

Department of Veterans Affairs
Tuscaloosa VA Medical Center

Human Research Protection Program SOP #2

September 28, 2009

**THE ORGANIZATIONAL STRUCTURE OF THE
INSTITUTIONAL REVIEW BOARD**

1. POLICY

The Tuscaloosa VA Medical Center (TVAMC) Human Research Protection Program (HRPP) is committed to protecting the rights and welfare of human research subjects by outlining policies and delineating the organizational structure of the Institutional Review Board (IRB; also previously and elsewhere referred to as the Subcommittee on Human Studies). When veterans take part in VA research, they rely on us to keep them safe and they entrust us to safeguard the quality, safety and integrity of our research program.

It is the policy of the TVAMC HRPP to ensure that the applicable Federal, state, and local regulations are carried out in protecting the rights and welfare of subjects who voluntarily participate in investigational studies within this Medical Center. This Standard Operating Procedure (SOP) is a written documentation of the organizational structure, process, roles, and responsibilities of the IRB.

This policy establishes procedures that ensure research at the TVAMC is conducted in accordance with the requirements of the TVAMC HRPP, as well as state and federal regulations. The Department of Veterans Affairs was one of 16 departments and agencies that agreed on August 19, 1991 to follow the Federal Policy for the Protection of Human Subjects [21 CFR 56.109(a)]. This policy is incorporated in [38 CFR 16, 17]. Each VA Medical Center that conducts human research is required to have an IRB, also called the Subcommittee on Human Studies [VHA Handbook 1200.05].

The Purpose of the IRB: It is acknowledged by the TVAMC, that the purposes of the IRB is to review, approve, require modifications of (to secure approval), or disapprove all human research activities that are proposed to take place at the TVAMC regardless of whether research is funded or non-funded. The IRB assures that the rights and welfare of individuals involved as subjects of research under Federal auspices are being protected in accordance with federal regulations, VA [38 CFR Part 16,17], FDA [21 CFR Part 50,56] and DHHS [45 CFR Part 46]. This is in keeping with the commitment of the TVAMC to provide the highest quality care possible to those who authorize and entrust themselves to this institution for medical treatment.

Scope of Authority of the IRB Defined: (38 CFR 16, 17; 21 CFR 50, 56; 45 CFR 46) The TVAMC IRB is the official Research Review Unit for the TVAMC. It is organized and

empowered to act under the authority of regulations specified by the Department of Veterans Affairs Health and Research Services, a Department of the United States Federal Government. The TVAMC IRB functions independently of other TVAMC organizational entities in its role in protecting research participants. The TVAMC IRB, as designated by the TVAMC Director and the R&D Committee and as named in the FWA, will prospectively review and make a decision concerning all human subject research conducted at the TVAMC, or by TVAMC employees or agents, or otherwise under the auspices of the TVAMC. Furthermore, the TVAMC IRB has statutory authority to take any action necessary to protect the rights and welfare of human subjects in TVAMC's R&D program. The TVAMC IRB has the authority to approve, require modifications of, or disapprove a research study or modification to an approved research project; and to conduct continuing review of each study at intervals appropriate to the degree of risk, but not less than once per year. The TVAMC IRB has authority to suspend, or terminate, the enrollment and/or ongoing involvement of human subjects in the facility's research as it determines necessary for the protection of those subjects. The TVAMC IRB has the authority to observe and/or monitor the TVAMC's human subject research to whatever extent it considers necessary to protect human subjects. The scope of the authority includes all research involving human subjects conducted at, supported by or otherwise affiliated with the TVAMC [38 CFR 16, 17], FDA [21 CFR Part 50,56] and DHHS [45 CFR Part 46].

Although the IRB is a subcommittee of the R&D Committee (VHA Handbook, 1200.05), neither the Director nor the R&D Committee can reverse a negative decision by the IRB or approve research involving human subjects that has not been approved by the IRB (38 CFR 116.112; M-3, Part1, Chapter 3.01(e)).

The TVAMC IRB was established on August 25, 1997 by the R&D Committee and the TVAMC Director (R&D minutes 8/5/97 and 8/14/97; Director's memo 8/7/97; and Subcommittee minutes 8/27/01). The IRB was empowered to protect the rights and welfare of human research subjects.

Statutory Basis for IRB Authority: The statutory bases for these authorities are as follows:

- Statutory provisions for protection of VA patient rights, *U.S.C. (United States Code) Sections 7331 through 7334*
- VA (Department of Veterans Affairs) regulations pertaining to protection of patient rights. [38 CFR 17.34 and 17.34a]
- VA (Department of Veterans Affairs) regulations pertaining to rights and welfare of patients participating in research. [38 CFR 16 - *Federal Policy for the Protection of Human Subjects*]
- VA (Department of Veterans Affairs) requirements for the protection of human subjects in research. [VHA Handbook 1200.05]
- FDA (Food and Drug Administration) regulations pertaining to rights and welfare of patients participating in research involving investigational drugs and devices. [21 CFR 50, 56]
- DHHS (Department of Health and Human Services) regulations pertaining to rights and welfare of patients participating in research supported by DHHS. [45 CFR 46]

2. RESPONSIBILITIES

The TVAMC Director is responsible for making final decisions concerning research studies based on recommendations from the IRB and the R&D Committee; this is accomplished through the approval or disapproval of the actions listed in the R&D Committee minutes, through the Chief of Staff. The Director reviews, and approves, the minutes of the R&D Committee prior to their submission to VA Headquarters, which includes approval or disapproval of IRB approved actions. The Director is also responsible for ensuring that the IRB is free from undue pressure in discharging its responsibilities. The Director cannot approve an action that has been disapproved by the IRB. The Director is responsible for ensuring that adequate resources for the IRB to discharge its obligation are available.

The Research and Development (R&D) Committee reviews all activities of the IRB and recommends to the Director approval or disapproval of the actions of the IRB. The R&D Committee may not approve human research that has been disapproved by the IRB, but it may disapprove a previously IRB approved study. The R&D Committee is responsible, through the TVAMC Chief of Staff to the Director, for maintaining high standards throughout the R&D program and for the adequacy of the IRB's policies and procedures.

TVAMC Institutional Review Board (IRB) is a subcommittee of the R&D Committee and reports directly to the R&D Committee. However, the IRB functions independently and is responsible for the initial evaluation and subsequent progress reviews of investigational studies involving humans. The IRB has the responsibility and specific authority to approve, require modifications (in order to secure approval), disapprove, suspend, or terminate approval of any TVAMC human subject research activity. The IRB has the specific authority to observe, or have a third party observe, the consent process or the research activities. It makes recommendations concerning approval, disapproval, modifications, restrictions, or termination of such studies to the R&D Committee. Within the review process, the IRB is responsible for safe-guarding human subjects in the areas of informed consent, voluntary participation, confidentiality, and ensures that human experimentation is performed under stipulation and procedures of the written protocol as approved. All protocols involving human research must be reviewed and approved by the IRB prior to submission to the R&D Committee for review and approval. Initiation of human research studies may proceed only after review and approval by the IRB and the R&D Committee. The IRB Approval Letter issued to investigators informs Principal Investigators that studies may only be initiated after R&D approval is obtained.

The IRB Chairperson is responsible for chairing IRB meetings in an orderly manner with procedures defined by Robert's Rule of Order and following the SOPs as published. The IRB Chair person (or designee of experienced IRB member) is responsible for conducting expedited reviews, reviews of exempt research, and determination of when studies meet the regulatory definitions of human research and require IRB review.

IRB Members are responsible for following all HRPP SOPs in regard to review of research activities, requirements for continuing education, requirements to disclose potential conflict of interests, and other requirements set forth in the HRPP SOPs.

Investigators (Principal and Co-investigators) are responsible for conducting their research in accordance with all agreements with the IRB and all HRPP SOPs. Investigator responsibilities are detailed in TVAMC SOP # 13. All investigators are required to comply with all relevant research-related policies and procedures. All requests to conduct research involving human subjects must be submitted in accordance with the requirements set forth in the TVAMC HRPP SOPs.

The Principal Investigator is responsible for submitting the proposal and all relevant documentation, to the IRB for evaluation and approval before the research can be initiated. Under no circumstances may an investigator begin a study involving human participation without approval from the IRB, the R&D Committee, and the Director who endorses the R&D Committee Minutes. The IRB recognizes one Principal Investigator (PI) for each project. The PI has ultimate responsibility for his/her research project; all official IRB correspondence is addressed to the PI. Co-investigators communicate with the IRB through the PI. Students can serve as PI under the supervision of a VA investigator (Part Time (PT), Full Time (FTE), or WOC [Without Compensation] appointed). All investigators (PI and co-investigators) must be under a VA-approved appointment while participating in a TVAMC research project.

The IRB Staff carry out the mission of the IRB and reports directly to Chief for Research and Development. These duties include maintenance of all IRB files, correspondence, and documents, taking and preparing minutes of IRB meetings, maintaining electronic files/systems, tracking files for review and signatures from responsible individuals, and other duties described below.

Research Compliance Officer reports directly to the Director and conducts compliance oversight duties.

Other Optional Committees. The IRB may require projects to be reviewed and approved by the Safety Committee, Occupational Health and Fire Committee, the Ethics Committee, or the Pharmacy and Therapeutics Committee.

Other Institutions: The IRB has no authority over or responsibility for research conducted at other institutions. At this time, the TVAMC IRB has no affiliated Human Research Protections Programs. If future affiliations are needed or requested, the TVAMC's IRB SOP and FWA would need modifications to address the nature of the relationships.

Regulatory Agencies: The IRB and R&D records are subject to regulation and inspection by accreditation agencies and governmental regulatory agencies, e.g. Food and Drug Administration (FDA), General Accounting Office (GAO), Veterans Administration Inspector General (VAIG), Office for Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the VA Office of Research and Development (VA ORD). Copies of any reports or correspondence to and from such agencies concerning the VAMC's R&D Committee must be provided to the IRB and to the R&D Committee, which shall determine if any additional notifications are necessary. The TVAMC IRB and R&D Committees will comply with the VHA Handbook 1058.01 "Requirements for Reporting

Research Events to Facility Oversight Committees and the Office of Research Oversight”.

3. **DEFINITIONS**

- a. **Research:** VA regulations at 38 CFR 16.102(b) defines research as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge". VA regulations at 38 CFR 16.102(f) define human subject as “a living individual about whom an investigator (whether professional or student) conducting research obtains 1) data through intervention or interaction with the individual or 2) identifiable private information. Private information includes information that an individual can reasonably expect will not be made public and information about behavior that an individual can reasonably expect will not be observed or recorded. Private information must be individually identifiable. Identifiable means that the identity of the individual is or may readily be ascertained by the investigator or associated with the information.”
- b. **If an FDA-regulated test article is involved,** the FDA regulations will apply. The FDA regulations define research as “any experiment that involves a test article and one or more human subjects.” The FDA regulation further states that “the terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.” 21 CFR 56.102(e) defines human subject as “an individual who is or becomes a participant in research, either as recipient of the test article or as a control. A subject may be either a healthy individual or a patient.”
- c. **Human Subject:** VA policy (VHA Handbook 1200.05) highlights that the definition of human subject includes investigators, technicians, and others assisting investigators, when they serve in a “subject” role by being observed, manipulated, or sampled.

4. **PROCEDURES**

- a. **Determination of When Studies Meet the Regulatory Definitions of Human Research:** The definition of “Research” and “Human Subject” as listed above appears straightforward and fairly well confined. However, translating these definitions in the everyday practice of a VA Medical Center setting can often illustrate the broader meaning of these definitions, which intentionally provides increased protections for human subjects. The TVAMC HRPP encourages open and frequent discussion on the topic of whether an activity meets the definition of research with human subjects, which means the TVAMC HRPP has both an informal approach and formal procedure in determining when activities or studies meet the regulatory definitions of human research. Informally, these discussions should initially take place at the source of the activity, such as during a quality management or performance improvement planning meeting, at a clinical staff meeting, between an individual and their supervisor, or at a treatment program planning meeting. The R&D and IRB members are selected (as described below) from diverse clinical settings and may often be present at these meetings and serve as a front-line source to answer questions about whether an activity approaches the definition of human research. Should an activity be brought into question, the individual in charge of that activity or

program should seek advice from someone expert in the definitions and regulations, i.e. the Chair of the IRB, Chair of the R&D Committee, Chief of R&D, or R&D Administrative Officer. More formally, any activity that remains unclear in whether it meets the definition of human research can be referred in writing to the IRB Chair or convened IRB meeting. See TVAMC HRPP SOP #3 on the procedures, definitions, and flowchart regarding the determination of when research meets the definition of human research. All activities that meet the definition of human research must go through one of the mechanisms outlined in separate HRPP SOPs, i.e. initial review, expedited review, or review of exempt research.

- b. **Prohibited Undue Influence:** Any attempt by an individual or group to unduly influence the deliberation and determinations of the IRB and the IRB staff is strictly prohibited and will not be tolerated. Any such attempts must be reported promptly to the Chief of R&D and the TVAMC Director. Once an allegation is made to the Chief for R&D and the TVAMC Director, the allegation will be investigated by the Research Compliance Officer (AO for R&D) to the fullest extent possible with the findings listed in a report to the R&D Committee, Chief for R&D and TVAMC Director, for appropriate actions to be taken in response to any legitimate attempts to unduly influence the IRB. The response may include a verbal counseling, written counseling, letter of reprimand, or other administrative or disciplinary action issued to the individual or group from the Chief of Research and Development or the TVAMC Director, in collaboration with other necessary parties, such as supervisors or Service Chiefs. If the attempt to unduly influence the IRB is deemed as serious or continuing noncompliance with HRPP policies, further details of procedures are given in TVAMC HRPP SOP#18.
- c. **The Membership of the IRB (38 CFR 16.107; VHA Handbook 1200.05):** The TVAMC IRB shall consist of a minimum of five members and a maximum of twenty members. Membership is selected to ensure appropriate sensitivity to community issues and/or attitudes with respect to the rights and welfare of human research subjects and to assure appropriate diversity. The membership will promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The membership shall possess the professional competence necessary to review the types of research activities that are submitted to the TVAMC IRB. The IRB shall have individuals with the appropriate scientific or scholarly expertise required to review the protocols. The IRB shall be able to ascertain the acceptability of proposed research in terms of medical center commitments and policies, applicable law, and standards of professional conduct and practice, and therefore will include persons knowledgeable in these areas. No single investigator shall be responsible for the selection of members who will review his/her investigational studies. The IRB chair, members, and staff must have the knowledge, skills, and abilities (KSAs) appropriate to their respective roles.

The membership roster is maintained in an Excel spreadsheet and includes sufficient information (i.e. demographics, diversity, experience, expertise). about members to permit review by the R&D Committee to evaluate the composition and by the IRB Committee to ensure that appropriate representation is present at the meeting for each the protocols under review. The IRB's roster contains the individuals' name, alternate names (with

corresponding regular member name for whom they serve), specialty qualification, and area of scientific or scholarly expertise and whether they are a non-scientist member, a non-affiliated member, knowledgeable about or experienced in working with participants vulnerable to coercion or undue influence, or a representative of the perspective of research participants. Individuals with cultural diversity, knowledge of community values, and experience with vulnerable populations, medical expertise, and whom colleagues respect are represented in IRB membership. The roster is based on the information derived from the individual's curriculum vitae (CV) and an Addendum CV form that documents the individual's experience and knowledge of working with veterans, mentally ill, economically and educationally disadvantaged, and cognitively impaired adults. This form is completed by all members, alternates, and consultants. The IRB Program Assistant shall ensure that the current IRB membership roster is maintained.

The membership roster is periodically (at least annually or more often as needed) reviewed carefully by the R&D Committee to determine if changes are needed to adjust the composition to better meet regulatory requirements, TVAMC requirements, and the needs of the HRPP research portfolio. The IRB can also give input to the R&D Committee for consideration of membership composition. In addition, the R&D Committee will review the performance of, knowledge, skills and abilities of the IRB staff, chair, and members (appropriate to their respective roles) on a periodic basis (at least annually) and document this review in the R&D minutes. Performance of IRB members may include, but is not limited to, timeliness, attendance at IRB meetings, attention to detail, adherence to proper review procedures, adequate documentation of reviews, being prepared at the meeting, and compliance with training requirements. Based on this performance review, the R&D Committee will make appropriate adjustments (i.e. terminate membership of members who are not performing and add new members or advance well-performing alternates to full member status). The R&D Chair will provide feedback to the IRB

The membership shall include representation by:

- Multiple professions
- Multiple ethnic backgrounds
- Both genders
- Those with knowledge of institutional commitments
- One or more who are knowledgeable about or experience in working with vulnerable subjects/populations involved in research conducted at the TVAMC (i.e. mentally ill, terminally ill, medically ill, veterans, or other vulnerable populations)
- At least one member whose primary concerns are scientific
- At least one member whose primary concerns are non-scientific
- At least one or more community member who is not otherwise affiliated with the TVAMC and who is not a part of the immediate family of a person who is affiliated with the medical center (i.e. neither an employee of the VA nor directly connected with any research within the institution), such as clergypersons, attorneys, representatives of legally recognized veterans organizations, or practicing physicians.
- At least one member who also serves concurrently on the R&D Committee.

- d. **Appointment of Chairperson and Vice-Chair, Length of Service, and Duties:** (VHA Handbook 1200.05). The IRB may nominate the Chair and Vice-Chair from the IRB membership, by a simple majority of the membership. After the qualifications and experience of the person have been assessed by review of their curriculum vitae and determined to be appropriate for the position, the R&D Committee endorses the nominee and forwards the nominee to the Director. The individuals selected will hold a VA appointment (VA employee or without compensation employee) of the TVAMC. The IRB Chair must be appointed by the Director for a term of 1 year and may be re-appointed indefinitely. The Vice-Chair must be appointed by the Director for a term of three years and may be re-appointed indefinitely. The Chairperson has primary responsibility for conducting IRB business. He/she directs IRB proceedings in accordance with institutional and federal requirements. He/she works with IRB members, institutional officials, and investigators to ensure that the rights and welfare of research subjects are protected. He/she functions as a role model and conducts business fairly and impartially. He/she is the signatory official for official IRB correspondence. He/she or the Chief for R&D orients new IRB members to their responsibilities as members of the IRB. At each IRB meeting the Chair will educate the IRB members with respect to changes in the laws and regulations governing either experimentation involving humans or laws and regulations governing the composition and procedures for IRB. The Vice Chair has the primary responsibility for conducting IRB business in the absence of or at the request of the Chair, or in the event of the Chair's removal until a new Chair is elected. The R&D Committee may remove the Chairperson and/or the Vice-Chair with the concurrence of the Director for failure to perform the duties defined above.
- e. **Appointment of IRB Members, Length of Service, and Duties:** (VHA Handbook 1200.05). IRB members are nominated by the IRB and/or R&D Committees, approved by the R&D Committee and appointed by the Director. Other VA personnel may submit names to the IRB or R&D Committee to be forwarded to the Director for consideration. The Director must officially appoint members in writing. Members of the IRB must be appointed by the Director for a period of 3 years and may be re-appointed indefinitely. The members must have the knowledge, skills, and abilities appropriate to their respective roles, as determined by a review of their curriculum vitae (CV) and Addendum CV form.
- f. **Alternate IRB Members:** Alternate members are nominated by the IRB and/or R&D Committees, approved by the R&D Committee and appointed by the Director. These alternate members replace regular IRB members who are unable to attend convened meetings of the IRB. IRB members have assigned alternate(s). The selection, length of term, duties, removal, grounds for removal, resignation terms, education requirements, compensation, liability coverage and conflict of interest policies of the alternate(s) are the same as a regular IRB member. An alternate may only substitute for his/her designated member.
- g. **The Periodic Review of the IRB Membership:** The IRB chair, membership and composition are periodically (at least annually) reviewed by the IRB and R&D Committee and adjusted to meet regulatory and organizational requirements. These committees

review the membership roster and determine if the membership is appropriate; includes the expertise required; and meets with sufficient frequency to review the amount and type of research conducted at the TVAMC. If an investigator proposes research in a specialty not regularly represented on the IRB, the R&D Committee may change the IRB composition to include the specialty area. The review of the membership composition and any suggested changes in membership are documented in the minutes and thereby communicated to the appropriate institutional officials.

- h. **Attendance Requirements and Membership Removal:** IRB members are required to attend monthly meetings. Each member is responsible for notifying the Chair and their designated alternate at least one week, or as soon as possible in advance of an anticipated absence. The R&D Committee may remove IRB members with the concurrence of the Director. An IRB member may be removed if 1) there are unexcused absences for more than three meetings in one year, 2) the member knowingly provides the IRB with false information, or 3) the member fails failure to accept and perform responsible assignment of IRB tasks as determined by the Chair or Vice-Chair. Any member may resign from the IRB at any time, by written or verbal means of communication. The R&D Committee will officially terminate the member and then submit the termination to the Director, through the Chief of Staff via the R&D minutes.
- i. **Member Orientation:** The IRB Chairperson or the R&D Chief orients new members. IRB members and investigators receive the TVAMC HRPP SOPs, and the TVAMC pertinent Center Memorandums. Web Site references will be provided for the VHA Handbook 1200.05, The Belmont Report, the 1998 FDA Information Sheets, the Institutional Review Board Guidebook (DHHS), as well as FDA [21 CFR 50,56] and DHHS [45 CFR 46].
- j. **Continuing Education:** All IRB members and IRB staff must receive training on the protection of human subjects in research and Good Clinical Practices every year or as required by Federal agencies and the FWA and outlined in SOP #12.
- k. **Compensation for IRB Service:** Currently, the IRB members are not compensated, except for the IRB Community members (non-VA-affiliated members). Community members receive a flat-rate compensation through TREAC for each monthly IRB meeting that they attend.
- l. **Liability Coverage for IRB Members:** Currently there is no liability coverage for the IRB members. VA IRB members (including those with a WOC appointment) are officially carrying out the VA mission and are protected from liability under the US Federal Tort Claims Act.
- m. **Consultants:** The IRB is authorized to obtain the services of ad hoc reviewers, outside peer review or consultation when additional expertise is required to adequately review a specific protocol. An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues, which require expertise beyond or in addition to that available on the IRB. The need for such an individual may be identified

by the IRB staff prior to the initial IRB review or by the IRB members at the time of initial IRB review. The IRB office maintains a file of consultants and their curriculum vitae/biosketch for reference, if needed by the IRB member to select an outside consultant. In addition, the IRB member or the Chief of R&D can also identify consultants in specific areas, when needed, from known colleagues or experts in the field. These individuals are sent the study submission materials to review in advance of the next scheduled IRB meeting. The criteria for selection include, but are not limited to, known or credentialed expertise in the area of concern, availability and willingness to serve in this capacity within a timely manner, and no conflict of interest with the study under review. These individuals are subject to the same conflict of interest policies as IRB members. These individuals may send a written report to the IRB regarding their review and recommendations or they may personally attend the IRB meeting to deliver their written report and communicate their review and recommendations verbally. These individuals may not vote, however may participate in the IRB discussions. Legal counsel (such as VA Regional Counsel) may be retained on a consultant basis, if needed.

- n. **Conflict of Interest(s):** All IRB members and consultants must complete a financial disclosure form (as described in SOP # 9A), which will be kept on file with their curriculum vitae (CV) and certification of education on the protection of human subjects in research. In addition to financial conflicts of interest, a conflict of interest (as defined in SOP #9A) would exist if an IRB member or consultant were an investigator or co-investigator, research assistant, or spouse of an investigator on a specific protocol under review. At the beginning of every meeting, the IRB Chair shall ask the IRB members and consultants to disclose any potential conflict of interest(s) related to any protocols that the IRB is about to consider. The IRB minutes will document identified conflict of interests. An IRB member or consultant who is identified as having a conflict of interest may not participate in the IRB's initial or continuing review discussion or vote on the project in which a member has a conflicting interest, except to provide information requested by the IRB. IRB members or consultants who have a conflict of interest are required to absent themselves from the meeting room during deliberations and voting, abstain from voting, and not be counted towards a quorum for voting purposes. Abstentions are recorded in the IRB minutes. In addition, IRB members or consultants with a conflict of interest on a specific protocol are not allowed to participate in the approval process for its continuing review, expedited procedures, review of modifications, review of unanticipated problems involving risks to participants or others, or review of non-compliance with the regulations or the requirements of the IRB.
- o. **IRB Primary Reviewer Assignment System:** For initial and continuing reviews, the IRB Program Support Assistant will assign primary reviewers on a case-by-case basis as authorized by the IRB Chair. Primary reviewers are assigned by the IRB Program Support Assistant after consideration of protocol content and primary reviewer's scientific or scholarly expertise or experience. The IRB Program Support Assistant consults with the IRB Chair, Vice-Chair, or C/R&D if needed in determining the appropriate primary review for a specific protocol. Assignment of primary reviewer is documented in the agenda and minutes. The primary reviewer is responsible for an in-depth review of the research proposal (as described in SOP #3 and #6; using the primary reviewer checklist as

an aid and means of documentation) and for leading the discussion during the IRB meeting. The primary reviewer system does not take the place of a review by the convened IRB for actions that require a full convened IRB review and action.

- p. **IRB Meetings, Minutes, Materials and Documentation:** The IRB is required to conduct initial and continuing reviews of all non-exempt research at convened meetings at which a majority of the members are present, unless the research falls into one or more categories for expedited review. Prior to the convened meeting, all members of the IRB shall be provided with sufficient information to substantially and meaningfully evaluate the proposed research and determine appropriate action during the convened meeting. The agenda and all supporting documentation to be reviewed are made available to all IRB members at least 4 days in advance of the meeting.

The IRB meets every month on a regularly scheduled basis. Scheduled meetings will be canceled or rescheduled for federal holidays, for lack of a quorum, or at the discretion of the Chair. All canceled meetings must have a full written explanation for doing so recorded in the minutes of the next meeting. The Chair will give notification to members in a timely manner of any rescheduled meeting. As deemed necessary to accomplish the responsibilities of the IRB, the Chair may call additional meetings.

Meetings are considered appropriately convened when the following requirements are met:

1. At least one non-scientific member is present
2. More than half of the membership is present (i.e. a simple majority or quorum), even during actions in which a member(s) are recused due to conflict of interest(s).
3. At least one licensed physician must be present for review of protocols utilizing FDA regulated test items.

Although not required, a non-affiliated member is highly recommended at convened meetings. Frequent absence of the non-affiliated member is unacceptable.

Quorums can be lost if a member or members have to leave a meeting early or absent themselves due to conflicts of interest. In such circumstances, affected projects may be deferred until a quorum can be re-established or postponed until the next meeting. Votes by proxy are not permissible. Written review of an assigned protocol from an absent member is permissible and will be reported to the IRB by the Chair. IRB members can attend by conference call and count towards quorum if the member has a copy of the same material that the IRB has at that actual meeting.

The conditions for an appropriately convened meeting are documented in the IRB minutes. Minutes of the meeting, including all recommendations, shall be prepared by the R&D Program Support Assistant and forwarded to the Chairperson of the IRB for approval prior to distribution. Once approved, copies will be distributed to IRB members and R&D Committee Chairperson and members. All IRB findings and actions are communicated in the IRB minutes and forward to the investigator in memorandums. The IRB minutes are

forward to the R&D Committee for their review and are attached to the R&D minutes for review by the Chief of Staff and the TVAMC Director.

- q. **IRB Actions:** The IRB has specific authority to approve, require stipulations, contingencies, or modifications (in order to secure approval), table, disapprove, suspend, or terminate approval of any TVAMC human subject research activity, at any point in the course of submission or course of the study, i.e. initial review, expedited review, continuing review, or elsewhere during the course of the study. For studies of greater than minimal risk research that the IRB approved contingent upon substantive modifications or clarifications to the protocol or the informed consent, IRB approval must not occur until subsequent review by the convened IRB of the materials the PI submitted.

- r. **IRB Record Keeping and Required Documentation:** The IRB records, including the investigator's research records and reports of injuries to participants will 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), and consistent with applicable FDA and DHHS regulations, sponsor requirements, and organizational policies and procedures. The stored IRB records will also include the specific category of exemption cited for exemption determinations (when applicable) and determinations required by the regulations and protocol-specific findings supporting those determinations for waiver of alteration of the consent process (when applicable). All records shall be accessible for inspection by authorized persons at reasonable times and in a reasonable manner. Records will then be archived according to VA regulations. The IRB maintains a complete set of materials relevant to review of the research study in each protocol file.

IRB records are the property and the responsibility of the local research office and are maintained and/or stored as required to protect the privacy and confidentiality of subjects. IRB records are stored in locked filing cabinets in the locked IRB office with limited access keys. The IRB records may be accessed by the Chief for R&D, Research Compliance Officer (RCO), R&D Administrative Officer (AO), Chair or Vice-chair of IRB, IRB members, Chair or Vice-chair of R&D, R&D Committee members, IRB Program Assistant and staff, Director, accrediting agencies, Federal (OHRP, FDA), State, or VA (local, VISN 7 RACO, ORO) authorized persons. Research investigators shall be provided reasonable access to files related to their research, with access supervised by the IRB Program Assistant or staff member. All other access to IRB records is limited to those who have legitimate need for them, as determined by the Director, the Chief of R&D, the R&D AO, the R&D or IRB Chair person, and VA Central Office. Appropriate accreditation bodies shall be provided access and may recommend additional procedures for maintaining security of IRB records. Records are accessible for inspection and copying by authorized representatives of VA and other Federal regulatory agencies at reasonable times and in a reasonable manner. The IRB controls access to protocol files and the IRB Administrative Staff tracks the following by written log: 1) who, other than IRB members and office staff, accessed the files, 2) what files were accessed, 3) when the files were accessed, and 4) for what purpose the files were accessed. IRB records include written IRB standard operating procedures, IRB membership rosters, training records, IRB correspondence, IRB research application files, active research tracking system,

documentation of exemptions and exceptions, documentation of expedited reviews, IRB minutes, FWA, serious adverse event reports, and membership CVs.

- s. **IRB Correspondence:** The IRB Program Assistant shall ensure that accurate records are maintained of all correspondence to or from the IRB. IRB correspondence regarding a specific study is kept in the specific study file. All decisions are reported to the investigator and the appropriate institutional officials in writing (memo or email). All correspondence will be maintained in a computer database or study specific file, and will be easily retrievable. The IRB may request (by memo, letter, or email) additional information from the PI or sponsor to enable appropriate review.
- t. **Correspondence to the Investigator Conveying IRB Decision:** IRB actions and all decisions about a research protocol are promptly conveyed to the PI in writing. Communications conveying stipulations for approval or reasons for disapproval/tabling include the reasons for non-approval and may suggest changes to the protocol and/or consent form needed before approval will be reconsidered. Contingent Approval Memo or electronic mail message is issued with instructions to modify the protocol or consent form according to IRB stipulations. All IRB actions and communications are maintained in a study specific file and are easily retrievable. The Chairperson may designate a member to work with the PI on making the recommended changes. After any and all stipulated changes are made to the protocol and/or Consent Form and are verified by the Chair or Vice-Chair, a formal IRB Approval Memo is issued to the PI. If a submission is disapproved a written memo is issued to the PI. The study may be revised and resubmitted.
- u. **IRB Approval Letter/Memo:** The IRB Approval Letter includes the Conditions of IRB Approval and the Penalties for Noncompliance.
- v. **Correspondence to the Institution Administration Conveying IRB Decision:** The IRB submits reviewed and approved minutes that report all decisions of the IRB to the R&D Committee. R&D Committee minutes are reviewed and approved by the Director. When approved, project data information is submitted to the Department of Veterans Affairs Headquarters, Chief, Research Support Office through the National VA Research and Development Information System (PROMISE). Terminations and suspensions are reported to the R&D Committee, institutional officials responsible for the assurance and HRPP, and to the appropriate VA Central Office officials, Federal agencies and departments.
- w. **Correspondence To Sponsor of Research Conveying IRB Decision:** Unless specifically required by a sponsor or the IRB no written notifications of IRB decisions will be provided to sponsors. The PI usually serves as the communications link between the IRB and the sponsor. For FDA regulated test articles the sponsors and PIs agree to such linkage when they sign Form 1572.
- x. **IRB Research Application Files:** The IRB shall maintain a separate file for each research study application. Protocols are numbered sequentially in the order in which they

are received. Each IRB research study file contains the following materials: protocol, informed consent (all approved versions), sponsor's protocol or Investigator's Brochure (in an associated 3-ring binder), any grant applications, advertising or recruitment materials, correspondence of protocol amendments or modifications, reports of unanticipated problems involving risks to subjects, reports of SAEs (local and external), Data and Safety Monitoring Board (DSMB) reports (if any), results of any internal or external quality control and monitoring activities, all IRB correspondence to and from the investigator, approval letters, study related forms, continuing review forms and information, and final study close-out correspondence.

- y. **Research Study Tracking System:** The IRB Program Support Assistant shall maintain a tabulated tracking system (electronically maintained on Microsoft Access MIRB 2002) of all research protocols, listing PI, protocol name, date of initial protocol review and approval, and date of latest continuing review.
- z. **Documentation of Exemptions:** (38 CFR 16.101; M-3, Part 1, Chapter 9.06) The IRB office maintains documentation of protocols submitted in writing by the investigator, as well as the IRB Chair/designee and R&D approval of exempt status on appropriate studies. The IRB Chair or designee must approve the exempt status and communicated that status in writing to the investigator. See HRPP SOP#5 Exempt Research.
- aa. **Documentation of Exceptions/Waivers from Informed Consent:** The IRB maintains documentation of protocols submitted in writing by the investigator, as well as the IRB and R&D approval of exempt/waiver of informed consent status on appropriate studies. The IRB must approve the exempt/waiver of informed consent status and communicate that status in writing to the investigator. See HRPP SOP#7 Research Informed Consent.
- bb. **Documentation of Expedited Reviews:** The IRB must maintain documentation of submitted expedited reviews and the status or approval of such a review. The actions are communicated in writing to the investigator (i.e. copy of the memo with approval or disapproval indicated at the bottom). See HRPP SOP #4 Expedited Review.
- cc. **Institutional Forms/Reports:** VA Form 10-1086 (VA Research Consent Form) and VA Form 10-9012 (Investigational Drug Information Record) are utilized. The Research and Development Information System (RDIS) is linked to the VA Headquarters computerized project reporting system. The IRB has developed multiple forms to assure that investigators provide the information required for review and continuing review activities.
- dd. **Adverse Reactions Reports and Documentation that the IRB Reviews such Reports:** All SAE (TVAMC serious adverse events) are reported in the SAE form, signed by investigators, reviewed under expedited review by the Chair or experience member and reported at convened meetings and/or continuing review. Reviews are documented in IRB minutes, filed in the IRB investigator study file and written notifications of review and approval or actions required are sent to the investigator.
- ee. **Statements of Significant New Findings Provided to Subjects:** The "new findings"

statement is included in the Consent Form template provided to investigators. The IRB verifies that this statement is included in the approved Consent Form. The method and urgency of conveying significant new findings varies depending on safety specifics. For example, if new information indicates that study medication is harmful then subjects will be contacted immediately. In less urgent cases, for example a change in PIs, written notification may be appropriate. A phone call in addition may be appropriate. A revised Consent Form and re-consenting all affected subjects may be necessary. All actions will be maintained in the IRB's investigator project file.

- ff. **Documentation of Convened IRB Meetings Minutes:** the IRB Program Assistant prepares meeting agendas and minutes for each convened IRB meeting. Minutes of the previous meeting are reviewed and approved at each succeeding meeting. The minutes could not be altered by anyone including a higher authority once approved by the members at a subsequent IRB meeting. Minutes include documentation of:
- Members present, absent/excused, alternate(s) present (when replacing a primary member), others present
 - Number of members present and statement of quorum requirements to transact business (including a non-scientific member)
 - Conflict of interest disclosure (and circumstances in which members with conflicts of interest did not participate in deliberations or voting).
 - Names of IRB members who leave the meeting because of a conflict of interest along with the fact that a conflicting interest is the reason for absence
 - Approval/modifications of prior meeting minutes
 - Old business
 - Previously TABLED items identified
 - Continuing reviews (3, 6, 9, 12 months or other but at least annually; separate deliberations for each review)
 - Items reviewed (Abstract, Protocol, Consent Form, etc.) including dates and version of items reviewed
 - New business
 - Initial reviews (separate deliberations for each review)
 - Protocol submissions to include: Title of Project, Investigator Name, Primary Reviewer, Sponsor Name
 - Objective of the project
 - Details of pertinent discussions including risk and benefit analysis, Assessment of informed consent document, controverted issues and their resolution. An issue is controverted when there is a split vote, in which some IRB members vote for approval and other IRB members vote against approval. When a split vote is recorded, the summary of the controverted issue must be documented.
 - Discussions of appropriateness and rationale for elements requiring special attention, if any
 - Changes required prior to final approval, if any
 - Basis for requiring changes in research and disapproving research
 - Basis of allowing exempt status, waiver of informed consent, or alteration of informed consent process (if applicable).

- Approve/Contingent Approve/Table/Disapprove Action taken by the IRB; including the approval period for approved protocols
- Records of voting (number of members for, against, abstained, recused, and excused on each action) that meets the required quorum to be present for each vote, including a non-scientific member
- Expedited reviews or reviews of Exempt Research and actions taken (e.g. advertisements, amendments, Investigator Brochure updates, protocol deviations, modifications, notifications, Sponsor SAEs, TVAMC SAEs)
- Members who recused/excused themselves by name
- Determination of the frequency of continuing review of each project based upon the degree of risk
- Noncompliance or complaints, if any
- Education In-service discussion, if any
- Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document

gg. **Other IRB records** include the following: progress reports submitted by investigators; reports of injuries to participants; investigator brochures; any supplemental information; all correspondence; and any other records relevant to IRB business or review of the research studies.

hh. **IRB Functions:** The IRB has and follows written policies and procedures that are specifically described in separate SOPs and include the following functions:

- To conduct initial reviews of research studies (SOP#3, SOP#7, SOP #8, SOP#9A, SOP #10, and SOP#12) to ensure that all safeguards and requirements for ethical research and protection of vulnerable subjects are met prior to approval
- To conduct continuing reviews of research studies and to determine which projects require continuing review more often than annually (SOP#6)
- To conduct review of proposed informed consent forms/process involving human subjects and review proposed exemptions to informed consent (SOP#7)
- To conduct review of modifications and amendments to previously approved research; to ensure that changes in approved research are not initiated without IRB review and approval; and to determine whether projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review (SOP #11 and SOP #17)
- To conduct reviews by the expedited process, when appropriate (SOP #4)
- To conduct review of study closures (SOP#6)
- To conduct review of and ensure that unanticipated problems involving risks to subjects, protocol deviations, and adverse effects, whether research related or not, are promptly reported to the IRB (SOP #11 and SOP #17)
- To conduct review of allegations and findings of noncompliance (SOP #18)
- To conduct review of participant recruitment and outreach materials (SOP #8 and SOP#14)

- To conduct review of reports of budget, resources, compliance audits, and quality improvement activities (SOP #17 and SOP #19)

5. REFERENCES

- a. VHA Handbook 1200.05
- b. VA Center Memorandum No. 11-14, Subcommittee on Human Studies (IRB)
- c. TVAMC Federal Wide Assurance
- d. TREAC Federal Wide Assurance

6. ATTACHMENTS

Membership Roster

7. RESCISSIONS

HRPP SOP #2 The Organizational Structure of the Institutional Review Board dated March 23, 2009.

8. REVIEW DATE

January 1, 2012

Signature on File in R&D Office

Lori L. Davis, MD

Chief of Research and Development

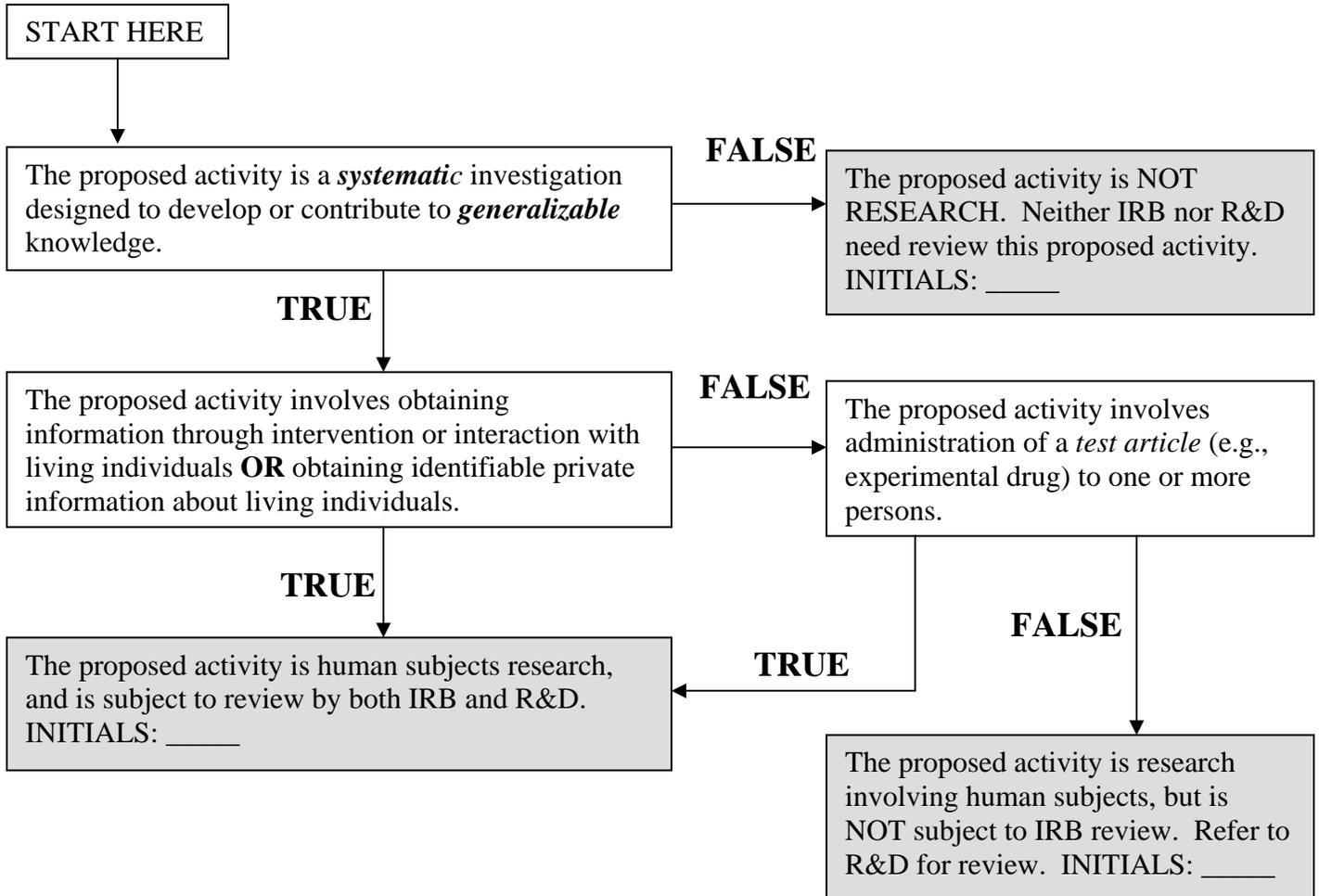
TVAMC HRPP FLOWCHART

Worksheet for Determination of Whether a Proposed Project Meets the Definition for Human Subjects Research

PROJECT TITLE: _____

PRINCIPAL INVESTIGATOR: _____

INITIAL THE SHADED BOX INDICATING THE STATUS OF THIS PROJECT



WORKSHEET COMPLETED BY: _____

DATE: _____