

**Department of Veterans Affairs
Tuscaloosa VA Medical Center**

Human Research Protection Program SOP #8

October 7, 2007

Participant Selection, Recruitment, and Vulnerable Subjects

1. POLICY

The Tuscaloosa VA Medical Center (TVAMC) 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 TVAMC 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 TVAMC 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.

TVAMC Research Offices and 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.

TVAMC Institutional Review Board (IRB) is responsible for assuring that the recruitment and selection methods are consistent with IRB policy. An 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, TVAMC HRPP and TVAMC 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 TVAMC 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**

Vulnerable Subject: See list below and HRPP SOP #7 Research Informed Consent.

Legally Authorized Representative: See HRPP SOP #7 Research Informed Consent.

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 TVAMC 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 ***Nuremberg Code***, the ***Declaration of Helsinki***, and 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 TVAMC 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 and to state if there is exclusion of classes of persons who might benefit from the research. The primary reviewer documents the review of this item on the primary reviewer's checklist and documents if this item is clearly and thoroughly described. The IRB review evaluates 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.

- e. **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 to 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 TVAMC).
- 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 TVAMC).
- Children or Human Fetal Tissue (Note: research on children or human fetal tissue is not conducted at the TVAMC.)
- Employees
- Students
- Economically or educationally disadvantaged persons
- 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 TVAMC does not conduct research on prisoners, pregnant women (as the focus of research), children (persons under the age of 19), fetuses, or embryos. If research with these populations were ever being considered, the TVAMC HRPP would revise or develop SOPs for procedures and policies specifically for these populations.

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.

- f. **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 primary reviewer documents the review of these items on the primary reviewer's checklist and documents confirmation 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 reviewer 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

g. 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.

h. 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 primary reviewer documents the review of this item on the primary reviewer's checklist and documents if this item is clearly and thoroughly described. Advertisements and incentives must be directly related to the Informed Consent process and must be consistent with prohibitions on coercion and undue influence. 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. Direct advertising for research subjects, i.e., advertising that is intended to be seen or heard by prospective subjects to solicit their participation in a study, is not in and of itself, an objectionable practice. Direct advertising includes, but is not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects. **Not included** are: (1) communications intended to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor letters (even when soliciting for study subjects), (2) news stories, (3) publicity intended for other audiences, such as financial page advertisements directed toward prospective investors, (4) exculpatory language, and (5) offer by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing

The IRB must review the final copy of printed advertisements, or the final audio/video taped advertisements.

IRB review and approval of listings of clinical trials on the internet would provide no additional safeguard and 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. Examples of clinical trial listing services that do not require prospective IRB approval include the National Cancer Institute's cancer clinical trial listing (PDQ) and the government-sponsored AIDS Clinical Trials Information Service (ACTIS). However, when the opportunity to add additional descriptive information is not precluded by the data base system, IRB review and approval may 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.

The TVAMC IRB considers direct advertising for study subjects to be the start of the informed consent and subject selection process. Advertisements should be reviewed and approved by the IRB as part of the package for initial review. If, at a later date, the clinical 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 other designated IRB member, may review and approve by expedited means. When the IRB reviewer 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 TVAMC 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.

- i. **Payment to Research Subjects:** The IRB shall review any proposed payments to research subjects associated with the research study. 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.

5. **REFERENCES**

21 CFR, 38 CFR 16, 45 CFR 46, 56 CFR, The Belmont Report, Declaration of Helsinki, The Nuremberg Code, The VHA Handbook 1200.5, FDA 1998 Information Sheets

6. **ATTACHMENTS**

None.

7. **RESCISSIONS**

TVAMC HRPP SOP#8 Participant Selection Recruitment Vulnerable Subjects May 7, 2007

8. **REVIEW DATE**

January 1, 2012

Signature on File in R&D Office

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