Department of Veterans Affairs
Birmingham VA Medical Center

Human Research Protection Program SOP #8 Revised March 3, 2016

Participant Selection, Recruitment, and Vulnerable Subjects

1. POLICY

The Birmingham VA Medical Center (BVAMC) Human Research Protection Program (HRPP) is committed to the protection of research participants while affording them the opportunity to participate in research.

It is the policy of the BVAMC to ensure the protection of research participants by compliance of written policies and procedures to evaluate the impartial selection of participants from various populations and sub-populations, when applicable; consider whether inclusion and exclusion criteria impose fair and equitable burdens and benefits; ensure appropriate recruitment practices; and protect vulnerable subjects.

This standard operating procedure (SOP) establishes procedures that ensure the protection of human participants recruited and selected for research, particularly vulnerable subjects.

2. RESPONSIBILITIES

The BVAMC Medical Center Director has the ultimate responsibility for ensuring that the selection and recruitment of human subjects, particularly vulnerable subjects, are protected in accordance with federal policies.

Associate Chief of Staff, Research and Development (ACOS/R&D) and the Research and Development (R&D) Committee must ensure responsibility for the overall policy, planning, coordination, and direction of research activities within VHA, including those pertaining to recruitment and participant selection practices for human subjects, in particular those with additional vulnerabilities. Recruitment and selection of participants must be done in a fair, equitable, and non-misleading manner.

Institutional Review Board (IRB) is responsible for assuring that the recruitment and selection methods are consistent with IRB policy. BVAMC has two IRB’s of record, the local BVAMC IRB and Central Office IRB (CIRB). The IRB is required to ensure that appropriate safeguards exist to protect the rights and welfare of research subjects [21 CFR 56.107(a) and 56.111]. In fulfilling these responsibilities, an IRB is expected to review all the research documents and activities that bear directly on the rights and welfare of the subjects of proposed research. In addition to the protocol and consent form, the IRB should review the methods and material that investigators propose to use to recruit subjects. The
IRB determines whether the recruitment and selection strategies are fair, equitable, and non-misleading. The IRB also evaluates the inclusion of vulnerable populations and safeguards to protect these populations.

**Principal Investigators** are responsible for recruiting participants in a fair and equitable manner, while weighing the potential benefits of the research to the participants against their vulnerability and the risks to them. Each Investigator affirms that they agree to uphold the protection of the rights and safety of human research participants through adherence to federal, state, and local laws, the VHA, BVAMC HRPP, CIRB SOP's and BVAMC IRB policies and procedures, for defining purposes of the research, the recruitment methods and materials, payment arrangements, the consent process, inclusion/exclusion criteria, and protection of vulnerable populations. **Anyone involved in VA research** must comply with the BVAMC HRPP comprehensive system to ensure the protection of human subjects participating in research, including the selection of subject, recruitment practices, and protection of vulnerable subjects as outlined in this SOP.

3. **DEFINITIONS**

   See HRPP SOP# 24 – HRPP Definitions

4. **PROCEDURES**

   a. **Participant Selection, Recruitment Practices, and Vulnerable Subjects Plan:**
   During the early stages of planning a research project, an investigator should determine if any element of research involves any activity with human subjects. If so, the activity must undergo prospective IRB review, which includes a review of the equitable participant selection, recruitment practices and protection of vulnerable subjects. See HRPP SOP #3 Initial IRB Review, SOP #4 Expedited Review, SOP #5 Exempt Research, SOP #6 Continuing Review, and SOP#7 Research Informed Consent.

   b. **Statement of Principles Concerning Protection of Human Research Participants:**
   The BVAMC HRPP is designed to assist all members and staff within its purview to adhere to the *Belmont Report* principles which are the basis for the current regulations and guidelines established to protect human research participants. VHA research must be carried out in an ethical manner. The basic ethical principles guiding research involving human subjects are provided in the *Belmont Report*. Three basic principles contained in the *Belmont Report* are central to the ethics of research involving human research and guide the IRB in assuring that the rights and welfare of subjects are protected: The *Belmont Report* of the National Commission for the Protection of Human Participants of Biomedical and Behavioral Research articulates these basic ethical principles that guide the conduct of research with human participants. They are:

   - **RESPECT FOR PERSONS:** In consideration of respect for persons, investigators are required to seek voluntary, written informed consent from potential research participants. Voluntary informed consent means that potential participants are given explicit assurances of the voluntary nature of their
participation in terms that are easy to understand and when they are not under duress. The informed consent form includes adequate information about the study that will assist potential participants in intelligently deciding whether or not to take part in the research. In addition, respect means honoring the privacy of individuals and maintaining their confidentiality. Respect for minors and mentally disabled persons require taking extra precautions. Individuals who are immature or incapacitated must be protected, perhaps even to the extent of excluding them from participation in certain research. The extent of the protection depends on the potential risks and benefits of the research to the participant.

- **BENEFICENCE:** The principle of beneficence requires that researchers do not harm participants and that they maximize potential benefits to participants while minimizing any potential risks of harm. Where there are any risks resulting from participation in the research, there should be equally corresponding and greater benefits, either to the participant and/or to the society at large. Benefits must outweigh risks to a large enough extent to justify the conduct of the research.

- **JUSTICE:** The principle of justice requires that participants be selected fairly and that risks and benefits of research be distributed equitably. Investigators are bound by the principal of justice to incorporate special precaution and procedures designed to ensure that, through the conduct of research, they are not systematically selecting participants simply because of easy availability, compromised position, and/or because of racial, sexual, economic and/or cultural biases in society. Investigators should base inclusion and exclusion criteria on factors that most effectively and soundly address the research problem while concurrently maximizing benefit and minimizing risks to any potential research participant.

Based upon the above principles from the *Belmont Report*, the IRB, under the authority of the BVAMC Director, examines selection criteria, recruitment procedures, proposed remuneration, and the informed consent process, in tandem with evaluating the risks and potential benefits to participants as outlined in each research protocol. IRB review is designed to assure that 1) investigators recruit participants in an equitable, non-coercive manner; 2) participants are fully informed about the potential risks and benefits entailed in the research; and 3) through voluntary research participation, human participants will not be exposed to disproportional risks and that precautions for vulnerable populations are considered.

d. **Equitable Selection of Participants:** The PI includes a section in the protocol to address selection of participants (also referred to as subjects) and to state if there is exclusion of classes of persons who might benefit from the research. The IRB documents the review of this item on the Protocol Review Standards/Risk-Benefit Assessment checklist and documents if this item is clearly and thoroughly described. Non-veterans may be entered into VA-approved studies only when there are insufficient veterans available to complete the study in accordance with 38 CFR 17.45 and 38 CFR 17.92. All regulations pertaining to the participation of veterans as research subjects including
requirements for indemnification in case of research related injury pertain to non-veteran subjects enrolled in VA- approved research. The IRB members review and evaluate whether equitable selection of participants from various populations and sub-populations, when applicable, and considers whether selection criteria impose fair and equitable burdens and benefits.

c. **Equitable Selection of Participants for Department of Defense (DOD) Research:**
When research involves U.S. military personnel additional protections for military research subjects is necessary to minimize undue influence. Please note the following:

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment.
- Officers and senior non-commissioned officers have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.

f. **Potentially Vulnerable Subject Groups:** The IRB and PI must identify vulnerable populations and ensure that they are not being taken advantage of or being coerced. The IRB assures that appropriate safeguards have been included to protect the welfare of subjects likely to be vulnerable to coercion or undue influence and may ask investigators or sponsors to address this issue in detail. The IRB may require special precautions or safeguards to be taken by the investigator to protect the rights and welfare of potentially vulnerable populations (i.e. require a patient advocate or legally authorized persons to witness consent; require a waiting period between initial contact and enrollment; require oversight of the Informed Consent process). Investigators are required to identify use of vulnerable populations and state the compelling reason to include them as research participants as well as explain extra precautions taken to prevent coercion and to protect potentially vulnerable populations.

Examples of vulnerable populations include:

- Mentally challenged, disabled, or incompetent (including psychiatric subjects)
- Prisoners (Note: research on prisoners is not conducted at the BVAMC).
- Institutionalized
- Receiving inpatient care for long-term chronic illness (e.g. Spinal Cord Injury, Nursing Home, Palliative Care)
- Terminally ill (including cancer, HIV, genetic studies)
- Pregnant women (Note: research on pregnant women is not conducted at the BVAMC).
- Children or Human Fetal Tissue (Note: research on children or human fetal tissue is not conducted at the BVAMC.)
- Employees
- Students
- Economically or educationally disadvantaged persons
• Incompetent individuals or persons with impaired decision-making capacity
• The involvement of prisoners of war as human subjects of research is prohibited in all DOD Research. The IRB is aware of the definition of “prison of war” for DOD component granting addendum.
• Vulnerability is a relative term, however veterans as a whole should be considered "vulnerable". Veterans have a long history of obeying orders and making sacrifices.

The BVAMC does not conduct research on prisoners, pregnant women (as the focus of research), children (persons under the age of 19), fetuses, or embryos.

See HRPP SOP#7 Research Informed Consent for definition and description of the policy and procedures regarding decisionally-impaired participants and legally authorized representative surrogate consent.

g. **Additional Safeguards To Protect Vulnerable Subjects:** In addition to safeguards outlined in HRPP SOP #3 Initial IRB Review and HRPP SOP #7 Research Informed Consent, the IRB may require additional safeguards to protect vulnerable subjects, if needed. The IRB documents the review of these items on the IRB Protocol Review Standards/Risk-Benefit Assessment checklist, and in the IRB minutes that these items are clearly and thoroughly described in the protocol and/or consent. Other than the safeguards described in SOP #3 and SOP #7, examples of additional safeguards that may be planned by the investigator or recommended by the IRB include:

• Ensuring subjects’ understanding by requiring prospective subjects to take a test or to independently write or dictate their understanding of the research and risks
• Obtaining an independent assessment by a physician not involved in the study
• Employing a consent monitor to independently verify that informed consent has taken place
• Providing prospective subjects with an advocate during the consent process
• Providing additional opportunities for prospective subjects to decline to participate or to end their participation in the study
• Constructing an assent mechanism for subjects with limited autonomy
• Requiring a ceiling for level of risks of nontherapeutic procedures
• Requiring that research be limited to the medical conditions affecting the subjects
• Requiring that research not be performed on subjects who are unable to provide consent for themselves
• Re-consenting previous decisionally- incapable subjects who were enrolled via proxy consent, who become competent during the time of the study

h. **Telephone Contact with Potential Participants:** Contact with veterans is limited to those clinically essential or as outlined in IRB approved protocols. Contacts do not solicit sensitive information (e.g., Social Security Numbers [SSNs]). During the recruitment process, researchers make initial contacts with veterans in person and/or by IRB-approved letter prior to any telephone contact and provide a telephone number or other means that veterans can use to verify the validity of the study. After recruitment and
during follow-up phase, researchers begin calls by referring to previous contacts and the information provided on the informed consent document.

i. **Advertisements and Recruitment Incentives:** At the time of initial review, continuing review, or expedited review of amendments, the IRB shall review advertisements and recruitment incentives associated with research studies. The IRB documents the review of this item on the IRB review checklist and documents that advertisements are clearly written with thorough descriptions excluding exculpatory language. Advertisements and incentives must be directly related to the Informed Consent process and must be consistent with prohibitions on coercion and undue influence. The IRB members review payments to determine that any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn. Investigators are prohibited from paying participants to participate in research when the research was integrated with a patient’s medical care and when it made no special demands on the patient beyond those of usual medical care. There shall be no payments to investigators, physicians, or other health care providers for identifying and/or enrolling subjects (i.e. “no finder’s fees” or “bonus payments” tied to referrals or rate of recruitment). When appropriately worded, the following items may be included (but not all are required):

1) The name and address of the clinical investigator and/or research facility
2) The condition under study and/or the purpose of the research
3) In summary form, the criteria that will be used to determine eligibility for the study
4) A brief list of participation benefits, if any (e.g., a no-cost health examination, DO NOT USE THE WORD “FREE”)
5) The time or other commitment required of the subjects
6) The location of the research and the person or office to contact for further information
7) All advertisements must be IRB approved prior to public display; Expedited review and approval by the IRB Chair is allowed

Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. The IRB must review the final copy of printed advertisements, or the final audio/video taped advertisements.

Advertisements should be reviewed and approved by the IRB as part of the package for initial review. If, at a later date, the investigator decides to advertise for subjects, the advertising may be considered an amendment to the ongoing study. When such advertisements are easily compared to the approved consent document, the IRB chair, or alternate chair, may review and approve by expedited means. When the IRB Chair or alternate has doubts or other complicating issues are involved, the advertising should be reviewed at a convened meeting of the IRB.
When direct advertising is to be used, the BVAMC IRB reviews the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting subjects is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. This is especially critical when a study may involve subjects who are likely to be vulnerable to undue influence. When advertisements are to be taped for broadcast, the IRB reviews the transcript of the audiotape. No claims should be made, either explicitly or implicitly, that the investigational drug is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug. Advertising for recruitment into investigational drug study should not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational. A phrase such as "receive new treatments" leads study subjects to believe they will be receiving newly improved products of proven worth.

Advertisements should not promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation. Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.

j. **Payment to Research Subjects:** The IRB shall review any proposed payments to research subjects associated with the research study. Payment may be permitted, with IRB approval, in the following circumstances:

1) No Direct Subject Benefit. When the study to be performed is not directly intended to enhance the diagnosis or treatment of the medical condition for which the volunteer subject is being treated, and when the standard of practice in affiliated non-VA institutions is to pay subjects in this situation.

2) Others Being Paid. In multi-institutional studies, when human subjects at a collaborating non-VA institution are to be paid for the same participation in the same study at the same rate proposed.

3) Comparable Situations. In other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate.

4) Transportation Expenses. When transportation expenses are incurred by the subject that would not be incurred in the normal course of receiving treatment and which are not reimbursed by any other mechanism.

Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive. Financial incentives are often used when health benefits to subjects are remote or non-existent. The amount and schedule of all payments should be presented to the IRB at the time of initial review. The IRB should review both the amount of payment and the proposed method and timing of disbursement to assure that neither is coercive or present undue influence. Payments to subjects may not be of such an amount as to result in coercion or undue influence on the subject's decision to participate or continue in the study. Payments may not be withheld as a condition of the subject completing the research. If the subject withdraws early, payments must be prorated to
reflect the time and inconvenience of the subjects participation up to that point. The payments must be reasonable and commensurate with the expected contributions of the subject; must be outlined in the informed consent; must be fair and appropriate.

When research involves U.S. military personnel, individuals may not receive pay of compensation during duty hours. U.S. military personnel may be compensated for research if the subject is involved in the research when not on duty.

k. Recruitment Only Studies: "Recruitment Only" studies are permitted at the BVAMC on a case-by-case basis (to be reviewed by the IRB). There is no guarantee the IRB will approve a recruitment only study.

1) The IRB Initial Review Application must be completed as with all other studies. All components of the IRB Initial Review Application submission are required for "recruitment only" studies. As part of the IRB Initial Review Submission process, the PI is required to provide:
   a) The rational of the benefits being offered to BVAMC Veterans,
   b) Why the research cannot be performed at the BVAMC,
   c) A complete copy of the affiliate’s proposed protocol

2) The BVAMC application must clearly differentiate between what activities will take place at the BVAMC and what activities will take place at the affiliate. The IRB initial review application and study protocol must clearly indicate the purpose of the study and highlight the need for recruitment only for the affiliate’s study. The application and informed consent must indicate that the subject:
   a) Is specifically being recruited for a study at the affiliate;
   b) Agrees to be recruited and the subject’s contact information will be forwarded to the affiliate (per a HIPAA Authorization). At which time, the affiliate will contact the potential subject;
   c) Will not be active in BVAMC research once the subject’s name is released to the affiliate.

3) Recruitment materials may highlight the affiliate’s study; however, it must contain the BVAMC logo.

4) The PI must designate an Assistant or Associate to be the acting PI at the VA that is an employee of the BVAMC (WOC, IPA status is not permitted).

5) The only activities allowed to take place in Recruitment Only studies are:
   a) Obtaining a subject’s name and contact information (through consent or HIPAA Waiver) and
   b) Releasing subject’s name and contact information to the affiliate, or
   c) Providing recruitment materials to potential subjects to allow subjects to contact the affiliate; and
d) Closing recruitment activities once names and contact information has been provided to the affiliates or when recruitment materials have been provided to potential subjects.

5. REFERENCES

- Title 21 CFR
- Title 38 CFR 16
- Title 45, 46 and 56 CFR
- The Belmont Report
- Declaration of Helsinki
- The Nuremburg Code
- VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research

6. ATTACHMENTS

Protocol Review Standards/Risk-Benefit Assessment

7. RESCISSIONS


8. REVIEW DATE

February 5, 2019

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