPAA Privacy Rule* (February 2004) NIH Publication #04-5495
7. HHS HIPAA webpage *Research* (HIPAA as it relates to research) (Revised December 2017)
8. HHS *Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule Health Services Research and the HIPAA Privacy Rule* (NIH Publication #03-5388)
9. HHS *Research Repositories, Databases, and the HIPAA Privacy Rule*. (January 2004) NIH Publication #04-5489