

# TVAMC IRB CHECKLIST FOR SUBMISSION OF RESEARCH STUDY/PROJECT

## New Application

Please verify that this application is complete and accurate by 1) filling in the blanks and double clicking the boxes, then choose "checked" for the default value (leave unchecked if not applicable) and 2) signing/date below. Please attach this checklist to the original application. **PLEASE MAKE 15 COMPLETE SETS OF ENTIRE SUBMISSION (except where noted below).**

Principal Investigator's (PI) Name: \_\_\_\_\_  
 PI's email address: \_\_\_\_\_  
 PI's mobile number: \_\_\_\_\_. PI's office number: \_\_\_\_\_  
 Sponsor of Research Project: \_\_\_\_\_  
 Title (175 characters maximum): \_\_\_\_\_

- Certification of Exemption (original +15 copies)
- Abstract\* (original +15 copies) (One-page, 500 words or less, Title: 175 characters maximum)
- Protocol\* (original +15 copies)
- VA Research Consent Form (VA Form 10-1086)\* with HIPAA Authorization (last page of consent) OR Request for Waiver of Consent and HIPAA waiver Memorandums (original +15 copies)
- Full Sponsor Protocol (3 copies only!)
- Investigator's Drug Brochure (3 copies only!)
- TVAMC Assessment of Clinical Impact Form (Original + 15 copies)  
(All signatures except Chair, R&D, must be obtained prior to submission; Submit separately with submission)
- Request to Review Research Proposal/Project (Pages 3&4) **SUBMIT ORIGINAL ON GREEN PAPER ONLY!**
- Research & Development Information System (RDIS) Investigator Data Form (Page 18)  
(Submit original **ONLY ONCE** in a calendar year unless information changes)
- Investigational Drug Information Record (10-9012) (Chairs signatures obtained at meeting) (Original +15 copies)
- Investigator(s)/Co-investigator(s) Financial Disclosure Form (Original + 15 copies)
- TVAMC Research Safety (SRS) form (If applicable) (Original + 15 copies)  
(Submit separately with submission; attach a copy of the Abstract to back of SRS form)
- Advertisements and other recruitment materials (15 copies)
- Subject's surveys or questionnaires (if applicable) (15 copies)
- Abstract ONLY, (Save a copy to the K-drive [ePROMISE folder] or see pg. 2)
- Budget Page (Original + 15 copies) (Submit separately with submission)
- Complete grant submission (If applicable; 3 copies only)
- Curriculum Vitae (CV) (DO NOT SUBMIT if copies of the PI, Co-Investigators, &/or  
Consultant's CVs are already on file with the IRB Office [Please verify])
- Collaborative IRB Training Initiatives (CITI) & VA Information Security 201 for R&D Personnel (1 copy; DO NOT  
SUBMIT if Certificates of Completion for PI/Co-Investigators are already on file with the IRB Office [Please verify]); these  
courses does not replace the annual training requirement for Cyber Security Awareness Training Course or VHA Privacy  
Policy Training. Those two courses must also be completed annually.
- Data Security Checklist for Principal Investigators & Principal Investigator's Certification: Storage & Security of  
VA Research Information (Submit original + 15 copies; R&D Committee approval date will be entered by IRB Staff)
- A Data Safety Monitoring Board (DSMB) is planned for this study
- VA Appointment: (Check One) Full-Time; Part-Time; WOC (Submit 1 copy of Appointment letter)
- Union (AFGE and/or ASNA) Review (If applicable; your research project involves employees as subjects)  
Submit written copy of union review (Original + 15 copies)

<b>IRB Staff Use Only:</b> <input type="checkbox"/> Reviewed by AO/R&D <input type="checkbox"/> CV(s) on file or submitted <input type="checkbox"/> Research mandatory educational training verified by IRB and/or RCO <input type="checkbox"/> Request to Review Research Proposal/Project (Green Form) complete <input type="checkbox"/> Page 18 RDIS Investigator Data form complete <input type="checkbox"/> Verify ePROMISE folder K-drive for Abstract <input type="checkbox"/> SRS Form (If applicable) <input type="checkbox"/> WOC Appointment (If applicable)
--

By my signature/date below, I attest that this application is complete, true, & accurate and that I will make available the informational brochure, "Volunteering in Research – Here are some things you need to know," to potential research participants in settings where participants may be recruited (e.g., clinic waiting areas), and to each prospective participant when that individual is approached to take part in a project.

I understand that as Principal Investigator, I have ultimate responsibility for the conduct of the study, the ethical performance of the project, the protection of the rights and welfare of human subjects, and strict adherence to any stipulations imposed by the IRB.

I agree to comply with all VA policies and TVAMC Standard Operating Procedures, as well as, with all applicable Federal, State, and local laws regarding the protection of human subjects in research, including, but not limited to, the following:

- Performing the project with qualified personnel who have been credentialed and privileged by the Tuscaloosa VA Medical Center,
- Implementing no changes in the approved protocol or consent form without prior IRB approval,
- Obtaining the legally effective informed consent from human subjects using only the currently approved, date-stamped, consent form,
- Promptly reporting serious adverse events to the IRB in writing,
- If I will be unavailable to direct this research personally, as when on research travel, leave, or vacation, I will arrange for a co-investigator to assume direct responsibility in my absence. This person is named as a co-investigator in this application,
- If I leave the Tuscaloosa VA Medical Center, I will make arrangements to turn over original study records that have been organized and cataloged to the Research Office for storage until the appropriate record destruction time.

Principal Investigator's  
signature: \_\_\_\_\_

Date: \_\_\_\_\_

## Guidelines for Submission of Research Proposals

The Subcommittee on Human Studies functions as the Institutional Review Board (IRB) for the Tuscaloosa VA Human Research Protection Program (HRPP). Its purpose is to assess acceptable levels of risk in research to human subjects and the presentation of that risk to the subjects. All studies involving human subjects must be reviewed and approved by the IRB before enrolling participants. Refer to the HRPP Standard Operating Procedures for specifics on the types of IRB review and all regulations. The IRB meets on the first Thursday of every month. **Therefore, materials for the meeting must be submitted to the IRB Office (151), Darlene S. Knox, HRPP Administrator/Program Support Assistant, Tracy Dent-Rivers, IRB Clerical Assistant, or Julie Wakefield, MA, Research Administrative Officer, fourteen (14) days prior (by close of business; excluding holidays, if it falls on Monday - Friday) to the IRB meeting.** The submission is then forwarded to the Research and Development (R&D) Committee that meets on the fourth Monday of every month for their review. Approved research projects will also undergo continuing review and progress report (an update of number of patients enrolled, number of adverse events, and findings to date, etc.). Any modifications to the Abstract, Protocol or Consent Form **must** be submitted via Amendment to the IRB Office prior to implementation. **A copy of the signed consent form for participants of approved research projects must be filed in their VA Medical Records and kept in the investigator's records. A copy of the informed consent must be given to the participant (signed or unsigned according to patient's preference).**

Studies submitted to the IRB must contain three main parts: abstract, protocol, and consent form (VA form 10-1086). **An electronic copy of the Abstract must be included with the submission. Please save a copy to the K-drive, ePROMISE folder; Pls not in the Research Department should submit Abstract via Microsoft Outlook to VHATUA\_CLSTUDIES (Darlene.Servant@va.gov, Tracy.Dent@va.gov, and Julie.Wakefield@va.gov).** Submissions must comply with the following format (See pages 3-14) and be typed, single-spaced, 12-point font. Investigators will be notified about the IRB's recommendations within two weeks after the meeting. The IRB Office Staff contact information and mailing address is as follows:

- Julie Wakefield, MA, Research Administrative Officer, (205) 554-3674
- Darlene S. Knox, HRPP Administrator/Program Support Assistant, (205) 554-3675, Fax (205) 554-2002
- Tracy Dent-Rivers, IRB Clerical Assistant, (205) 554-2000, ext. 3273
- Veterans Affairs Medical Center  
Research and Development Service (151-IRB)  
3701 Loop Road East  
Tuscaloosa, Alabama 35404

## **\*ABSTRACT**

The abstract must be no longer than 500 words (**one page**). It should summarize the study in the following format. Do not use underline, italic, subscripts, superscripts, symbols or Greek letters. **Abstract should be dated and must list principal investigator and co-investigators and/or consultants. Please leave a 1-inch margin at the bottom of your document for the IRB approval stamp.**

1. Objectives: State clearly the precise objective or question address in the study.
2. Research Design: Describe briefly the design of the study (i.e. use of randomization, blinding, retrospective or prospective, patient population, type of evaluation, and length).
3. Methodology: Summarize the methods used (i.e. study setting, level of care, selection procedures, entry criteria, numbers of subjects, interventions, duration, primary study outcome measure, and the hypothesis formulated).
4. Significance: State the anticipated contributions of the proposed study, i.e., how the study results may be used in the VA health care system.

## \*PROTOCOL

The protocol should be written with sufficient detail to enable a fair assessment of the risks and benefits to human subjects. The protocol should address each of the following points in the following order given. **EACH PAGE OF THE PROTOCOL MUST BE NUMBERED. Please leave a 1-inch margin at the bottom of each page of your document for the IRB approval stamp.**

1. Title of the study (175 characters maximum)
2. Principal Investigator
3. All co-investigators and/or consultants (list the role of the consultants)
4. Sponsor of the study
5. Research setting
6. Purpose of the study including hypothesis to be tested
7. Background, including results of relevant research, gaps in the current knowledge.
8. Potential benefits to the research subject and the knowledge to be gained (**Choose from the following: Prospect for direct benefit to participants [include knowledge to be gained], Little prospect for benefit to participants, but likely to yield generalizable knowledge, No prospect for direct benefit to participants, but likely to yield generalizable knowledge, No prospect for direct benefit to participants, and unlikely to yield generalizable knowledge**)
9. Definition of population to which study is directed and justification
10. Number of the subjects that will be recruited for study
11. Subject inclusion/selection criteria
12. Subject exclusion criteria
13. Subject exit criteria
14. Justification for use of special subject populations who may present informed consent issues (for example, incompetent patients, children, elderly, etc.) and reason for inclusion

When incompetent individuals or persons with impaired decision-making capacity as participants are included in the study, describe the compelling reasons to include incompetent individuals or persons with impaired decision-making capacity as participants and address the following items:

- The subjects were not being proposed as participants simply because they were readily available.
- The proposed research entailed no significant risks, tangible or intangible, or if the research presents some probability of harm, there is a greater probability of direct benefit to the participant.
- The research does not impose risk of injury, unless that research is intended to benefit that participant and the probability of benefit is greater than the probability of harm.
- Procedures are devised to ensure that participants' legally authorized representatives are well informed regarding their roles and obligations to protect incompetent participants or persons with impaired decision making capacity.

15. Scientific and ethical justification for excluding classes (gender, race, etc) of persons who might benefit from the research
16. Appropriateness of Impact of Study design on risk
17. Description of procedures to be performed and specify what procedures are being performed already for diagnostic or treatment purposes
18. Description of the anticipated data and how the data will be analyzed to test the specific hypotheses
19. Risks (physical, psychological, social, and economic) and steps taken to minimize these risks (refer to page 13 and 14 **[all four types of risk must be stated in consent form]**)
20. Describe in detail the provisions for managing adverse reactions and for monitoring data to ensure the safety of participants
21. Planned procedure for obtaining informed consent and if someone other than the investigator conducts the informed consent, define the formal delegation of this responsibility and the training or credentials of the person delegated to perform this activity.
22. Compensation for participation, if offered, and amount **(include when participant will be paid [i.e., after each visit, at end of study, etc.]) Note: Information here should also be listed identically in the Consent form.**
23. Plans for protection of patient privacy and confidentiality (The following issues **must** be addressed: Will you collect individually identifiable information that may be transferred/transmitted to the Sponsor or outside the Tuscaloosa VA Medical Center? Clearly delineate how you will secure/store the data? Explain how you will destroy the Patient Health Information when it is no longer needed? Explain limits to Confidentiality – who may look at the records: e.g., a Sponsor, the FDA, and the IRB. Specify that the Research Compliance Officer examines all completed Research Consent forms during the year). Complete Data Transfer Agreements, if applicable. Note: The required records, including the investigator's research records, must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA's Records Control Schedule (RCS 10-1). Therefore, at this present time all research records must be retained indefinitely. Please DO NOT destroy any research records. At study closure or at the Principal Investigator's expiration of Veteran Affairs (VA) appointment (including Without Compensation [WOC} appointments), the investigator's research records **MUST** be retained by the research office for storage at the completion of the research study. Records are the property of the Tuscaloosa VA Medical Center's Research Office. Any documents with private health information data that is NOT part of the research must be placed in the Shred-it boxes located throughout the Medical Center. Use of personally owned shredders is prohibited.  
FYI: Privacy is in regard to subjects' personal space, dignity, and need for modesty. Confidentiality is subjects' personal identity and health information.
24. Methods used to identify and recruit patients
25. Safeguards to prevent coercion or undue influence for study participants.
26. Resources: (i.e., all investigators and research assistants are currently qualified and are trained and experienced in clinical research of Bipolar I Disorder. No new staff will

need to be trained. They all have adequate offices and space and adequate access to patient's needed for the study. The TVAMC has the staff and experience in the pharmacy to complete the study procedures under strict blinded conditions.)

27. Safeguards to protect the rights and welfare of mentally disabled and/or decisionally impaired subjects (vulnerable patient populations)

28. Plans for Adherence to VA Policies and Regulations Regarding Research Involving Controlled Drugs [N:\HRPP POLICIES\Use of Controlled Substance in Research 102706.TIF](#): All Tuscaloosa VA Medical Center (TVAMC) policies and regulations and all other VHA policies regarding research involving controlled substances/drugs will be followed (if controlled drugs are included in the study).

29. Research at external sites and multi-site research in which the investigator is lead investigator.

When the investigator plans to conduct research at external sites, list the contact information for the site and whether the site has granted permission for the research to be conducted. Describe whether or not the TVAMC IRB will be the IRB of record or state otherwise.

If the TVAMC investigator is the lead investigator of a multi-site study, include information about the management of information that is relevant to participant protections, such as:

- Unanticipated problems involving risks to participants or others
- Interim results
- Protocol modification

30. References: Include references.

## **\*VA RESEARCH CONSENT FORM (10-1086)**

**A copy of the signed consent form for participants of approved research projects must be 1) filed in their VA Medical Records, 2) kept in the investigators records (original), and 3) given to the participant and/or legally authorized representative (LAR). One of the Investigators must certify in a progress note in the medical record that the subject has read the consent and has reasonably understood the protocol, its risks and benefits, prior to any study procedures being conducted. All sections of the consent form must be read and the final page signed and dated prior to the subject being enrolled in a research study. The investigator will provide for the prospective subject or the LAR to have sufficient opportunity to consider whether or not to participate. All subjects must give consent without coercion or undue influence.**

The consent form is one of the focal points for the IRB's ethical and legal scrutiny of the study; since it is the formalization of the process of obtaining the informed consent of the research subject to participate in the study. **Please leave a 1-inch margin at the bottom of each page of your document for the IRB approval stamp.**

1. The consent form must be on VA Form 10-1086 (**Consent template available from one of the IRB Staff [Darlene S. Knox, ext. 3275/3675, Tracy Dent-Rivers, ext. 3273, or Julie Wakefield, MA, ext. 3674] or the Chief, R&D [ext. 3819]).**
2. Type size at least 12 points.
3. Understandable to someone with 6<sup>th</sup> grade intelligence and language skills. If medical procedures are mentioned, they must be initially defined, and then the name of the procedure may be used throughout the remainder of the consent.
4. The title of the study must be the same title as in the written protocol.
5. The names of all investigators involved in the study must be included on all pages.
6. The final page of the consent form must be completed with accurate phone numbers. The after hours phone number must be stated.
7. **Information on the page of the Informed Consent form beginning "RESEARCH SUBJECTS' RIGHTS" and ending with the signature and date lines should be on a single page, immediately preceding the Health Insurance Portability and Accountability Act (HIPAA) Authorization.**
8. The consent form must follow the outline below.

**Submission also should include a HIPAA statement page (last page).**

**Route submissions to the Research Office (151) or mail to:**

**VA Medical Center  
Research & Development Service (151)  
3701 Loop Road, E.  
Tuscaloosa, AL 35404  
ATTN: IRB Administrative Staff (Julie Wakefield, MA, Darlene S. Knox, or Tracy Dent-Rivers)**

**In addition to elements in the Informed Consent Template, the required elements of informed consent are:**

1. Names of all investigators
2. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
3. A statement of the approximate number of subjects involved in the study.
4. A description of any reasonably foreseeable risks or discomforts to the subject.
5. A description of any benefits to the subjects or to others, which may reasonably be expected from the research.
6. A disclosure of appropriate alternative procedures or courses of treatment, if any that might be advantageous to the subject.
7. Right not to participate and that participation is voluntary
8. Right to terminate participation at any time without jeopardizing continuing care as a patient.
9. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and notes (if applicable) the possibility that the FDA may inspect the records.
10. Indication of a willingness to answer questions by the investigator
11. An explanation of how and to whom to contact for answers to questions or if problems occurs.
12. For research involving more than minimal risk, an explanation as to whether and compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained.
13. An explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
14. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and who to contact in the event of a research- related injury to the subject.
15. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
16. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation will be provided to the subject.
17. When appropriate a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable.
18. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

19. Any additional costs to the subject that may result from participation in the research (if applicable).
20. A statement concerning the amount of payment to subjects, with schedule of payments. **Also include when subjects will be paid (i.e., after visit, end of study, etc).** **Note: Information here should also be listed identically in the Protocol.**
21. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject (if applicable).
22. There may be no exculpatory language through which the subject or the subject's legally authorized representative is made to waive or to appear to waive any of the subjects' legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

**EXAMPLE TEXT FOR CONSENT FORM FOR COMMON PROCEDURES:**

- random assignment:  
“You will be randomly assigned (as by the flip of a coin) to receive either....”
- placebo:  
“blank pill or inactive medication”
- Intravenous catheterization:  
“You will have a small plastic tube inserted into an arm vein.”
- Quantity of blood drawn (15ml = tablespoon; 327 ml = cup; 480ml = pint)  
“total amount of the blood drawn will be \_\_\_\_\_ml or \_\_\_\_\_ (tablespoons/cup/pint).”
- venipuncture or IV catheterization:  
“Effects of the blood drawing (or intravenous (catheter) tube placement) may include mild pain on puncture (or insertion), and sometimes faintness, inflammation of the vein, bruising, or bleeding at the site of puncture (insertion). Rare complications of intravenous catheter placement may include infection or formation of blood clots.

**EXAMPLE OF TEXT FOR USE IN PROTOCOL, IF APPLICABLE**

**THE FOLLOWING IS PROVIDED AS EXAMPLE TEXT. PLEASE EDIT CAREFULLY TO PERTAIN TO THE POPULATION UNDER STUDY.**

**SAFEGUARDS TO PROTECT THE RIGHTS AND WELFARE OF MENTALLY DISABLED AND/OR DECISIONALLY IMPAIRED SUBJECTS**

Protection of subjects from harm must be balanced against the potential for benefit to subjects themselves, and to other persons with their disorders, that may arise from research participation. Since new treatments must eventually be tested in persons suffering from the condition, a policy totally excluding vulnerable subjects from research would preclude the development of improved treatment for persons with serious psychiatric disorders.

In establishing a patients' ability to make a decision in all populations of research, an autonomous choice to enter a research study is both informed and voluntary. To be capable of informed choice, it is generally agreed that prospective subject should demonstrate the ability to understand the nature of the research participation; appreciate the consequences of such participation; exhibit ability to deliberate on alternatives, including the alternative not to participate in the research; and evidence ability to make a reasoned choice. Subjects also should comprehend the fact that the suggested intervention is in fact research, and that they may decide against participation without jeopardizing the care and concern of health care providers. If a patient is deemed incapable of independent decision making, the use of a surrogate will be implemented. These major points are carefully explained in the written informed consent as well as verbally explained in the initial consent process and ongoing assessment of consent to participate in the study at each follow-up visit.

Decisions against participation or early withdrawal requests will be accepted without hesitation or consequence. Continued voluntary participation is also obtained by verbal agreement at each clinic and/or phone visit. Patients are given additional opportunities to decline to participate or to end their participation in the study. This aids in ensuring that a subject's continued involvement is truly voluntary by giving "permission" to leave the study. This also gives the opportunity to reassess decision-making capacity, which could introduce the need for surrogate arrangement. Patients may choose to involve a family member or advocate in the consent process.

Unless research is to be limited to the mildest forms of the disorders, which may differ substantively from more chronic or severe forms, persons whose decision making capacities may be impaired, are likely to be involved in research studies. Protection of subjects from harm must be balanced against the potential for benefit to subjects themselves, and to other persons with their disorders, that may arise from research participation. Since new treatments must eventually be tested in persons suffering from the relevant condition, a policy totally excluding incapable subjects from research would preclude the development of improved treatment for persons with serious psychiatric disorders, dementia, and other mentally debilitating conditions.

Risks to subjects range from physical injury to inconvenience. Physical, social, psychological and economic risks including benefits, violations of privacy, effects upon the subjects' relationship with family members, and anxiety associated with being asked to participate in research before coming to terms with one's affliction, should be considered. Evaluation of risks should include patients' perception. What may be a rather small inconvenience to ordinary persons may be highly disturbing to some subjects. Evaluation should incorporate reliable knowledge on the range of anticipated reactions subjects may have to study procedures.

Because persons with psychiatric and other disorders undergo treatment and tests involving some discomfort and risk, a study presenting similar procedures and potential for harm may qualify as presenting a minor increase over minimal risk to them. For subjects not accustomed to, or in need of such medical interventions, however, the same study could present a higher level of risk.

**Populations of subjects that could be considered decisionally impaired include the following:**

**Dementias** are characterized by multiple cognitive impairments, most prominently however, is that of memory. The best known of these is dementia of Alzheimer's type. Those persons with even a mild dementia may show deficits in understanding relevant information and reasoning sufficient for decision-making, although their choices about treatment and research may not differ at this point from non-impaired populations. However, dementia at a moderate stage, deficits are expanded, and ability for decision-making may be further impaired.

Persons considered seriously mentally ill include diagnoses of **schizophrenia** or **Bipolar disorder**. Those with Schizophrenia may have decision – making abilities that wax and wane. Acute exacerbations of the illness may substantially impair decision-making abilities by decreasing level of understanding and reasoning. However, the level of capacity of those that are stabilized is likely to be much higher. A lack of insight into illness and need for treatment is rather common among persons with Schizophrenia and this may make it difficult for them to anticipate consequences of their decisions.

Another disorder that is likely to impair capacities is Bipolar disorder. It results in alternating states of depression and mania. During a manic episode attention is reduced, impulsiveness is increased, and manic patients are well known for making poor decisions about money and personal affairs.

Persons considered moderately mentally ill include diagnoses of **depression** and **PTSD**. Those with depression have feelings of worthlessness, diminished interest, and difficulties concentrating. It has been suggested that decreased motivation to protect their own interests may reduce their abilities to make decisions, increase their willingness to take risks, or to simply not care that possible risks are present. Those with PTSD have some similarities, including diminished interest levels, and difficulties in concentration. The degree of impairment relates to the intensity of depressive and/or PTSD symptoms.

Another population to be included is that of the **veterans**. They are accustomed to taking and following direct orders, thus introducing a further need for researchers to prevent coercion, directly, or indirectly. Patients will be given ample time to read and consider informed consent, with other treatment options presented by investigators. Family members, significant others, and primary treatment teams may also be involved in the decision-making process if veteran wishes. They are also informed that refusal to participate will be accepted without hesitation at any time and will not change their eligibility for VA services, treatment, disability payments, or other related VA benefits.

Another population that may be considered vulnerable are those who are **economically or educationally disadvantaged**. The VA patient population includes individuals who are economically or educationally disadvantaged. The study keeps payments to

participation at a minimum in order to avoid coercion based on economic conditions. In addition, the informed consent is written at a grade-school level of education to minimize the vulnerability of the educationally disadvantaged.

In addition, those subjects involved in a **blinded or placebo study**, impose a need for additional safeguards. These will include rescue medications to be allowed, which are based per study specific protocols. Symptoms of illness and side effects are monitored very closely, and with frequent clinic visits.

In establishing a patients' ability to make a decision in all populations of research, an autonomous choice to enter a research study is both informed and voluntary. To be capable of informed choice, it is generally agreed that prospective subject should demonstrate the ability "to understand the nature of the research participation; appreciate the consequences of such participation; exhibit ability to deliberate on alternatives, including the alternative not to participate in the research; and evidence ability to make a reasoned choice." Subjects also should "comprehend the fact that the suggested intervention is in fact research (and is not intended to provide therapeutic benefit when that is the case)," and that they may decide against participation without jeopardizing the care and concern of health care providers. If a patient is deemed incapable of independent decision making, the use of a surrogate will be implemented.

Decisions against participation or early withdrawal requests will be accepted without hesitation or consequence. Continued voluntary participation (re-consent) is also obtained by verbal agreement at each clinic and/or phone visit. This aids in ensuring that a subjects continued involvement is truly voluntary by giving "permission" to leave the study. This also gives the opportunity to reassess decision-making capacity, which could introduce need for surrogate arrangement.

### **Risk/Benefits:**

**Potential Physical Risks:** The physical side effects of the study medication are listed in the attached informed consent. Physical risks of placebo are remote and negligible. Study medication will be started at low dose and titrated gradually in order to minimize risks of physical side effects. Risks to blood collection may include minor pain, bruising, or discomfort. These physical risks are usually transient and tolerable. A trained phlebotomist or clinician will perform the blood draw in order to minimize these physical risks. A trained investigator will be available to assess these risks and make adjustments to study medication dose or study procedures in order to minimize these physical risks.

**Potential Psychological Risks:** There are possible psychological risks associated with this study. Patients may experience transient anxiety during the clinical interviews when answering questions about their symptoms. Patients may experience embarrassment when their symptoms of psychiatric illness are being evaluated. Patients may feel that participation in the study is an invasion of their privacy. The study team will minimize these potential psychological risks by maintaining a pleasant and professional

demeanor, conducting the interviews and physical assessments in a private clinical office, and allowing the patient to discuss these reactions and feelings if they occur. Patients are allowed to take breaks during the interviews and assessments if needed to avoid or minimize discomfort.

**Potential Social and Economic Risks:** Participation in a study for psychiatric conditions may involve risk of feeling “labeled” or “stigmatized.” Confidentiality safeguards will be strictly maintained to prevent such risks. A HIPAA authorization page is also included in the informed consent to inform the patient of the use of identifiable personal health information. This informed consent and HIPAA authorization page outlines in detail the provisions for protecting the confidentiality of research data. The methods used to obtain information about the participants include direct patient query and medical record review. Participation in the study may involve economic risk of missing work or having to pay for transportation. The study team will work with the patient to minimize these inconveniences by seeing the patients outside their work hours and by minimizing clinical appointments to those necessary to adhere to the protocol. Also patients will be seen in a timely fashion upon arrival and appointments will be kept as short as possible to minimize inconvenience of attending appointments. Patients are paid in order to offset the economic burden of attending the study-mandated clinic appointments.

**Anticipated Potential Benefits:** The actual patient participant may benefit from further reduction in underlying psychiatric symptoms. There is substantial potential for knowledge about treatment to be gained by the cumulative data gathered in this study that may improve the health care of veterans and non-veterans in the future. **(Choose from the following: Prospect for direct benefit to participants [include knowledge to be gained], Little prospect for benefit to participants, but likely to yield generalizable knowledge, No prospect for direct benefit to participants, but likely to yield generalizable knowledge, No prospect for direct benefit to participants, and unlikely to yield generalizable knowledge)**

**Recruitment Practices:** Patients will be recruited from the mental health and primary care clinics by the following means:

- Direct referral from their providers
- Direct patient self-referral
- IRB-approved patient education pamphlets or flyers **(Must include advertisements with submission)**
- Study team members’ direct patient contact made in screening and/or follow-up clinics

There will be no compensation for recruitment paid to referral sources or persons. There will be no direct compensation to investigators or other health care providers for identifying and/or enrolling subjects. (In other words, there will be no “finders’ fees” of any sort to any person).

Participants will be paid minimal fees to offset their time and inconvenience due to participation in the study. This payment is not for use as a method of recruitment.