CARILION CLINIC INSTITUTIONAL REVIEW BOARD
Standard Operating Guidelines

Title: 2.3: Review of Research: RECRUITMENT OF STUDY SUBJECTS	
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Primary Sponsor: Human Research Protections Office	**Approved By:** Director of the Human Research Protections Office

Objective:

To establish guidelines for the recruitment and enrollment of potential human subjects into research activities and for the use of protected health information (PHI) as it relates to research recruitment practices.

General Description:

Recruitment of subjects is one of the most challenging aspects of research involving human subjects. According to federal regulations on human subjects research, all research in which individuals are contacted or recruited for enrollment must be prospectively reviewed and approved by an Institutional Review Board (IRB). Because recruitment is an essential part of the research protocol, all matters of recruitment must be presented in sufficient detail to allow the IRB to assess fully the investigator's plan. Recruitment of subjects must be equitable and include racial, ethnic, educational, socioeconomic, and gender diversity appropriate to the condition that is studied. Exclusion of any specific group (e.g., women of child-bearing potential) must be justified in the protocol. This is done in an effort to assure that both the benefits and risks of research participation are fairly distributed. The recruitment plan must avoid coercion or undue influence of subjects, which includes consideration of such matters as financial compensation, reimbursement for expenses, or other inducement for participation, each of which must be reasonable for the expenses, discomfort, or inconvenience of participating.

The Privacy Rule (HIPAA) mandates an additional privacy focus to this review. For a protocol to qualify for IRB approval, all recruitment efforts must respect personal rights to privacy and confidentiality and be compliant with HIPAA regulations and the policies and procedures of the institution and the IRB.

Procedure:

RECRUITMENT METHODS

There is benefit to involving the treating clinician in discussions of research participation, particularly for studies involving treatment interventions. This policy, acknowledging these benefits and an existing culture at Carilion, encourages treating clinician involvement in recruitment discussions and processes for this type of research.

Recruitment includes identifying potential subjects through review of records to determine eligibility or any contact to determine a potential subject's interest in a research study. The following are recruitment methods for human research studies at Carilion. All recruitment methods must be described in the narrative of the IRB protocol and/or application. Recruitment materials must be reviewed and approved by the IRB.

Recruitment Material may not be used prior to IRB Approval. After Approval, if a researcher intends to change or add new Recruitment Material, it must be reviewed and approved by the IRB prior to implementation using a Change Update form in PRIS3M.

It is recommended that potential participants are contacted no more than three times in total per research study to solicit their participation. Potential participants who receive multiple requests for participation may feel harassed.

No Treating Clinician Involvement

- **Use of advertisements, notices, and/or media to recruit subjects.** Examples include flyers posted in public settings, newspaper ads, radio and television advertisement. All advertisements and recruitment materials (e.g., video, audio, telephone scripts) require prior IRB approval.
- **Direct recruitment of subjects unknown to the researchers.** Examples include random digit dialing, approaching people in public settings, snowball sampling, use of social networks.
- **Maintain a separate IRB-approved recruitment protocol** to develop a database of potential subjects. The subjects/patients provide consent ahead of time to be contacted for future research studies. Researchers contact patients about participation in IRB-approved studies in accord with the signed consent. No waiver of informed consent or partial waiver of HIPAA authorization is required.
- **Utilize a clinical trial website.** Researchers posting information on such a website should submit the content of postings to the IRB for approval. However, IRB review and approval of listings of clinical trials on an internet clinical trail website is not required when the system format limits the information provided to basic trial information, such as: the title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information. When the opportunity to add additional descriptive information is not precluded by the data base system, IRB review and approval is needed to assure that the additional information does not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document.
- **Contact of potential subjects by researchers who ARE NOT health care providers of patients. Researchers are Carilion employees or workforce members.** Contact will be via letter, phone, or email. These communications must be approved by the IRB. (Use templates available on the IRB web site) Contact information will be obtained through review of medical records, clinic schedules or databases established for health care operations or quality improvement or provided by a patient's Carilion health care provider without the patient's knowledge. This method requires the IRB to grant a waiver of informed consent for recruitment purposes and a partial waiver of HIPAA authorization to identify and contact subjects because Protected Health Information will be accessed and used. In addition, these research personnel must be approved to have access to protected health information.

The IRB considers this method most appropriate for minimal risk studies that do not involve the use of investigative drugs, devices, biologics or medical or surgical procedures.

For studies that involve greater than minimal risk investigative procedures or interventions, there should be greater treating clinician involvement using one of the methods outlined below.

Non-Carilion employed research team members can contact potential subjects after the Carilion employed researcher/treating clinician has received permission from the patient. Verbal permission is allowed with appropriate documentation.

- **Cold calling:** Cold calling is the act of researchers calling potential subjects on the phone without providing them with prior information about the study before contact. Carilion does not permit cold calling of patients (including leaving voicemails) who are outside of the principal investigator's clinical practice or department. Permission to contact participants must either involve the treating care provider receiving permission from the patient for the researchers to contact the patient OR a letter to be sent to the patient from the treating clinician with information on how the participant should contact researchers if interested. The study team may also include a letter of support from an outside Department Chair or Clinical Manager to recruit from their patient population for minimal risk studies.

<u>Treating Clinician Involvement</u>

- **Provide colleagues with an IRB-approved recruitment letter or flier for patients** describing the study. This letter can be signed by the treating physicians and would explain the purpose and procedures of the study and inform patients how to contact the research team. Researchers are prohibited from having access to subject/patient names, addresses, or phone numbers; interested patients must initiate contact.
- **Send an IRB-approved letter to colleagues asking for referrals of eligible individuals/patients** interested in the study. The research team may provide the referring colleague an IRB-approved information sheet about the study to give to the individuals/patients. If interested, the individual/patient contacts the researcher. Also, the treating clinician may discuss possible patient eligibility with the research personnel in a de-identified manner, i.e., with all specified subject identifiers removed. If the research personnel believe the de-identified patient would be eligible for the trial, the treatment personnel could then give the research personnel the patient's name with documented permission from the patient (e.g., documentation in research record or medical record that the care provider spoke with patient who agreed to be contacted). The researcher could then be allowed to contact patients about enrollment. Note: A waiver of informed consent and a partial waiver of HIPAA authorization must be granted by the IRB if treatment personnel provide researchers with patient contact information.
- **Send a letter from the treating clinician to the patient** indicating how to join an IRB-approved study so long as this process and the content of the letter are approved by the IRB. While this letter can be co-signed by the investigator, only the treating clinician/personnel (i.e. those who already have reason to know the patient's identifying information) are authorized access to this PHI, and thus they must send the letters.
    - If the letter indicates that the prospective subject will be approached (usually via telephone) regarding study participation, the letter must clearly detail that participation is voluntary and that if they are not interested in discussing study participation they are free to say no. The recruitment letter should include a telephone number to call or a postcard to return if the prospective subject is not interested in participating in the study. If no telephone call is received or postcard

returned, the prospective subject may then be contacted by the investigator to determine whether the subject is interested in learning more about the study. This process requires prior IRB approval of a telephone script that will be utilized as part of the recruitment process.

- When research involves sensitive information (e.g. illegal behavior, drug or alcohol use, mental illness, sexual behavior or other sensitive issues) the recruitment letter should include a telephone number to call or postcard to return if the prospective subject is interested in learning more about the study. The investigator may NOT contact prospective subjects who have not called or returned a postcard indicating interest in learning more about the study. The IRB will determine when this approach should be used.

- **Treating clinician approaches own patients.** Direct recruitment of patients by a treating clinician/researcher, his/her treatment personnel, or his/her Carilion research personnel for his/her own research protocols is not affected by HIPAA provisions. These personnel already have a reason to know the patient's PHI and, assuming the study (and the recruitment process) has been approved by the IRB, these personnel may approach the patient about participating in the trial without any further implications resulting from HIPAA. If identifying information from a medical record is recorded about a patient for recruitment purposes prior to obtaining informed consent, a waiver of informed consent must granted by the IRB.

  This method may raise ethical concerns because individuals may have difficulty saying no to an authority figure. To protect against even the appearance of undue influence or coercion, Carilion researchers should use caution in actively recruiting their own patients. A description must be provided in the IRB application or protocol narrative of what precautions will be taken to avoid undue influence during recruitment (e.g., research staff obtaining signatures after the consent discussion).

  Note: If a prospective subject refuses to participate, no identifiable information may be kept about the individual unless s/he consents to allow retention of this information. The protocol narrative should include a description of this consent process. With IRB approval, de-identified information about those who refuse to participate may be retained/collected; otherwise all information obtained from charts, records, registries must be destroyed.

  Note: Per this policy, treatment relationships at Carilion extend to group practices where providers cover for each other and can treat each other's patients.

- **Approach own students or employees.** This method raises ethical concerns because individuals may have difficulty saying no to an authority figure. To protect against even the appearance of undue influence or coercion, Carilion researchers should use caution in actively recruiting their own students or employees.

  An investigator, research coordinator, or other member of the research team that does not have direct authority over the students or employees should obtain informed consent from these individuals. A discussion must be provided in the IRB application protocol narrative of the precautions that will be taken to avoid undue influence during recruitment.

- **Request a Waiver of Consent/HIPAA Authorization, if applicable, for recruitment purposes.** In all cases the waivers must be justified in IRB application and protocol narrative. Waivers may be granted under the following circumstances:

- **Minimal risk studies** (i.e., expedited level of review) in which subjects will not be contacted (e.g., retrospective chart review studies) researchers request a complete waiver of consent/HIPAA authorization, if applicable. Justification for the waiver must be included in the IRB Application.
- **Review of charts, medical records, clinic schedules or clinical databases to identify prospective subjects who will then be contacted and asked to participate in the study.** Justification for the waiver to review charts must explain why the study cannot be done without the waiver. A partial waiver may be granted to allow collection of only the minimum amount of information needed to make contact; informed consent is obtained before additional information is gathered.

  For studies that are greater than minimal risk and involve use of investigative drugs, devices, biologics or medical or surgical procedures, patients identified through review of clinical records must be approached by someone already involved in their care (e.g., treating physician and other health professionals directly involved in care as well as administrative and Carilion research staff working for the treating physician).

  In some circumstances for greater than minimal risk research it may be necessary for members of the Carilion research team who are not involved in the patient's care or who do not work for the treating physician to make the approach, either in person or by phone or letter. The application should explain why the study cannot be done unless the researchers approach subjects directly. Direct approach by someone not involved in the patient's care for greater than minimal risk research is unusual but may be approved under exceptional circumstances (e.g., emergency care research).

- **Large-scale epidemiological studies and other population-based studies** may need to identify subjects through registries, medical records in multiple institutions, or other sources. The researchers may need to contact prospective subjects directly rather than through professionals involved in the prospective subjects' health care. This approach involves a greater invasion of privacy than other methods, because researchers without approval from patients gather significant personal health information about the patients, and then contact the patients directly. Justification in the application must explain in detail why it is impossible to do the study unless the IRB grants (1) a partial waiver of informed consent/ HIPAA authorization to obtain subjects' identities and (2) allows researchers to contact subjects directly. Written informed consent and HIPAA authorization is required before additional information is gathered and/or research procedures are initiated.

ADVERTISEMENTS AND RECRUITMENT MATERIALS REQUIREMENTS

Advertisements and recruitment materials for human research subjects (posters, flyers, newspaper/magazine ads, scripts for radio/TV, electronic mail, or solicitations from outside sources) are considered an extension of the informed consent and subject selection processes. Accordingly, they require IRB review and approval.

Recruitment materials are reviewed by the IRB to ensure that:

- They are neither misleading nor coercive to potential subjects.

- They make no claims either explicitly or implicitly that might lead a subject to believe that an investigational/experimental treatment is proven safe and effective and/or equivalent or superior to other treatments.
- If the study involves an investigational drug, biologic or device, the advertisement may not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational. Phrases such as "receive new treatments" or "receive new therapy" mislead study subjects to believe they will be receiving newly improved products of proven benefit.
- They do not promise "free medical treatment," when the intent is only to state that subjects will not be charged for taking part in the study.

All Recruitment Materials Should Contain, at Least, the Following Information:

- The name of the institution, the name of the Department or Division, the name of the researcher and the name of a contact person with a telephone number (including area code) to call for information about the study;
- The purpose of the research and, in summary form, the eligibility criteria that will be used to admit subjects into the study (e.g., adults on medication for high blood pressure, diabetic patients on insulin; normal, healthy adults; etc.);
- A straightforward, truthful description of the benefits, if any; and
- The location of the research and time commitment, if appropriate (e.g., subjects will have to come to X on 4 separate occasions; the research will take 2 hours on one day, etc.)
- If monetary compensation is offered, it must not be presented as an inducement to participate. For example:

  Acceptable: Subjects will be financially compensated for their participation; subjects will receive $5.00 for each blood sample; subjects will receive a $25 gift card as a thank you gift for their participation; subjects will receive a free tote bag and water bottle for taking part.

  Unacceptable: EARN $500! Get FREE medical care!

Submission and Approval

Recruitment materials should be included with the original IRB submission. If the researchers need to add additional recruitment materials after IRB approval has been granted, a copy of the advertising or recruitment materials should be submitted along with a change/update form. The IRB will send a letter to the investigator stating which materials have been approved. A copy of the materials will be stamped as approved, dated, and placed in the IRB protocol file.

Changes to Recruitment Materials

Any subsequent changes in the content of an approved advertisement must also be submitted for IRB review and approval prior to use.

PAYMENTS TO SUBJECTS

Payment to research subjects for participation in studies is not considered a benefit; rather, it should be considered compensation for time and inconvenience or a recruitment incentive. The

amount and schedule of all payments should be described in the IRB protocol at the time of initial review, including a summary of both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive or present undue influence. Procedures for prorating payment should the subject withdraw should be included in the IRB application and informed consent document(s).

Timing of Payments

Credit for payment should accrue as the study progresses and not be contingent upon the subject completing the entire study. Unless it creates undue inconvenience or a coercive practice, payment to subjects who withdraw from the study may be paid at the time the study would have been completed had they not withdrawn. For example, in a study lasting only a few days, it would be permissible to allow a single payment date at the end of the study, even to subjects who withdraw before completion. However, for a study lasting several months, it would not be permissible to allow a single payment date. Subjects who withdraw before completion of the study should receive accrued compensation in a timely manner.

Completion Bonus

While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion is acceptable, providing that such incentive is not extreme. The IRB will determine whether the amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.

Disclosure of Payments

All information concerning payment, including the amount and schedule of payment(s), should be described in the informed consent document and research protocol.

Alterations in Payments

Any changes in subject compensation or flexibility of the payment schedule must be reported to the IRB as a modification prior to implementation.

Payment Methods and Fund Management

Payments to research subjects must be in accordance with Carilion accounting policy and procedures for payments to research subjects. Carilion does not permit the use of raffles as a form of compensation as it is not seen as equitable compensation.

Reporting Payments to the IRS

The Internal Revenue Service (IRS) requires that Carilion (or whoever is paying the subjects for their participation) report payments in excess of $600 per calendar year on Form 1099-Misc. The filing of these forms necessitates that the name and social security number of the subject be collected and released to the Accounts Payable department to process the Form 1099-Misc. The collection and release of this information must be addressed thoroughly in the informed consent document so that it is clear to the subject that his or her identity will be released for the purpose of payment and reporting.

PAYMENT OF FINDER'S FEES AND BONUS PAYMENTS

The payment of a finder's fee is prohibited when it involves a health care professional with a treatment and/or counseling relationship to a patient being referred for enrollment to a research study. In addition, bonus payments to investigators or study staff that are beyond compensation for actual work performed are prohibited.

Individuals participating in the conduct of research should be reimbursed only for activities directly related to the performance of the research and at a rate not exceeding fair-market value for the level of activity being performed. All payments for the conduct of a research project must be negotiated at the beginning of the study and not provide for additional payments based on either the number or rate of subject enrollment. Expenses of a research study defrayed on a per-subject payment schedule should be fixed for each subject and may not increase as a result of subject enrollment meeting specific thresholds unless the increase is based on a documented increase in direct expenses.

The prohibition against finder's fees is supported by the American Medical Association's Code of Medical Ethics which states that "a physician may not accept payment of any kind, in any form, from any source, such as a pharmaceutical company… for prescribing or referring a patient to said source" and that "offering or accepting payment for referring patients to research studies (finder's fees) is also unethical." In addition, the American College of Physicians is against this practice, stating that "giving finder's fees to individual physicians for referring patients to a research project generates an unethical conflict of interest."

The prohibition against enrollment bonuses is prompted by the risk that such incentives are real or perceived conflict of interest that might lead an investigator or research staff to influence inappropriately a potential subject's decision to take part in research.

The prohibition of payment for finder's fees and enrollment bonuses includes but is not limited to compensation, stock options, travel opportunities, educational stipends, merchandise, vouchers, gift certificates, medical care or other services, discount coupons, extra vacation time, academic awards such as class credit or anything else of value.

References: Carilion Clinic Policy System-Wide Privacy & Research; University of California Irvine IRB Policies and Procedures on Subject Selection, Recruitment and Compensation; The Metro Health System IRB Guidelines; Institutional Review Board Management and Function, 2nd Edition, Chapter 5-11, pp. 173-176; University of Pennsylvania IRB Policy on Payment for Referral/Recruitment of Subjects in Human Subjects Research; University of Miami Human Subjects Research Office Policy 22.2 (C); Recruitment Incentives/Compensation, Bonuses, Referral Fees or other Inducements to Investigators or to those Referring Subjects; Brown University IRB Policy on Recruitment.