

Human Research Protections Program Investigator Handbook

Harry S. Truman Memorial Veterans' Hospital
Research and Development
Columbia, MO
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<http://www.va.gov/columbia-mo/>

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Overview of the HRPP

Letter from the Research Compliance Officer (RCO)

Welcome to the Research and Development's (R&D) Human Research Protection Program (HRPP) Handbook! Here at the Harry S. Truman Memorial Veterans' Hospital (HSTMVH; also known as Truman VA), we strive to be on the forefront for the advancement of protections for human participants in research. The HSTMVH is committed to conducting all research activities with integrity and with adherence to scientifically sound practices and ethical principles. We have an excellent record of compliance with human research protection rules, regulations, and policies, and we are working to continually improve in this area. This Handbook has been prepared to aid you in your work as a researcher. It should be a reference that will help fulfill your obligations regarding human participant protections. This Handbook is a testament of R&D's strong commitment to develop a community of researchers that are exceptional with regard to implementing human research protections. Please know that the R&D staff is here to assist you when needed. Thank you for your commitment to research and to the protection of human participants.

Karen L. Smarr, Ph.D.
Research Compliance Officer
Harry S. Truman Memorial Veterans' Hospital

What is HRPP?

The continual pursuit of knowledge that can help not only VA patients, but also other healthcare consumers is highly valued and supported throughout the VA system, and at the HSTMVH. One of the most important qualities of a researcher is the “intention to do careful, ethical work” (Parker & Katz, 1998*). Protecting the welfare of our patients who accept or decline to participate in research must be the primary concern of every research protocol involving human participants. All health science professions have ethical principles and guidelines that guide the behavior of those practicing in that profession. There are also principles (like those in the Belmont Report) and regulations (such as the Common Rule) that guide the ethical behavior of those conducting human participants research. Three basic principles of respect for persons, beneficence, and justice, discussed in the Belmont Report, relate to the ethics of research involving human subjects and these will be the ethical principles that must be adhered to by all VA investigators.

At the national level, the Veterans Health Administration (VHA) is committed to being at the forefront of strategies for the protection of human participants in research programs. One of the responsibilities of the R&D Committee is ensuring the welfare of all human subjects. Therefore, the HSTMVH Director has designated a Research Compliance Officer (RCO), who oversees all aspects of the VA human research portfolio. The RCO oversight includes ensuring proper credentialing, educational verification, and training for human researchers, in addition to investigator compliance with all regulatory guidelines. There also is a major emphasis on close interaction with the Institutional

Review Board (IRB) of record, either the University of Missouri-Columbia's Health Sciences-Institutional Review Board (HS-IRB) or the VA Central Institutional Review Board (CIRB), and the Research and Development (R&D) Committee. The R&D Committee serves as the oversight committee for all research conducted at the HSTMVH. The Research Office has developed policies regarding the conduct of human research in support of the HRPP which are available on the Research Office's web page.

*Parker, J.C., & Katz, R.T. (1998). Strategies for an academic career. In J.K. Silver (Ed.), The Business of Medicine (pp. 279-291). Philadelphia: Hanley & Belfus.

Who are some of the staff responsible for the HRPP?

Sallie Houser-Hanfelder, FACHE, HSTMVH Director

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Ms. Houser-Hanfelder is the Institutional Official for the HRPP. She is ultimately responsible for the overall conduct of the Research and Development Program, including the welfare of human participants. She is responsible for ensuring that adequate resources and facilities are provided for the HRPP. Ms. Houser-Hanfelder is advised and assisted by the R&D Committee, the Research Compliance Officer, and the Associate Chief of Staff for Research & Development (ACOS/R&D).

John D. Whited, MD, MHS, Associate Chief of Staff/R&D (ACOS/R&D)

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Dr. Whited is responsible for the daily operations of the Research Program providing administrative support, and implementing the decisions of the R&D Committee and the HS-IRB. He provides assistance to investigators on scientific and administrative matters including research involving human participants. Dr. Whited serves as the HSTMVH Research Integrity Officer and the Conflict of Interest Administrator. He also is responsible for ensuring that decisions of the R&D Committee are communicated to investigators, that proper records are maintained, and implementation of the HSTMVH Outreach Program. He communicates with investigators new directives pertinent to the investigator's program of research. Dr. Whited is the facility liaison to the CIRB (an IRB of record).

Lawrence Propp, Administrative Officer/R&D (AO/R&D)

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Mr. Propp supervises the day-to-day operations of the Research Office. He is responsible for the deployment of resources, as required, to maintain compliance with HRPP activities. He advises the ACOS/R&D, the R&D Committee, the HS-IRB, CIRB, and investigators concerning relevant regulations, and their interpretation, for conducting VA human studies research at HSTMVH.

Karen L. Smarr, Ph.D., Research Compliance Officer (RCO)

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Dr. Smarr is responsible for the development and review of HRPP policies and procedures. She monitors compliance with IRB of record policies, investigator compliance, and is the Hospital's liaison to the HS-IRB. She also develops and implements the quality assurance/improvement program for HRPP, which includes the required annual auditing of research studies (per VHA Handbook 1058.01) and ensuring that training requirements are met by all research administrative staff, investigators, and research team members. The RCO is a consultant to all HRPP committees, monitors research compliance for the Hospital Director, and educates and advises investigators of relevant VA regulations pertaining to the conduct of human research.

Nancy Dietz, Ph.D., R.Ph., Research Pharmacist

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Dr. Dietz is responsible for ensuring that all relevant Pharmacy staff are trained in the procedures for the dispensing and storage of investigational drugs and devices, and that all related recordkeeping practices are followed and consistent with hospital policies. She works closely with the MU Investigational Pharmacist, as applicable. The HSTMVH Pharmacy will dispense all investigational drugs and devices (unless delegation authority has been granted) to research subjects seen at HSTMVH.

T. Renee Nichols, Research Secretary

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Ms. Nichols initiates the process for new research applications. She coordinates the process of research staff appointments and two-year reappointments. She also oversees staff compliance with training requirements, and assisting with primary source verification (e.g., verifying the education and certification).

Karen Iadanza, Program Assistant
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Ms. Iadanza serves as the Research and Development (R&D) Committee, SRS, and SAS Recording Secretary. Ms. Iadanza handles all R&D, SRS, and SAS communications. She monitors the status of research projects within the Research Office, works closely with the ACOS/R&D regard notifying investigators of their R&D project status, and will facilitate R&D review of amendments and unanticipated problems. She will request annual project updates for review by the R&D committee, SRS, and SAS. She will facilitate the review of all IRB of record amendments by SRS and other applicable R&D subcommittees, as well as the R&D committee for all substantial amendments.

What committees or other partner are involved in the HRPP?

There are several committees that must approve all research conducted at the HSTMVH. The R&D committee is the oversight committee for all research conducted at the HSTMVH and must approve all research before initiated. There are several subcommittees that must approve proposed research prior to R&D approval. The subcommittees consist of the HS-IRB or CIRB (IRBs of record which focus on human subjects protections), the Subcommittee for Research Safety (SRS; which focuses in personnel safety), the Subcommittee for Animal Safety (SAS; which focuses on animal safety), Radiation Safety Committee (RSC: which focuses on studies involving any type of radiation), and MU Institutional Biosafety Committee (IBC; which focuses on genetic research).

Other parties that must approve your research before initiating include the Information Security Officer (ISO) and the Privacy Officer (PO). The ISO and PO serve as ex-officio members of the R&D Committee. These two individuals ensure information/data security, confidentiality, and privacy matters meet all VA standards. All sensitive VA Data must stay within the VA, unless a waiver has been obtained from the Hospital Director OR there MUST be a valid, signed HIPAA authorization explicitly indicating what sensitive data can be removed from the HSTMVH and where data will be stored outside the VA. With the participant's release (the later above scenario), the data will no longer be considered VA sensitive data and the VA will not be responsible for its protection

What are the responsibilities of the Principal Investigator in relation to the HRPP?

The Principal Investigator (PI) maintains the ultimate responsibility for ALL aspects of the research, including the protocol and ensuring the protection of all human participants involved in VA-approved research (that is research approved by the R&D committee). The PI is expected to abide by the highest ethical standards. The responsibilities of the investigator and the required protocol content are listed in VHA

Handbook 1200.05 found at:

http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2326.

Some of the PI's responsibilities in relation to protecting human participants include:

1. Developing and executing research that incorporates the principles of the Belmont Report.
2. Conducting research in accordance with an R&D Committee approved protocol.
3. Overseeing all aspects of the research, including supervision of the research team members, residents, and other staff involved in conducting human research, and implementation of the research study in accordance with the approved protocol. Ensuring adequate resources and qualified staff are available to execute the research safely.
4. Completing functional statements for all research staff delineating their authorization and responsibilities on the research study.
5. Ensuring that the informed consent process approved by the IRB of record is followed and properly documented, per VHA Handbook 1200.05. Ensuring that written consent is obtained prior to initiation of any study procedures, unless a waiver has been granted by the IRB of record. Ensuring that study team members who consent subjects have been designated by the PI to consent eligible subjects into the research study and that the IRB of record has approved such delegation. Ensuring that the correct version of the informed consent is used in all cases (initial consent and re-consenting). Ensuring the consent process minimizes the possibility of coercion or undue influence and that eligible subjects are allowed adequate time to consider whether or not to participate. The informed consent process must denote to subjects which potential risks are related to the research versus those associated solely with usual care provided by the subject's health care provider. Ensuring that all required element of consent are obtained (i.e., subject or legally authorized representative's signature and date, signature and date of person obtaining consent, and signature and date of witness [if required by IRB of record]), as well as the HIPAA authorization being signed and dated (if applicable). The original signed/dated consents and HIPAA authorization (when applicable) must be maintained in a secure location (and approved by the PO and ISO).
6. Establishing and maintaining open lines of communication with research participants throughout their research participation.
7. Complying with institutional policies and administrative requirements, including complying with all requirements of the IRB of record (e.g., submitting documentation for amendments, continuing reviews, all unanticipated internal (i.e., local) serious adverse events [SAEs], whether related or unrelated to the research, deviations from the protocol, subject complaints, and unanticipated problems involving risks to subjects or others) for conducting research. Promptly reporting to the IRB of record any changes in

the protocol, consent, staff changes, and PI or local site investigator. The only exception is when it is necessary to change the protocol to eliminate apparent immediate hazards to the subject. The investigator must promptly report these changes to the IRB of record.

8. Ensuring the protections of sensitive VA data and the confidentiality of research participants. (see Appendix A)

9. Acknowledging contributions of the VA when presenting results of studies in publications, presentations, media interviews, and other public activities as outlined in VHA Handbook 1200.9.

10. Distributing the VA publication entitled "Volunteering in Research: Here are some things you need to know" to all prospective subjects as part of HSTMVH's Outreach Program.

11. Ensuring that all research activities have been approved by IRB of record AND that written notification from the Associate Chief for Staff for Research and Development (ACOS/R&D) in the VA Research Office has been obtained before initiating the conduct of research

12. Ensuring that all research staff complete required human research trainings.

13. Ensuring that the VA Pharmacy has received copies of all IRB-approved documents, including updated consents, amendments, protocol updates, Continuing Research Report (CRR), and the Investigator Brochure.

14. Obtaining the required administrative (Director waiver) or participant approval (HIPAA authorization) for the transport or removal of all sensitive VA data outside the protected environment of the HSTMVH.

15. Disclosing conflicts of interest to the IRB of record and VA Research Office any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research.

16. Maintaining records that can be inspected by the IRB of record, RCO, and other applicable entities upon request. The specific requirements regarding investigator research records depend upon the research. See the specifics in VHA Handbook 1200.05 (see link above).

17. Maintaining a master list of all subjects for whom informed consent has been obtained whether or not IRB granted a waiver of documentation of informed consent. Waiver from maintaining of the master list can only be granted by the IRB of record. The master list will be all persons after being consented (using an IRB-approved informed consent process [documentation or waiver of documentation of consent]) to be

in the study, regardless of their status in the study (e.g., withdrawn, ineligible, screen failure, completed, etc). The investigator must secure the master list appropriately in compliance with all VA confidentiality and information security requirements in the investigator's file for each study.

18. Ensuring that language in the protocol, consent document, IRB application and HIPAA authorization (when applicable) are consistent.

19. Collection and use of social security numbers (SSN) should be minimized. The collection and use of real SSNs must be approved by the IRB of record, and the investigators must follow all applicable VA and other Federal requirements for obtaining and using real SSNs.

20. Ensuring that initial phone contact to prospective subjects was preceded with a letter and that research team members do not request SSNs during any phone conversation. Later phone contacts must refer to previous phone contacts and, when applicable, the information provided in the informed consent form, and ensuring that the scope of telephone contacts with the subject is limited to topics outlined in IRB-approved protocols and informed consent forms. Scripts of phone contacts must be submitted and approved by the IRB of record.

21. Ensuring submission of the required paperwork to close a study at IRB of record and by the R&D committee. Ensuring investigator records are transferred to the VA Research Office for long-term retention and storage by the VA at closure and departure of the PI, per VA and Federal records retention requirements and as stated in a Memorandum of Understanding between the HSTMVH and University of Missouri Office of Research. Ensuring that VHA Handbook 1200.05 is followed when an investigator leaves the VA and requests to transfer records to another VA facility. Specifically approvals must be obtained from the first VA facility's research office, any other relevant individuals or offices according to VA and local requirements (e.g., compliance, privacy, or Information Security Officers [ISOs]) and the sponsor. Understanding that the investigator does not own the data and research records must be retained by the VA where the research was conducted.

22. If appropriate, communicating the results to subjects or the community from which subjects were recruited.

23. Ensuring that all laboratory results that are used for diagnosis, treatment, and prevention of disease in patients are properly accredited and meet all requirements of 42 CFR 493 (see VHA Handbook 1106.01).

24. Ensuring that the research protocol is scientifically sound, complies with all applicable local, VA, and other Federal requirements, involves a recruitment plan that is just, fair, and equitable in the selection of subjects, minimizes risks to the subjects or others, and includes a data and safety monitoring plan (DSMP) (the minimum

requirements for DSMP for prospective and retrospective studies can be found in VHA Handbook 1200.05).

25. Ensuring that the research protocol is: (a) scientifically sound, minimizes risks and provides for special safeguards; (b) compliant with all applicable local, VA, and other Federal requirements; (c) clear regarding differentiating the research intervention(s) from “usual care” (whether the “usual care” is limited to one “arm” of the study or is being delivered to all study subjects); (d) designed to contain a data safety monitoring plan that is based on the potential risks, complexity, and nature of the study; (e) clear regarding enlisting the indicated services of a clinician with appropriate expertise and privileges; (f) complaint with the provision of dedicated privacy, confidentiality and data/information security sections (separate or combined) which are part of the IRB protocol file; and (g) complaint regarding the reuse of data and describes the research data repository in which the data is to be stored (as applicable).

26. Ensuring that the VA Pharmacy has received the original VA Form 10-9012(s) (if applicable), specifying all authorized prescribers, in addition to allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements,

27. Ensuring that the VA Pharmacy has received signed/dated informed consent form for each participating subject prior to dispensing of study medication, copies of sponsor-related correspondence specific to the drug(s) (if applicable), and copies of all correspondence addressed to the investigator from the FDA (and other involved authorities) specific to the investigational drug(s) (if applicable).

28. Informing the IRB of record and when applicable, the VA Chief of the Pharmacy Service or research pharmacist, in writing when a study involving investigational drugs has been suspended, terminated, or closed.

29. Following all VA pharmacy requirements regarding receiving, dispensing, storing, and record-keeping for investigational drugs, as well as making relevant records accessible to the investigational drug pharmacist (when requested).

How Can HRPP Questions, Suggestions, or Concerns be Addressed?

Any person listed as a staff member responsible for the HRPP is available to answer questions, accept suggestions, or consider concerns voiced by investigators, their team members, or current or prospective research participants. In addition, the IRB of record administrator's (either Ms. Michele Kennett, at HS-IRB, 573-882-3181 or Ms. Annette Anderson at CIRB, 202-443-5649) are available as a point of contact for members of any human research team. Questions, suggestions, or expressions of concern/violation of any type are welcomed and encouraged by the HSTMVH Research staff and one of the IRBs of record.

R&D Application

What are the steps in the application process?

Completion of the entire packet is required for review of research projects by the Research and Development (R&D) Committee. Complete applications must be received at a minimum of four (4) weeks prior to the R&D Committee meeting (see schedule on HSTMVH Research website at: <http://www.va.gov/columbia-mo>). Final R&D approval will not be given until approval by all required subcommittees of the R&D Committee have been obtained. The R&D subcommittees include the IRB of record, MU Institutional Biosafety Committee (IBC), Subcommittee on Animal Studies (SAS), Subcommittee on Research Safety (SRS), and Radiation Safety Committee (RSC). The Privacy Officer (PO) and Information Security Officer (ISO) must approve your data security plan, HIPAA authorization, and any transport or storage of sensitive VA data off-site. Routing to the required subcommittees (except Radiation Safety and MU IRB of record) will be handled internally by the Program Assistant in the Research Office. The research may not begin until the R&D committee and all appropriate subcommittees have approved the project.

Application Parts

- Part I: Research and Development Committee
- Part II: Subcommittee on Research Safety (SRS)
- Part III: Human Studies Subcommittee/ (HS-IRB or CIRB Forms)
- Part IV: Subcommittee on Animal Studies (SAS)
- Part V: Abstract and Full Proposal, Data Security Plan
- Part VI: Conflict of Interest (COI) Statement(s)

Steps

1. Complete Part I (R&D Committee) through Part VI (Conflict of Interest Statement) for all projects.
2. All project staff who will access VA patients/data or will access VA space for Research activities are considered "on-site" personnel and will be required to hold VA appointments (Paid or Without Compensation [WOC]). Detailed information on the procedure can be obtained at the HSTMVH Research website <http://www.va.gov/columbia-mo>. Prior to submitting the R&D application, all VA "on site" staff appointments must be initiated and completed before initiating the research activities. All staff without access to VA patients/data or VA space will be considered "off-site" personnel. All "on-site" and "off-site" personnel must be listed on the R&D application and IRB of record and the listing of personnel must be consistent.
3. All "on-site" project staff on human research protocols must complete Human Research training modules as stated on the HSTMVH Research Service website. Provide the training certificates to the Research Secretary during to the submission of the completed R&D application. NOTE: IRB of record and R&D approval will not be granted until required training has been completed.

4. If projects involve either ionizing or non-ionizing radiation, a separate application must be made to the Radiation Safety Committee (RSC). Contact Rich Poelling at (573) 814-6000 extension 52590 regarding the requirements and application to RSC.

5. Obtain a **concurrence signature from the Director(s) of participating VA Service Line(s)** (i.e. Primary Care, Specialty Care, Behavioral Health, Nursing Service, Pharmacy, Clinical Support, Information Management, Facilities Management, or Business Office) whose approval will be required for the project to be reviewed by R&D Committee.

6. Complete the R&D Application checklist to ensure all required materials are submitted to the Research Office. Incomplete application packets will be returned to the investigator.

7. Submit the original, and one copy of the application packet (which will include a hardcopy of the IRB of record Application, the IRB of record approval letter, and CV's for the PI and Co-PIs), as well as a CD of the entire application packet, to the VA Research Secretary, Room B012, HSTMVH (Phone: 573-814-6550). Applications with pending IRB of record approval can be submitted to the Research Office and will be considered complete for submission purposes only (not for R&D review purposes). The application will not be sent to R&D reviewers until approved by the IRB of record and other applicable subcommittees, which must occur at least two weeks prior to a R&D meeting.

Why must I also apply to one of the IRBs of record, either HS-IRB or CIRB?

The IRBs of record (a subcommittee of the R&D Committee) reviews all VA protocols involving human subject participants prior to review by the R&D Committee. The R&D Committee continually monitors ongoing research through periodic reviews, including the review of adverse events, audit finding, unanticipated problems and substantive amendments to the protocol. The IRBs of record are charged with the responsibility of protecting the rights and welfare of all HSTMVH research participants in VA-approved research as required by the Common Rule and the Federal-Wide Assurances (FWAs). Prior to initiation of the research, the R&D Committee must approve all research involving the VA, including projects deemed exempt by one of the IRBs of record.

What if my project appears to be Exempt?

All research involving human participants must be submitted to an IRB of record. Decisions regarding Exempt status can only be made by the IRB of record, not by the investigator. The IRB or record Chair or an IRB member designated by the chair must make the exemption determination. Submit projects deemed exempt by the IRB of record to the Research Office for R&D review following the steps outlined above.

How do I apply to the HS-IRB?

Part III of the VA Application to Conduct Research includes submitting the HS-IRB application, HS-IRB approval letter, and application signature page. The process of

applying for HS-IRB approval is electronic and completed on the e-IRB website (located at <https://irb.missouri.edu/eirb/gen4/User/Login/>). All submissions to the HS-IRB are electronic and are paperless..

Attach one copy of the HS-IRB application and related materials to Part III of the "Application to Conduct Research."

What are some tips for using the e-IRB Website?

Log-in

In order to use the system, an account must first be created by selecting the appropriate link on the log-in page. To log onto the e-IRB system, enter your username and password. If you are MU faculty, staff, or a student, your username is your MU Paw Print, and your password is your Paw Print password (this is the username and password used for your MU email account). If you are external to the University system, enter the username and password you supplied when your e-IRB account was created. Once you log in, you will see the "Main Menu."

HS-IRB Forms

To begin a new application, select "IRB Forms" from the Main Menu. Five types of applications are displayed at the top of the "Health Sciences IRB Forms" page. Select the appropriate link for the application you wish to submit (Application, Exempt, Records Review [applies to all retrospective chart reviews], Facilitated Review of NCI CIRB Research or HS Humanitarian Use Device). All questions regarding which application to complete should be directed to the HS-IRB at (573) 882-3181.

Document Storage

The HS-IRB application process is completely electronic. All supporting documentation (such as consent forms, debriefing statements, surveys, scripts) is electronically attached to the application as computer files. You can also attach files to the application such as those created in word processing programs, documents that are scanned, etc. in the "Submit/Print" portion of the application, there is a link to "Document Storage." Selecting this option will enable you to upload the appropriate supporting documentation. You can also access this feature by clicking on "Document Storage" from the "Main Menu." From this link you can upload and view supporting documentation.

Saving your work

The e-IRB system automatically saves each section of the application when you select the "Save and Continue" button at the bottom of each section. You can also begin an application and return at a later time to finish your work.

Submission

When you have completed all required information (including required training), submit the application. From the "Print/Submit" page, a copy of your application can be printed

before you officially submit it to the HS-IRB. You will not be able to submit the application if any required information is missing. Missing information will be listed in red on the "Print/Submit" page. You will not be able to submit if all staff members are not up-to-date on their required HS-IRB training.

Log-out

Remember to log out of the system. After two hours of inactivity, the system will automatically log you out.

Technical Support/Help with Application

When you are logged into the e-IRB system, each page has links at the bottom that will link to information to contact the HS-IRB and Technical Support. You will be able to send questions, feedback, and technical problems by completing the forms that are available through those links. The HS-IRB contact information is also available on the e-IRB website. Please note that the E-IRB website works best with version 5 or greater of Internet Explorer for PC and version 7 or greater of Netscape for Mac.

Dates for Submission

HS-IRB meeting dates and application deadlines for each meeting are available on the HS-IRB website (located at <http://research.missouri.edu/hsirb/dates.htm>).

How do I apply to the CIRB?

Go to <http://www.research.va.gov/vacentralirb/default.cfm> and look under Important Links for specifics, including directions regarding how to apply to initially to CIRB at: <http://www.research.va.gov/vacentralirb/policies.cfm>. The CIRB requires local conflict of interest forms to be submitted as part of the initial CIRB application.

Attach one copy of the CIRB application and related materials to Part III of the "Application to Conduct Research."

What is a Conflict of Interest (COI)?

A Conflict of Interest is defined as any financial arrangement, personal obligation, situation, or action of the investigator that exerts, or is perceived to exert, inappropriate influence on the design, review, conduct, results, or reporting of research activities or findings. It will be the responsibility of the IRB of record to ensure that steps to manage, reduce, or eliminate potential, actual, or perceived conflicts of interest related to all aspects of the research (financial, role [investigator-patient relationships], and other professional, institutional, or personal roles) have been taken.

Conflicts of interest may arise although not limited to, the following:

1. Intellectual property involved in research and partnerships between industry and academia.

2. Financial incentives by pharmaceutical or biotech companies for investigators conducting clinical trials or enrolling participants into a clinical trial.
3. A particular role or relationship (i.e., board membership or executive relationship) an investigator has within the administrative structure(s) of the institutions(s) with whom they are affiliated.
4. Equity interest (i.e., stocks, stock options, or other ownership interests) an investigator, co-investigator or family member holds in a company with interest in the research.

How do I disclose a COI?

Investigators must submit COI documentation with their R&D application. This includes completion of the "Conflict of Interest Statement (VA Form 1313-9)" for each investigator (including PIs, Co-PIs, and other investigators/collaborators) with 5% or more effort on the protocol; and completion of Part VI of the R&D application ("Conflict of Interest"), which lists the proposed study's investigators, their role, and the percentage of effort on the protocol.

The ACOS/R&D is the designated COI Administrator. The ACOS/R&D reviews all COI disclosure statements and determines if there will be a negative impact on the research. Findings from these reviews are sent to the HS-IRB to determine how to handle any identified COI.

The IRB of record will review COI issues in the review of the protocol. The IRB of record considers any issues that raise the possibility of coercion or undue influence on the informed consent process. Necessary actions to minimize risks to subjects will be assessed. The IRB of record will initiate remedies to manage or eliminate COI through modifications in the protocol, change in consent to reflect the COI, and/or monitoring of the research by an independent reviewer. If a COI is not remedied through this process, a non-biased third party may be authorized to obtain informed consent from participants. The R&D committee will review the handling of COI's by the IRB of record as part of their oversight responsibilities.

The HSTMVH Director is informed of any inability to resolve a significant COI, and any investigator that fails to comply with the COI policy/remedies. The Director may impose remedies and/or restrictions including, but not limited to:

1. Termination of the research study.
2. Removal of the investigator from the research project.
3. Revocation of the privilege to conduct research.

4. Sanctions, which may include prohibition from submitting proposals to the IRB and/or R&D Committee.

The investigator is responsible for disclosing any type of COI. If a COI develops after IRB of record approval, it must be reported immediately. COI involving the investigator's spouse or dependent children that reasonably appears to affect the research must also be reported.

It is the investigator's ethical obligation to consider the potential effect that a financial relationship of any kind have on their study, including interactions with research participants.

Some examples of financial conflicts of interest:

1. Salary or payments for services (such as consulting fees or honoraria).
2. Compensation to the investigator(s) that is affected by the outcome of the study.
3. Stocks, stock options, or other ownership interests.
4. Patents, copyrights, or other intellectual property rights and any royalties from such rights.

For further information, see Conflict of Interest in Research Policy (HPM 589A4-339) located at <http://www.va.gov/columbia-mo/forms/conflict6.doc> .

Staff Appointments

Who must acquire a VA staff appointment?

For the HSTMVH to ensure that each member of the research team has the credentials, competencies, and qualifications to perform their assigned duties, all project staff who will access VA patients, and/or data, or who will access VA space for research activities must hold a VA appointment (Paid or Without Compensation [WOC]). In order to be compliant with VA Directive 0710, Special Agency Checks (SACs) must be completed before any new employee can begin working at the HSTMVH. Applicants must have their electronic fingerprints completed a minimum of seven (7) days prior to their appointment date. There will be NO exceptions to these requirements.

What are the procedures to receive a VA appointment?

1. Notify the Research Secretary **at least two weeks in advance** of the processing date and anticipated date to begin working.
2. The Principal Investigator (PI) should complete the Request for Staff Appointment and the Request for Functional Statement of Research Duties and Responsibilities for **all** research staff members (i.e. co-investigators and research staff). These forms are available at <http://www.va.gov/columbia-mo/forms/index.shtml>. Functional Statements must be updated every two years or when duties change.

Note. All research staff that hold a degree that may make them eligible for licensure, registration, or certification related to health care will have additional credentialing requirements. The VA Credentialing Office will communicate these credentialing requirements to staff with RN, MD, DO, and/or PhD degrees, and all others as applicable. These individuals must also complete a Functional Statement of Research Duties and Responsibilities.

3. Due to the confidential nature of the application materials, submit the following documents in person (by the applicant), to the Research Office: (a) Application for Federal Employment (OF612), (b) Declaration for Federal Employment (OF306), (c) Benefits Letter from HSTMVH, and (d) Minimum Necessary Standards. **THESE FORMS MUST BE COMPLETED IN BLACK INK ONLY** and are available at <http://www.va.gov/columbia-mo/forms/rfstatement.doc>.

Upon receiving a VA ID Badge, the applicant will be required to enter personal information into a secure web program (eQIP) on a VA computer. Instructions will be provided by the Research Secretary on completing these steps.

4. All new Research staff members who are not a U.S. citizen, are required to submit a copy of their Visa.
5. Complete all required training activities and deliver certificates to Research Secretary.

6. **ALL** required training must be completed, and eQIP signature pages submitted to the Research Secretary, before an access card for Research space will be issued.

What trainings will need to be completed?

The following training requirement instructions are available at <http://www.va.gov/columbia-mo/staffapps/training.shtml>. User IDs and passwords need to be stored in a secure environment since the web-based trainings below must be renewed as indicated below. .

1. **General Research Orientation:** This orientation is required for all new research staff members that will access VA Research Laboratories.

2. **Human Research Training:** Completion of the "Human Research Curriculum" web-based module is required for staff involved in human research protocols before they may participate in human subjects research. This training is located at <https://www.citiprogram.org/default.asp> and must be renewed every two years, specifically within 730 days after the previous training,.

Instructions to use <https://www.citiprogram.org/default.asp> are as follow. Copy the website and paste into your web browser. Register as a new user before beginning. **DO NOT SELECT A PARTICIPATING INSTITUTION.** Click on the drop down box for Veterans Affairs and select "Columbia, MO-543". Of Special note: Affiliate with the University of Missouri-Columbia as well as "Columbia, MO-543" if the HS-IRB is the IRB of record. Select a User Name and Password following the instructions on the page. Click Submit. Answer the questions on the next page. Click Submit. On the next page, select the applicable answer to Question #1 and #2, Question #3 will be "NO", skip Question #4, and select the third response to Question #5. Answer "yes" or "no" on the next page. The following page is your "Learner's Menu", under "My Courses" will be your training requirements, click "Enter" under the "Status" column to enter the Human Research training. All required modules must be completed beginning with "History & Ethical Principles". Once you have completed the training, print the Completion Report and provide to the Research Secretary.

3. **Radiation Safety Training:** This training is required for all staff whose duties will involve access to Research laboratory space. Appointments may be scheduled with the Radiation Safety Officer (RSO) at (573) 814-6000 Ext. 52590 or via email at Richard.Poelling@va.gov. The RSO will provide the required training manual to the staff member; once the training is complete, the RSO will provide a certificate to the PI and the Research Secretary.

4. **VHA Privacy Policy Web Training.** This training is required for ALL research staff and must be renewed annually (this is a facility requirement). If you are a VA-paid employee, this training must be accessed on the LMS Training website; if you are a

WOC, Resident, Medical Student, etc., the training may be accessed at <https://www.ees-learning.net/librix/loginhtml.asp?v=librix>. Provide the certificate to the Research Secretary.

5. VA Information Security 201 for Research and Development Personnel. This training is required for ALL research staff must be annually. If you are a VA-paid employee, this training must be accessed on the LMS Training website (ID #64879); if you are a WOC, Resident, Medical Student, etc., can be accessed at <https://www.ees-learning.net/librix/loginhtml.asp?v=librix>.

The instructions to use the above site follow. Check on "Available Courses"; type "Information Security" into Keyword and select "Information Technology" from the drop-down box under Content Area; click Search. Once the search is complete, select "Sign Me Up" next to the training. Note: Each slide will take 5 seconds to download. Allow time for each slide to download completely, or you will not receive full course credit. Again once completed, please provide the training certificate to the Research Secretary to fulfill this requirement.

6. Laboratory Safety Training: This training is required for all staff involved in laboratory-related activities and will be provided and documented (via checklist) by the responsible PI.

What do the IRBs of record require for members of my research staff?

The HS-IRB and CIRB requires that PIs and their research staff complete training. Per VHA Handbook 1200.05, all individuals involved in conducting VA human research are required to successfully complete training in ethical principles on which human research is to be conducted and accepted good clinical practices (GCP). The CITI Human Research Training is acceptable training to meet the GCP requirement for the IRBs of record.

HS-IRB applications will not be reviewed if PI(s) and staff have not completed the CITI training. Amendments, unanticipated problems, and continuing review reports also cannot be submitted to HS-IRB until all staff meet the training requirement.

The link to the directions for completing the CITI training that meets the HSTMVH and HS-IRB GCP requirements is located at: <http://research.missouri.edu/hsirb/training.htm>.

What trainings will need to be completed after initial appointments?

- CITI GCP "Human Research Curriculum" (biennially)
- VA Information Security 201 for Research and Development Personnel (annually)
- VHA Privacy Training (annually)

Informed Consent

How do I document informed consent?

The PI develops written informed consent documentation for participants to sign which must be approved by the IRB of record prior to enrolling patients in a study. The VA Research Consent Form template (available on the HS-IRB website at <http://irb.missouri.edu>) must be used to tailor written informed consent documentation or a script for waiver of consent documentation. The VA CIRB informed consent form guidelines and template can be accessed at <http://www.research.va.gov/vacentralirb/default.cfm>

When informed consent is obtained, it is best practice to have the participant sign and date three (2-3) copies, as applicable. Alternatively, multiple copies may be made of the original signature document. An original **MUST** always be placed in the participant's research file maintained by the PI. When the research requires the use of any clinical resources (radiology, cardiology [e.g., electrocardiogram, stress test, etc.], clinical laboratory, and/or pharmacy); or the research intervention may lead to physical or psychological adverse events (AE), a copy of the signed and dated informed consent form must be scanned into the participant's electronic medical record (see the CPRS Section of this Handbook for more information). Another copy is for the participant who must receive a signed and dated copy of the consent document for their reference. The only copy of the consent that should contain the SSN is the one hand-delivered to VA Medical Records for scanning purposes.

NOTE: PIs should minimize use of real Social Security numbers as much as possible. Only use real Social Security numbers when required to meet the specific aims of the research protocol or to enter information into the subjects' health records.

Remember to add the name of each individual who signs an informed consent document to the master list required to be maintained by the PI (see PI responsibilities).

Documentation of the informed consent process is very important! Document all aspects of the informed consent process in the PI research records and/or medical record. This includes initial contact/discussions with potential research participants and allowing the prospective participant to review consents with family and friends. There are required signatures on all VA written informed consents. These signatures are to be obtained on the same day and dated at the time of the informed consent process. If required by the IRB, the VA consent document must have a witness to the signature. The witness attests that the subject or subjects legally authorized representative signed the consent. The person obtaining the consent of the subject needs to sign as the authorized representative or person obtaining consent. The authorized representative or person obtaining consent must be either the PI or research staff who has the

delegated authority by PI and IRB to consent prospective subjects. Informed consent documents and the investigator's research records are required to be retained according to all applicable VA and Federal records retention requirements (and, if applicable, the Memorandum of Understanding between the HSTMVH and/or University of Missouri Office of Research) following the closure of the study by the IRB of record and the R&D Committee. The VA Research Office will maintain the long-term storage of all research participant records and PI files related to the study for the maximum length of time (e.g., per Food and Drug Administration regulations, VA Records Retention Schedule 10-1) indicated for all VA-approved studies.

How do I document that a participant understands their rights in relation to the Health Insurance Portability and Accountability Act (HIPAA)?

Research participants must sign a "HIPAA Authorization." The VA HIPAA Authorization template is available on the HS-IRB website at <http://irb.missouri.edu>. PI's should add study specific information to this template. The CIRB HIPAA form will be developed based the national PIs local IRB form and any specific state law that apply.

As with the informed consent document, it is best practice to also have the participant sign and date two (2) - three (3) copies of the HIPAA Form. Alternatively, multiple copies of an original signature document may be made. An original should be placed in the participant's research file maintained by the PI; if applicable, one signed and dated copy of the HIPAA authorization should be scanned into participant's electronic medical record (see the CPRS Section of this Handbook for more information); and one (signed and dated copy) provided to the participant.

When do I disclose conflict of interest?

Conflict of interest disclosure must be made to the IRB of record and the R&D Committee during the application process. If the application receives approval, any identified conflict of interest must be disclosed to the participant during the consent process (prior to obtaining written consent) or managed in a manner designated by the IRB of record.

What are the restrictions regarding social security number collection?

The collection of Social Security Numbers (SSN) should be avoided to minimize harm to participants. The IRB of record will require justification for collection of SSN for research purposes and will carefully weigh the risk/benefit ratio on this matter. Therefore, when obtaining written consent, the full SSN will need to be written only on the informed consent document only that will be scanned into the medical record. To protect participant's identifying health information, the written

informed consent and HIPAA form is to be hand delivered to HSTMVH Medical Records for scanning into the Computerized Patient Record System (CPRS).

Computerized Patient Records System (CPRS)

How do I gain access to CPRS for me and my staff?

The PI will indicate on an appointee's "Request for Functional Statement of Research Duties and Responsibilities" that he/she requires access to VISTA/CPRS. Following submission of these materials the PI should also send an email to the Research Secretary with a list of the staff who will require access to CPRS. The Research Secretary will then provide instructions for completion of additional CPRS-specific training requirements. These include web-based trainings in addition to a CPRS training session at the HSTMVH.

Once an individual has been authorized to use CPRS, they can access CPRS from the physicians' workstations in Release of Information/Medical Records (if computers are not available for them to use at other stations or clinic areas).

What is the documentation that will be required and how is it entered into CPRS?

There are CPRS notes that are required for VA-approved studies that involve the use of any clinical resources (radiology, cardiology [e.g., electrocardiogram, stress test, etc.], clinical laboratory, and/or pharmacy); or the research intervention may lead to physical or psychological adverse events (AE). These include at a minimum the research flagging note, consent note, and completion note.

1. Research Flagging Note: The IRB of record will specify whether or not the research record should be flagged (Level I). For HS-IRB, a Level I flagging note is required for all prospective studies, unless designated otherwise by the HS-IRB. A chart is flagged with a Level I flag (available under postings on cover page in CPRS) in the VA research participant's electronic medical record using the following note title: "CO-RESEARCH PARTICIPANT NOTE". Level I flagging notes always include names of research team members and their 24/7 contact information, as well as to describe the nature of the research. As applicable, in investigational drug trials the VA form 10-9012 will be included in the Level I flagging note for all medications (including placebo) used in the study.

Many significant risk studies also are required to have a Level II flag. The Level II flag is a pop-up alert that is a specific clinical warning that occurs before allowing access to the medical record. In the case of the Level II pop-up, the alert directs providers to the "CO-RESEARCH PARTICIPANT NOTE" (Level I) for the specific medication/dietary restrictions; the "CO-RESEARCH PARTICIPANT NOTE" specifies any contraindicated agents, information on possible drug interactions and/or toxicity of the pharmaceutical agents drugs that are listed in VA Form 10-9012(s). Level I and II flags alert providers and other medical personnel of the patient's participation in a study, although Level II flags are more visible to clinical staff. A Level II flag is particularly important for significant risk studies that can

involve contraindicated medications or other type of restrictions as part of study participation.

To complete the “CO-RESEARCH PARTICIPANT NOTE (Level I flag)” follow these steps:

1. Log onto CPRS.
2. Choose patient.
3. Select the “Notes” tab and then select the “New Note” button.
4. In the “Location of Current Activities” box, there is a place to type labeled “Encounter Location.” In that text box, type CO-A/S RESEARCH CLINIC. Then click “OK”.
5. In the “Progress Note Properties” box, type CO-RESEARCH PARTICIPANT. Then click “OK”. NOTE: This note is a non-encounter note (or non-bill event) which ensures the participant will not be billed for the research-related visit.
6. A list of studies will appear on the screen. Check the study title twice and then indicate "okay". The text will automatically populate the note. Review the content and edit as indicated.
7. For all studies involving an investigational drug or device, add the Research Pharmacist as a co-signer to alert her/him of enrollment of each subject into the study.
8. Level II flags are required all significant risk studies involving medications or dietary restrictions. By adding an additional Level II pop-up flag further sensitizes medical personnel of the cautions required for that research participant (while in the study, although also very important to ensure the pop-up is turned off at study completion-see below). Therefore to turn on a Level II clinical alert, include the RCO as a note co-signer so the RCO can initiate the Level II alert.
9. When the note is complete, sign it.

NOTE: To avoid multiple flags, for each participant the “CO-RESEARCH PARTICIPANT NOTE” must be completed only once! After the note is signed (and co-signed if required), you can view the Level I flag (on the cover page) by selecting the “Postings” button on the upper right hand side of the patient’s cover sheet in CPRS. The notes title will be listed in the “Crisis Notes, Warning Notes, Directives” box. Just select the title/flag to view the full note.

2. Research Consent note. The content of this note is required for all studies to explicitly document the informed process (which is a requirement and this will be audited by the RCO). VHA Handbook 1200.05 indicates that each study must update the medical record via creating a progress note, for all research subjects who are admitted to HSTMVH as an inpatient, treated as outpatients at HSTMVH, or when research procedures or interventions are used in the medical care of the VA research subject at HSTMVH or at facilities contracted by HSTMVH to provide services to Veterans (e.g., contract CBOCs or contract nursing homes). The note title of "Co-Research Consent" note should be used to

fulfill the documentation of study enrollment requirements, per VHA Handbook 1200.05.

At a minimum the enrollment/consent note must: (a) specify the name of the study; (b) state the name of the person obtaining the subject's consent; (c) state that the subject or their legally-authorized representative (LAR) was capable of understanding the consent process; (d) state that the study was explained to the potential research participant or their LAR; (e) state that the subject or their LAR was given the opportunity to ask questions; and (f) state that the subject or their LAR consented PRIOR to participation in the study. There is a generic Research Consent note available for use or you can choose to create a note that is tailored for the specific needs of your study (just ensure minimum requirements noted above are met). Contact Mark Kruse at 573-814-6504 to develop your own research consent note.

NOTE: If you decide to not use the Research Consent note to document consent and instead use a clinical progress note, it is the PIs responsibility to be sure that the subject is not billed for research only visits and research-related procedures (in other words not filling out a billing encounter for the visit-marking as a "historical" visit can accomplish this); the note must delineate between what is clinical and what is research, Remember, that the minimum requirements for the note that MUST be included are stated in the above paragraph.

4. Research Note or Research Follow-up Note(s): A blank "CO-Research Note" or "CO-Research Follow-up" note are available as progress notes to document research-related clinical interventions over the course of the study and each research-related participant contact; this note is a non-encounter (non-billing) note. These notes should be tailored to the study and can include, as applicable, a copy of any research results that are used for medical care and information on all research and experimental interventions including potential risks, indications, and references to applicable progress notes. Notes in the medical record should be written at each research visit when the research requires or involves any of the following: (a) use of any clinical resources or service(s) that will be used in the medical care of the subject, (e.g., ordering laboratory test results; x-ray; electrocardiogram; stress test; administration of a medication or treatment; use of an investigational device; or any other clinical intervention(s) that could interfere with or effect the other care the subject is receiving or may receive; (b) research intervention(s) that may lead to physical or psychological adverse event (AE); (c) any invasive research procedure (e.g., muscle biopsy or bronchoscopy); or (d) the use of a survey or questionnaire that may provoke undue stress or anxiety unless the IRB of record has determined that research flagging is not in the best interests of the subject (e.g., an interview study of victims of sexual assault or HIV study).

3. Research Completion note. A note entitled "CO-Research Completion" is available to document study completion, termination, or withdrawal. You are

required to document withdrawal, termination by participant or PI, or completion of the study. As stated above, study completion (including withdrawal and lost to follow-up) can be documented as an addendum to either the above notes or using a blank CO-Research Completion note or CO-Research Follow-up Note created for study documentation of this nature.

For all studies utilizing a Levels I and II flagging notes, the completion note or addendum to either a clinical or research note indicating withdrawal, termination, or completion MUST add the RCO as a co-signer to ensure the removal of the flagging of the medical record.

How do I get consents and HIPAA forms scanned into CPRS?

Signed consent forms are to be taken to Medical Records/Release of Information (E002) for scanning into CPRS. The consent and HIPAA forms must include the patient's name and full social security number on each page.

Once the forms are scanned, they can be viewed in CPRS using the following steps. When you are in the patient's record, select "Tools" in the menu at the top of the CPRS window, then select "VISTA Imaging Display." You may be asked to log on with your CPRS/VISTA access and verify codes. Scroll down the "Image Listing" box to find the document you wish to view. Click on it to view.

What about CPRS Encounters?

Research participants are NOT to be charged for their participation in research. Completing CPRS encounters prior to signing a note indicates the participant or their insurance will be billed. You should never complete encounters for research visits. Therefore, it is important to use a "non-billing" or "non-encounter" clinic for research visits. Always select CO-A/S Research Clinic as the location since it is a no count clinic and will never generate a bill. Be sure that CO-A/S Research Clinic appears on the top of the CPRS screen. If not, click on the encounter location and indicate under the "new visit" tab CO-A/S Research Clinic and specify date and time of visit. Checking the "Historical Visit" button when using a clinical, billable, encounter visit will also serve to generate no encounter and no bill for the visit.

What are other CPRS Research documentation options?

For other research documentation that should be included in the electronic record, you may simply choose a generic, blank progress note from the following research note titles: "CO-Research Note," "CO-Research Follow-up Note," or "CO-Research Completion Note." If you would like to develop a template to ease the study documentation burden, contact Mark Kruse, at 573-814-6504 for assistance.

Pharmacy

What information is maintained in the pharmacy regarding my research study?

The Pharmacy maintains an up-to-date protocol file for each study, which includes:

1. A copy of the HS-IRB-approved study specific Consent Form (VA Form 10-1086, VA Research Consent Form) that has been signed and dated by all the appropriate parties. All versions of the IRB-approved stamp dated informed consent document must be on file in the pharmacy, so the pharmacist can verify current version of consent was used prior to dispensing study medication(s).
2. The original of the Investigational Drug Information Record (VA Form 10-9012) for each drug (including placebo) used in the study. Each 10-9012 will be signed by the IRB or record Chair or IRB of record Member and R&D Chair signifying the approval by both committees.
3. A copy of the approved research protocol, all protocol updates, and any HS-IRB approved amendments.
4. A copy of the Investigator Brochure for the study, including all updates.
5. All investigational devices dispensed and stored by Pharmacy Service, unless a delegation of authority has been delineated.
6. A valid and updated Investigational Drug/ Device Dispensing Log for the protocol.

What information must be obtained for my study's Investigational Drug/Device Dispensing Log?

The following information is included in an *Investigational Drug Dispensing Log*:

Participant's name
Social Security number
Name of drug
Dosage form
Strength
Source of the drug (manufacturer, sponsor)
HS-IRB number and approval/review dates
Inventory notes
Amount and date of drug received
Expiration date of prescription
Lot/control number
Date of authority to use

Serial number and date of prescription dispensed
Pharmacist's verification signature
Inventory balance
Name of prescriber
Initials of dispensing pharmacist

The following information is included in an *Investigational Device Log*:

Name and identification number of the patient
Device name
Serial number
Model number
Manufacturer
Name of issuer
Inventory balances
Other relevant details specific to the appropriate use and dispensing of the device

What do I need to provide the Pharmacy after approval by R&D?

The following lists responsibilities of an investigator to ensure continued compliance:

1. Provide copies of all amendments and updates to the investigator's brochure, protocol, and informed consent document to the VA Pharmacy.
2. Ensure VA Form 10-9012 remains up-to-date (i.e., all contraindicated medications, side effects, and prescribers included). This form should be updated as personnel privileged to prescribe are removed or added to the project. Submit the original, modified 10-9012's to the VA Research Office to secure HS-IRB and R&D signatures. The original will be maintained by the Pharmacy.
3. All medication used at VA are to be dispensed by the VA Pharmacy. In the event MU Pharmacy will maintain primary dispensing responsibilities for the study, ensure that a Letter of Understanding (LOU) is on file with the MU Pharmacy and VA Pharmacy describing the handling of all medicines. All medications that will be used at the VA must be dispensed by the VA Pharmacy. The LOU will need to specify that drugs dispensed by MU Pharmacy will then be routed through the VA Pharmacy.

What do I need to provide to R&D Office after approval by the R&D Committee?

1. An electronic copy of all changes to the VA Form 10-9012 to update "Co-Research Participant" template note.

2. Any project amendments that will change the project description in the "Co-Research Participant" note will need to be provided in an electronic format to the Research Secretary and RCO.

3. Updated, signed original VA Form 10-9012 to obtain HS-IRB and R&D Committee chair signatures. Once signed the original VA Form 10-9012 will be maintained by the VA Pharmacy and the CPRS "CO-Research Participant" note modified accordingly.

What do I do when I close my study that involves an Investigative New Drug Application (IND) or Investigational Device Exemption (IDE)?

Notify the IRB of record by submitting a Completion/Withdrawal Form. At the HS-IRB submit the form at <http://irb.missouri.edu>. The R&D Committee will need to review and approve the closure of the study, following closure at the IRB or record.

The PI must also notify the Research Office and Pharmacy Service of his/her intent to close an IND or IDE study. Do this by sending an e-mail communication to the Research Office, the Chief, Pharmacy Section, and Research Pharmacist, Nancy Dietz, Ph.D., RPh., PhD of your intent to close and IND or IDE study. The Research Office will place the IND or IDE study closure on the next R&D committee agenda.

Continuing Review

What is continuing review?

The process of continuing review helps R&D and the IRB or record ensure that VA and/or MU policies and procedures are being followed for each research study, and that each study is conducted according to the protocol approved by the IRB or record.

What if I need to make a change in a component of the study?

To make changes to a study, follow HS-IRB policies and procedures regarding completing amendments, charging personnel, or closing a study. For additional information about changes in studies approved by HS-IRB see http://www.research.missouri.edu/policies/files/hsirb_SOP_Binder2.pdf. Contact the HS-IRB (882-3181) if you have any questions regarding which form to complete. See <http://www.research.va.gov/vacentralirb/forms/default.cfm> for information about changes to CIRB-approved studies.

What problems and events do I have to promptly report to the IRB of record?

Investigators must comply with the requirements of the IRB of record for the problems that require prompt reporting to the IRB of record. At HS-IRB see http://www.research.missouri.edu/policies/files/hsirb_SOP_Binder2.pdf for a list of problems that require reporting and the time frame for reporting. Reporting requirements are available for CIRB studies at <http://www.research.va.gov/vacentralirb/forms/default.cfm> .

The HSTMVH defers to the IRB or record policies and procedures for the review of these problems and the handling of problems determined by the IRB or record to be unanticipated problems involving risks to participants or others. As the oversight body, the R&D Committee will review all actions by the IRB of record and may request additional modifications, to ensure protection of research participants.

How is my study continually monitored by the R&D Committee and the IRB or record?

Both the R&D Committee and the IRBs of record require documentation to be completed for the continuing review process.

The ACOS/R&D reviews all studies annually (during the same month of the initial approval) on behalf of R&D Committee to verify staff compliance with training, any changes in COI, and study progress. When it is time for this annual review by the ACOS, the PI is sent a brief protocol survey that should be completed and returned to the Research Office. The RCO will also perform annual informed

consent audits and full study regulatory audits at least every three years. The results of the audits will be reviewed by the IRB of record and the R&D committee.

The IRBs or record reviews all studies at least every 12 months, but could require review more often. For additional information about continuing review procedures see

http://www.research.missouri.edu/policies/files/hsirb_SOP_Binder2.pdf

Failure to submit your Continuing Review Report (CRR) to the HS-IRB in a timely fashion will result in expiration of the study. A new HS-IRB application may have to be submitted and the study would have to start over. Be aware that R&D review is a separate procedure from the HS-IRB review and may have different deadlines. For additional information about continuing review procedures at CIRB see <http://www.research.va.gov/vacentralirb/forms/investigator-forms.cfm>.

What if there is a failure to follow the protocol or approved procedures for a study?

Failure to follow IRB or record-approved protocol procedures must be reported to the IRB of record in accordance with IRB of record policies and procedures. For additional information see

http://www.research.missouri.edu/policies/files/hsirb_SOP_Binder2.pdf and to

CIRB see <http://www.research.va.gov/vacentralirb/forms/investigator-forms.cfm>.

The R&D Committee will review the actions of the IRB of record on the matter at its next convened meeting.

Additionally, audit results that are considered serious or continuing non-compliance by the RCO will be reported promptly to the Hospital Director, Chief of Staff, ACOS/R&D, IRB of record Chair, R&D Chair, and all appropriate oversight bodies.

What is required when I complete a study?

When all data analysis, publications and patient interaction are completed, follow IRB or record policies and procedures for closing a study. For additional information about the HS-IRB see http://www.research.missouri.edu/policies/files/hsirb_SOP_Binder2.pdf and for CIRB see <http://www.research.va.gov/vacentralirb/forms/investigator-forms.cfm>. After closure of the study at the IRB of record, the project will be closed by R&D. PI's should alert the Research Office of a study closure.

What if an investigator does not comply or there is an allegation of non-compliance with IRB of record and VA policies or approved research protocol?

All complaints, or allegations of non-compliance are handled according to IRB of record policies and procedures. For additional information at HS-IRB see

http://www.research.missouri.edu/policies/files/hsirb_SOP_Binder2.pdf and at CIRB see <http://www.research.va.gov/vacentralirb/forms/investigator-forms.cfm> . The R&D Committee will review the IRB of record's handling of all complaints or allegations of noncompliance at its next convened meeting.

Possible consequences of noncompliance include:

- Termination of protocol(s)
- Restrictions on privileges to conduct research
- Potential disciplinary action

Data Security and Privacy

What constitutes VA Sensitive Information?

Sensitive VA information is all data, on any storage media/form/format that requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration, or destruction of the information. Sensitive information includes all information covered by various confidentiality provisions such as the Privacy Act of 1974 and the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. All protected health information (PHI) is considered sensitive VA data.

Sensitive VA research information consists of information that has been collected for, used in, or derived from the conduct of VA research that fits the definition of VA sensitive information. Personally-identifiable Information (PII) consists of any information, including health information, pertaining to a person that identifies the individual and, is retrieved by the individual's name or other unique identifier. De-identified health information is health information that does not use any of the 18 HIPAA identifiers and there is no reasonable basis to believe that the information can be used to identify an individual.

What are the Dos and Don'ts of Privacy?

E-mails	<ul style="list-style-type: none"> • Do use VistA within Veterans' Health Administration (VHA) to send and receive PHI and PII. • Do use only initial of last name and last 4 of SSN on subject line, in VistA e-mail. • Do remind patients that e-mail systems are not secure if patients contact you by e-mail. Request that patients call for information. • Don't send PHI or PII through Outlook unless it is de-identified or encrypted. • Don't send VistA or Outlook messages containing PHI AND PII or PII outside of VHA. • Don't display passwords and verify codes used for computer access.
Messages	<ul style="list-style-type: none"> • Do leave a message for the patient to call you back for healthcare information. • Do verify that the telephone number is correct. • Do repeat the call back telephone number • Don't leave PHI on answering machines or voice mail systems.
Faxes	<ul style="list-style-type: none"> • Do fax PHI only when necessary to provide information in a reasonable time. • Do verify fax numbers are correct. • Do make certain that faxes containing PHI or PII are not sent to public areas. • Do include confidentiality statement on cover sheet in event of error, or use the HSTVA Hospital fax cover sheet template available in the Office Word program. • Do remove faxes that include PHI or PII from public area fax machines. • Do call and confirm fax, if in doubt • Don't fax PHI unless you are sure someone is there to receive it.

Mail Directive	<ul style="list-style-type: none"> • Do place mail for internal delivery within the hospital and Community Based Outpatient Clinics in a Special Attention Envelope and seal it. • Do check name of addressee prior to opening mail. • Don't open mail unless it is addressed to you or are authorized to open.
Work Space	<ul style="list-style-type: none"> • Do turn all documents face down when leaving your work space for brief periods. • Do place all documents in a secure area at the end of shift. • Don't leave PHI or PII in public view.
Oral Communications	<ul style="list-style-type: none"> • Do use curtains, cubicles, offices, or other private area when possible to safeguard discussions. • Do speak in a low voice when discussing patient health information in public areas. • Do respect the privacy of our patients. • Don't use speaker phones with office doors open when discussing patient health information.
Telephone Calls	<ul style="list-style-type: none"> • Do take reasonable precautions to minimize the inappropriate disclosure of patient information.
Disposal	<ul style="list-style-type: none"> • Do place all paper documents containing PHI or PII in locked shred containers or shred documents daily. • Don't toss prescription bottles, IV bags, or other items containing PHI AND PII in regular trash, unless it has been de-identified.
Reporting	<ul style="list-style-type: none"> • Do report privacy violations or concerns immediately. • Do contact Ann Richmond, Privacy Officer, if you have questions or concerns at 573-814-6589.

What do I need to think about with HIPAA identifiers and de-identifying my research data?

Below is a list of 18 HIPAA identifiers that may not be used in a de-identified dataset. If you intend to remove any of these identifiers from the HSTMVH as part of your research, you must receive permission by obtaining a waiver from the Hospital Director (and other facility officials).

The 18 HIPAA identifiers are as follows:

1. Name
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except

that such ages and elements may be aggregated into a single category of age 90 or older;

4. Phone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social Security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)

What is a waiver to transport sensitive research data outside the HSTMVH?

The HSTMVH requires written permission by the Hospital Director, Information Security Officer, Chief of Staff, and Chief of Information and Technology to waive requirements to maintain all sensitive VA data within the facility. The waiver requires a detailed description of all sensitive data that will reside outside the protected environment of the VA facility. All off-site electronic storage systems will be inspected and approved by the ISO and/or RCO prior to approval of the waiver by the Hospital Director. To begin the process to obtain the waiver, complete the memorandum entitled "Authorization to Transport and Utilize VA Sensitive Information Outside Protected Environments" and submit to the Research Secretary. Include a full justification for specific PHI to be removed as well as the location of the PHI (i.e., room number, sponsor) outside the HSTMVH.

Any transport of sensitive VA data, (i.e., including SSN and other PHI) needs to be either hand-delivered to the intended recipient, mailed using "Special Attention" envelopes (used only within the HSTMVH), via courier, or traceable carrier.

What is my responsibility and role regarding Data Security and Privacy?

It is everyone's responsibility to handle sensitive VA data with care and be sure to protect it at all times using the approaches outlined above. Handle the PHI and data of your research participants as if it were your own. Always store hard copy data under double lock (locked cabinet in locked room) and electronic files must be password protected and stored on the HSTMVH Local Area Network

server (LAN) which is backed up nightly. It is the PI's responsibility to ensure that his/her staff following all procedures outlined in their data security plan and approval to remove PHI (if applicable). Every VA employee that identifies a privacy or information security violation is to report the violation within 1 hour to the Privacy Officer at 573-814-6589 or the Information Security Officer 573-814-6319.

What needs to be included in a data security plan?

Per VHA Handbook 1200.05, the investigator must either dedicate specific sections of the protocol to privacy and confidentiality, or must develop an additional document that specifically addresses all privacy and confidentiality issues in the protocol. This section must be in sufficient detail to appreciate how the PI protects the subject's privacy and the confidentiality of the data, in compliance with all applicable VA and other Federal requirements. Additionally, the PI may combine the privacy and confidentiality section with a section dedicated to information security, or must develop an additional document that specifically addresses all information security issues in the protocol. The plan must clearly identify and include, but not be limited to:

- (1) Whether or not individually identifiable information is to be collected or used;
- (2) How the data is to be collected or acquired;
- (3) Where the data (original and all copies) is to be stored and corresponding security systems;
- (4) How the data is to be transported or transmitted from one location to another;
- (5) Who is to have access to the data and how they are to access it (anyone who has access to the data is responsible for its security);
- (6) All entities or individuals outside VHA to whom the data is to be disclosed, and the justification for such disclosure and the authority (e.g., the HIPAA authorization);
- (7) Who is to have access and be responsible for the security of the information (e.g., the Coordinating Center, the statistician, and PI who has ultimate responsibility);
- (8) Mechanisms used to account for the information;
- (9) Security measures that must be in place to protect individually identifiable information if collected or used; and
- (10) How and to whom a suspected or confirmed loss of VA information is to be reported.

Also, see the Appendix A for specific details related to a data security plan and questions that the IRB of record will ensure are addressed in the study file.

Accreditation

What is the Association for the Accreditation of Human Research Protections Programs, Inc. (AAHRPP) and how is it related to the HSTMVH's HRPP?

AAHRPP is a not-for-profit organization, and its mission is to protect the rights and welfare of research participants. The U.S. Department of Veterans Affairs (VA) has awarded a contract to AAHRPP to operate an accreditation program to ensure that VA Medical Centers are in compliance with VA and other relevant federal regulations designed to protect human research participants. The HSTMVH's and MU HS-IRB's HRPP have received full AAHRPP accreditation.

References and Resources for More Information

Human Subjects Research Policies

Assurance of Compliance and Quality Improvement for Human Research Protection Program (HPM 589A4-340)

Conflict of Interest in Research (HPM 589A4-339)

Credentialing and Privileging of Research Staff (HPM 589A4-342)

Human Research Protection Program (HPM 589A4-321)

Institutional Conflict of Interest in Research (HPM 589A4-365)

Investigational Devices (HPM 589A4-338)

Outreach Program for Human Research Participants (HPM 589A4-366)

Required Education and Training for Research Activities (HPM 589A4-337)

Research Informed Consent (HPM 589A4-341)

Research Misconduct (HMP 589A4-362)

Review of Research Proposals (HPM589A4-042)

Review of Research Proposals for Compliance With Privacy and Information Security Requirements (HPM 589A4-391)

Sponsored Research (HPM 589A4-364)

University of Missouri-Columbia HS-IRB Policies

http://research.missouri.edu/policies/pol_dept.htm#cirb

VA Central IRB Policies

<http://www.research.va.gov/vacentralirb/sop/default.cfm>

VHA Handbooks Relevant to Research Activities

Research Misconduct (1058.2)

http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=1259

Research Compliance Reporting Requirements (VHA Handbook 1058.1)
http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2247

Requirements for the Protection of Human Subjects in Research (VHA Handbook 1200.05) http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2326

Presentation of Research Results Handbook (1200.19)
http://www.va.gov/portlandrd/pdf/publications/va_research_handbook.pdf#search='vha%20handbook%201200.19'

Inclusion of Women and Minorities in Research Handbook (1200.9)
http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=359

Other Websites

HS-IRB Website

VA Central IRB Website

Belmont Report

Declaration of Helsinki