VA Hospital Research – Special Considerations

Effective Date:  
Original Approval Date:  
Revision Date:  
   December 1, 2007  
   August 3, 2009

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1.0 Purpose

To assure knowledge and compliance by documenting the policies and procedures to be followed when conducting research within the Harry S Truman Memorial Veterans Hospital.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Policy/Procedure

The HS IRB has been appointed as the IRB of record for the Harry S Truman Memorial Veterans Hospital. The agreement has been outlined in a Memorandum of Understanding (MOU) signed by both parties. Further, the HS IRB agrees to comply with the federal regulations including 38 CFR 16 and with all applicable regulations as outlined in the VA Handbook 1200.5 “Requirements for Protection of Human Subjects Research in Department of Veterans Affairs (VA) Research. A commercial IRB is prohibited from being used to review VA research projects.

VA research will be reviewed and monitored in the same manner as all other research under the purview of the HS IRB. It will be expected to comply with the federal regulations and adhere to the HS IRB SOPs as outlined for all research. VA regulations have some additional requirements specific to VA research and these requirements are outlined in this policy.

For VA research, IRB approval may be granted pending approval of the R&D Committee. Research cannot commence until R&D Committee approval is granted. Therefore, research may not commence until R&D approval has been obtained. The R&D Committee will provide a written approval letter to the investigator with a copy sent to the HS IRB for inclusion in the study files.

IRB Composition

Each committee of the HS IRB is properly constituted to review VA research. As required by 1200.5, each committee of the HS IRB has appointed 2 full voting members from the VA Hospital to offer advice and counsel as to special circumstances of the VA population. At least one of the VA members must have scientific expertise. VA members will be appointed to the HS IRB by the VA Hospital Director with concurrence of the Vice-Provost for Research. Each VA representative is appointed for a 3-year term with re-appointment options.

Although representing VA interests, these members will also review and act upon non-VA activities coming before the full board or through expedited procedures. At least one of the VA representatives must be present at the IRB meeting when review of VA research occurs.

R&D Administration officials such as the ACOS R&D or AO R&D may not serve as a voting member of the HS IRB. However to facilitate communications with the HS IRB, the VA Human
Research Compliance Officer attends IRB meetings as an observer. A member of the HS IRB administrative office staff also attends the monthly R&D committee meetings as a non-voting member.

For VA research involving an FDA-regulated article, a licensed physician must be included in the quorum of the IRB meeting.

The membership of the HS IRB must include at least 1 with expertise in the area of research when VA research to be reviewed includes participants with impaired decision-making capacity.

The HS IRB has on file CVs for each board member to the HS IRB. These CVs are made available to the VA R&D as requested.

The HS IRB does not utilize alternate members. Therefore no alternate VA members have been named. In the event, alternate VA members become necessary, the HS IRB will follow appropriate procedures in working with the VA to appoint alternate members.

R&D Committee

In addition to review by the HS IRB, all VA projects must also be reviewed and approved by the VA R&D committee prior to initiation of the research. The main emphasis of R&D review is:

1) scientific merit
2) utilization of VA resources
3) impact on VA

The approved HS IRB minutes are provided on a monthly basis to the VA R&D Committee. As required by 1200.5, the R&D Committee reviews the minutes of the IRB to assure compliance with the regulations and consideration of VA interests. Minutes of IRB meetings must be documented and available for review within 3 weeks of the HS IRB meeting date. The IRB meeting minutes provided to R&D will be non-redacted minutes prepared in compliance with the federal regulations and HS IRB policies and procedures. The R&D Committee or higher VA authority may not alter the HS IRB minutes once approved by the HS IRB.

Procedures for interacting with the R&D Committee

For initial reviews, the VA R&D will only review a project once it has been approved by the HS IRB. The VA has a separate application form to be submitted with the completed HS IRB application form to the R&D. To ensure the R&D review occurs at the earliest opportunity after IRB approval, the VA application should be submitted to the R&D Committee at the same time as the IRB application. Any revisions or clarifications to the HS IRB application between submission and approval by the HS IRB should also be communicated between the investigator and the VA R&D.

The HS IRB will notify the R&D Committee in writing of its review and action of a proposed research activity or modifications required to secure approval. This notification will occur through completion of VA form 10-1223 provided to the VA R&D.

Research activities disapproved by the HS IRB may not be overruled by the R&D Committee or any higher VA authority. The R&D Committee may, however, strengthen requirements and/or conditions, or request other modifications to secure R&D approval. Any requests made by the
R&D Committee must be communicated to the HS IRB if they are relevant to the approval granted by the HS IRB which may necessitate a re-review by the HS IRB or involve amendments to the study. If the study is being conducted in both VA and MU venues, the R&D requests impact only the VA portion of the study.

The VA R&D also has a separate continuing review form. This VA continuing review form will need to be completed and submitted to the VA R&D in addition to the continuing review materials submitted to the HS IRB.

Other actions such as amendments, unanticipated events, etc. do not require separate forms submitted to the VA R&D in addition to those submitted to the HS IRB. Mechanisms are in place between the VA R&D and the HS IRB to convey this information. Notification of amendments and other actions are provided to the R&D by the VA Human Research Protection Compliance Officer in consultation with the HS IRB.

To facilitate interaction, the HS IRB has provided access to the electronic IRB (eIRB) system for projects that involve the VA to aid in monitoring the VA projects. The eIRB is paperless storage for all IRB files and documents, including but not limited to, correspondence between the IRB and R&D, unanticipated problems involving risks to participants or others, and other documentation of information to be provided to both the HS IRB and IRB. Upon request, the VA R&D is provided with complete access to the eIRB system for inspection and copying of records pertaining to VA-specific research.

Research Proposed for VA participants only

Non-veterans may not be enrolled into VA-funded research studies unless there are not enough veterans available to complete the study. Determination of the allowance to enroll non-VA participants will be decided upon by the VA R&D.

Additional VA Consent Requirements

The VA requires all consents to be on the VA Form 10-1086. To facilitate this, the HS IRB provides a VA consent template including all required elements of consent and VA-specific language.

The VA requires the IRB to determine if a subject’s medical record (paper or electronic) needs to be flagged and the source for additional information regarding the study. All medical records will be flagged with the required documentation according to the Harry S. Truman Memorial Veteran’s Hospital Investigator’s Handbook (http://www.va.gov/columbia-mo/humanres/cprs.shtml) and any relevant information (to be determined by the HRCO) unless there is a specific reason not to do so, such as a confidentiality issues. Only exceptions will be noted in the minutes.

All regulations pertaining to the participation of veterans as research subjects including requirement for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research. Additionally, every participant enrolled at the VA (veteran or not) must have a medical chart, and a copy of the consent form must be included in that chart.

There are also 3 areas of the consent which must contain VA specific language. The sections are “What are the Costs?”, “What if I am Injured?”, and the signature section.
What are the Costs?
There will be no costs to you for any of the treatment or testing done as part of this research study. However, medical care and services provided by the VA that are not part of this study (e.g., normal hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services.

What if I am Injured?

In the event that you sustain an injury or illness as a result of your participation in this VA approved research study, all medical treatment (emergency as well as medical treatment beyond emergency care) will be provided by the VA. You will be treated for the injury at no cost to you. However, no additional compensation has been set aside. You have not waived any legal rights or released the hospital or its agents from liability for negligence by signing this form.

In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor at (XXX) XXX-XXXX during the day and (XXX) XXX-XXXX after business hours. If you need emergency hospitalization in a private hospital because you are unable to come to the VA, have a family member or friend contact your study doctor so that the VA can coordinate care with the private hospital.

Signature

Research Subjects’ Rights

I have read or have had read to me all of the above. Dr. [ ] has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

It has been explained to me that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled. The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems or questions, I have been told I can call Dr. [ ] at [ ] during the day and Dr. [ ] at [ ] after hours. If any medical problems occur in connection with this study the VA will provide emergency care.

My rights as a research subject have been explained to me, and I voluntarily consent to participate in this study. It has been explained to me what the study is about and how and why it is being done. I will receive a signed copy of this consent form.

Are you participating in any other research projects? Yes No

Additionally, if appropriate, the Government Accounting Office (GAO) must be listed in the consent as an entity having access to the study records. All VA research must use the VA 10-1086 consent form including research using non-VA participants which is conducted within the VA facilities.

VA 1200.5 requires all participant signatures be witnessed. A witness line and prompt have been added to the 10-1086 consent template. There are no specific requirements on who the witness may be or stipulations as to the impartiality of the witness. It may be a member of the study staff.
and does not have to be an impartial third party unless the status of the participant requires an impartial, third party witness. If required by the study and the same person serves in the capacity of both witnesses, a note to that effect must be placed under the witness signature line.

VA 1200.5 requires the consent version approval date to be on every page of the consent. The 10-1086 template on the HS IRB website has provisions for the entry of this date. If an amendment or other action necessitates revision to the consent, the new consent version approval date must be entered on every page of the consent.

Handbook 1200.5 requires informed consent to be obtained by a person knowledgeable about the consent process and the research. If someone other than the investigator conducts the informed consent process and obtains consent, the investigator must formally delegate this responsibility. The delegated person must have appropriate training and knowledge of the study to perform this activity.

If the HS IRB has determined the research qualifies for a waiver of documentation of informed consent, the written summary presented to the participant will be on the VA 10-1086 form letterhead.

VA regulations require the consent process and study participation in all VA studies of greater than minimal risk to be documented in the Computerized Patient Record System (CPRS). The VA R&D Committee will determine whether certain studies should be additionally “flagged” based on participant safety needs.

VA Research with Persons of Impaired Decision-Making Capacity

VA research involving persons with impaired decision-making capability may only be approved by the IRB when the following conditions apply:

1) Only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.

2) The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

3) Procedures have been devised to ensure that participant’s representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. When appropriate, the IRB should consider whether other health care providers ought to be consulted to ensure that proposed research procedures will not be detrimental to ongoing therapeutic regimens. The legally authorized representative (LAR) must be given descriptions of both proposed research studies and their obligations as a LAR. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject’s wishes cannot be determined, what they think is in the incompetent person’s best interest.
4) In situations where there is a history or current presentation of mental illness or impaired decision-making capacity, the investigator will be obligated to obtain an appropriate assessment of the capacity to give informed consent. If there is medical evaluation and documentation in the medical record by two VA physicians that (a) the prospective research participant is incompetent or has an impaired decision-making capacity, (b) there is little or no likelihood that the person will regain competence within a reasonable period of time, or (c) incompetence already has been established by a legal determination, then consent may be requested from the legally authorized representative.

5) Consultation with a psychiatrist or licensed psychologist must be obtained when the determination that the prospective research subject lacks decision-making capacity is based on a diagnosis of mental illness.

6) If feasible, the practitioner must explain the proposed research to the prospective research subject even when the surrogate gives consent. Under no circumstances may a subject be forced or coerced to participate in a research study.

The IRB must make a determination in writing of each of the criteria listed above. If these criteria are met, the IRB may approve the inclusion of incompetent subjects or subjects with impaired decision-making capacity in research projects on the basis of informed consent from a VA approved LAR.

The VA, under VA policy follows the State of Missouri law applicable for research and legally authorized representatives. (See – Informed Consent Process and Issues SOP).

Refer to VA policies for further guidance on consent issues and legally authorized representatives.

The HSIRB staff will consult with the VA compliance officer for guidance on interpreting VA policies concerning consent, approved legally authorized representatives and other applicable areas, as needed.

Payment to Participants

VA policy prohibits payment to research participants when the research is integrated with a patient’s medical care and makes no demands on a patient beyond those of usual medical care. Payment may be permitted, with IRB approval, in the following circumstances:

1) no direct subject benefit – when the study to be performed is not directly intended to enhance diagnosis or treatment of the medical condition for which the patient is being treated and the standard practice in affiliated non-VA institutions is to pay participants
2) other participants being paid – in multi-institutional studies where human subjects at a collaborating non-VA institution are being paid for the same participation in the same study at the same proposed rate
3) comparable situations – in other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate
4) Transportation expenses – when transportation expenses are incurred that would not be incurred in the normal course of receiving treatment and are not reimbursed by any other mechanism.
VA investigators who wish to pay research subjects must, in their proposal:

1) substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject
2) state the terms of the subject participation agreement and the amount of payment in the informed consent form
3) substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure or influence on the prospective research subjects to volunteer for, or to continue to participate in, the research study; and that the payments do not constitute (or appear to constitute) coercion to participate in, or continue to participate in, the research study.

The VA has its own policies regarding the appropriate handling of payments to research subjects. The PI is responsible to contact the R&D office for information on the appropriate policies and procedures.

**HIPAA**

Any HIPAA authorizations for the VA study must also be provided on the VA 10-1086 letterhead. A template VA HIPAA Authorization may be found at [http://research.missouri.edu/forms/forms_dept.htm#hsirb](http://research.missouri.edu/forms/forms_dept.htm#hsirb). Any waiver of HIPAA Authorization or alteration in the content of the authorization will be documented in the HS IRB minutes of the meeting where action occurred or reported as an expedited review action.

**Study Personnel**

All research conducted at/by the VA must include a VA investigator as study personnel on the study. The VA R&D will be responsible for determining the qualifications and appropriateness of the VA investigator in relationship to the VA study.

All key personnel involved in VA research are required to complete the educational requirements of the VA in addition to the HS IRB educational requirements. The VA R&D Office should be consulted for additional educational, credentialing or appointment requirements.

**Conflict of Interest**

All VA investigators must comply with the VHA policies and procedures regarding conflict of interest. The VA R&D Office should be contacted for information on conflict of interest requirements.

**Obtaining and/or Banking of Tissue**

If investigators believe that the human biologic specimens obtained could be part of, or lead to the development of a commercially valuable product, involve genetic testing, or if the specimens are to be retained after the end of the study, current VA policy and VHA regulations must be followed. The VA R&D Office should be consulted for additional information on obtaining and banking of tissue.

Regulations require all human biological specimens and linked clinical data collected as part of research projects conducted by VA investigators in VA facilities or approved off-site locations will be maintained at either VA-sponsored tissue banks or VA (ORD) approved tissue banks.
Sites that may not be acceptable for storage of tissue specimens include non-academic, for-profit institutions, such as pharmaceutical or biotech companies. Therefore, research involving banking of tissue for future research purposes may only be conducted if the tissue is banked at a VA-approved tissue banking facility. The VA R&D Office should be contacted for more information on conducting research involving tissue banking and approved tissue banks.

Unanticipated Problems Involving Risks to Participants or Others

All unanticipated problems (per HS policy) involving risks to participants or others will be communicated by the HS IRB staff to the VA R&D.

Problems Involving Risks to Subjects or Others; (VHA Handbook 1058.01), Investigators, RCOs, and other members of the VA research community must report all problems involving, or suggesting, risks to subjects or others in VA research to the Associate Chief of Staff for Research (ACOS for R) and the IRB as soon as possible but no later than 5 business days after becoming aware of the problem.

SAE’s (VHA Handbook 1058.01): VA investigators must report all local SAEs in VA research to the ACOS for R and the IRB as soon as possible, but no later than 5 business days after the event has become known to the investigator.

The VA is responsible for reporting to other VA authorities as required by VA policy.

**HS IRB Procedure for IRB Review of SAE’s and Problems Involving Risks to Subjects or Others**

Within 5 business days after a report of a problem involving risks to subjects or others or a local SAE, a qualified IRB member-reviewer (or alternatively, the convened IRB) must determine and document whether or not the problem is (a) serious, (b) whether or not it is anticipated or unanticipated, and (c) whether it is related, possibly related, or probably not related to the research.

(a) The qualified IRB member-reviewer (or the convened IRB) must also document whether or not one of the following applies:

1. Immediate action (e.g., suspension of activities; notification of subjects) is necessary to prevent an immediate hazard to subjects in accordance with VA regulations at 38 CFR 16.103(b)(4)(iii), and review by the convened IRB is needed; or

2. Review by the convened IRB is needed, but immediate action to prevent an immediate hazard to subjects is not warranted.

(b) If the preceding determinations are made by a qualified IRB member-reviewer, the determinations must be reported to the IRB at the IRB’s next convened meeting.

(c) If the qualified IRB member-reviewer (or the convened IRB) determines that the problem or AE is serious, unanticipated, and related, or possibly related, to the research, the IRB Chairperson must report the problem or event to the Facility Director as soon as possible, but no later than 5 business days after the determination.
(d) If it is determined that an informed consent modification is warranted, the convened IRB must determine and document in its records whether or not previously enrolled subjects must be notified of the modification and, if so, when such notification must take place and how such notification must be documented.

Research Noncompliance

**Serious or Continuing Noncompliance.** Within 5 business days of becoming aware of possible serious or continuing noncompliance with VA or other Federal requirements related to human research (e.g., VHA Handbook 1200.5; the Common Rule at 36 CFR 16; Food and Drug Administration (FDA) regulations at 21 CFR 50 and 56) or with IRB requirements or determinations, members of the VA research community must report the possible noncompliance to the ACOS for R and the IRB.

The HS IRB Compliance Officer and the VA R&D Human Research Compliance Officer will interact to determine the extent of the possible noncompliance and which entity should take the lead in the investigation of the issue. The resolution of the issue will be discussed between all applicable parties and reporting to take place per this policy.

The VA is responsible for reporting to other VA authorities as required by VA policy.

**IRB Reporting Requirements**

**Serious or Continuing Noncompliance:** If the IRB determines that the possible noncompliance is or was serious or continuing, the IRB Chairperson must report the noncompliance to the Facility Director and the R&D Committee as soon as possible, but no later than 5 business days after the IRB’s determination.

**Terminations or Suspensions of IRB Approval.** The IRB Chairperson must report terminations or suspensions of IRB approval of any research related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others to the Facility Director as soon as possible, but no later than 5 business days after the IRB’s action.

**SAEs and Problems Involving Risks to Subjects or Others.** If the qualified IRB member-reviewer (or the convened IRB) determines that the problem or AE is serious, unanticipated, and related, or possibly related, to the research, the IRB Chairperson must report the problem or event to the Facility Director as soon as possible, but no later than 5 business days after the determination.

**Continuing Review Information**

VA research projects will be required to undergo an annual review through the VA R&D Committee in addition to the continuing review with the HS IRB. The VA R&D has a separate annual review form to supplement the information obtained on the HS IRB Continuing Review form. The HS IRB continuing review requests information on all information required in VA Handbook 1200. 5.

**Expired Research**
If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the unless the IRB or IRB chair, in consultation with the VAMC Chief of Staff, find it is in the best interests of individual participants to continue in the study. Enrollment of new subjects cannot occur after the expiration of IRB approval. The IRB Chair will notify investigators to immediately submit to the IRB, a list of participants for whom stopping research activities would cause harm. The investigator is required to promptly report the expiration to the study sponsor.

Research Suspension

VA research that has been suspended or terminated by the HS IRB will be promptly reported to the VA R&D. It is the responsibility of the R&D to report to other VA authorities, as required by VA policy.

The IRB Chairperson must report terminations or suspensions of IRB approval of any research related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others to the Facility Director as soon as possible, but no later than 5 business days after the IRB’s action.

For suspended research involving the VA, continuation of research interventions or interactions in already enrolled subjects should only continue when the IRB Chair, in consultation with the VA Chief of Staff, finds it in the best interest of the subject(s) to do so.

To facilitate the process, the PI or study staff must submit a list of participants for whom suspension would cause harm.

FDA requirements will be followed in FDA-regulated studies. The IRB will promptly report the suspension to the Sponsor, if applicable.

Record Retention

Records stored for VA research will include all records as described in the HS IRB policy of Record Retention and all correspondence between the HS IRB and the VA R&D committee.

Records for VA research must be retained by the investigator at the VA for a minimum of 5 years after the completion of the study and in accordance with VHA Records Control Schedule (RCS10-01), applicable FDA and DHHS regulations or as required by outside sponsors. Note: Under University of Missouri policy the investigator must retain records for 7 years. (See Record Keeping Policy for HSIRB and University of Missouri policies)

All records must be accessible for inspection and copying by VA, OHRP, FDA and other authorized entities upon request.

If the investigator leaves the VA facility, the original research records must be retained at the institution.

Exempt Status Research

See SOP-Exempt applications for regulatory and guidance criteria for exempt research
Projects classified as meeting the exempt criteria by the HS IRB must still be reviewed and approved by the VA R&D Committee.

The exempt application and supporting documents will be submitted the IRB administrative office for review. The HS IRB chair or designee will determine if it meets the criteria set forth in 46.101(b) and is compliant with guidance and policies. If the application meets the criteria for an exempted application, the IRB Chair or designee will determine the category of the exemption, document the determination and sign the application in the appropriate place indicating approval. The original approved application will be returned to the Principal Investigator for inclusion into the study file.

The Department of Veterans Affairs includes a possible loss of insurability as a possible risk not allowed by research being considered for Exempt status under category 38 CFR 16.101(b)(2)(ii). When the IRB chair or designee is making a determination of exempt status under this category, the research will be reviewed to make sure it does not include loss of insurability, in addition to the other exceptions required by the federal regulations.

Notification of the determination of exempt status is communicated to the Investigator through a letter from the HS IRB Chair.

**Research with special requirements by the VA**

Research involving a fetus, in-utero or ex-utero (including human fetal tissue) may not be conducted by VA investigators while on official duty, at VA facilities, or at approved off-site facilities.

Research related to in vitro fertilization may not be conducted by VA investigators while on official duty, by any investigator at VA facilities, or at approved off-site facilities.

Research involving prisoners must not be conducted by VA investigators while on official duty, or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer. The VA R&D Office should be contacted for more information on conducting research with prisoners as participants.

Research involving children must not be conducted by VA investigators while on official duty or at VA or approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer.

**4.0 Applicable Regulations**

- 45 CFR 46
- 21 CFR 56
- 38 CFR 16
- VA Handbook 1200.5

**5.0 Related SOP**

All HS IRB SOPs are relevant to the conduct of VA research

**7.0 Review Panel**