Human Research Protections Program Investigator Handbook

Harry S. Truman Memorial Veterans' Hospital (Truman VA)
Research and Development
Columbia, MO
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http://www.columbiamo.va.gov/services/Research.asp

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Overview of the HRPP

Letter from the Research Compliance Officer (RCO)

Welcome to the Research Service's Human Research Protection Program (HRPP) Handbook! Here at the Harry S. Truman Memorial Veterans' Hospital (Truman VA), we strive to be on the forefront for the advancement of protections for human participants in research. The Truman VA 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 or research team member. It should be a reference that will help fulfill your obligations regarding human participant protections. This Handbook is a testament of Research's (and Office of the Director's) strong commitment to develop a community of researchers that are exceptional with regard to implementing human research protections. Please know that the Research Office staff is available 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 (RCO)
Office of the Director
Truman VA

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 Truman VA. 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 prospective and enrolled research participants must be the primary concern of every research investigator engaged in human research, as well as ensure the maintenance of the highest ethical standards to ensure privacy and confidentiality when handling sensitive personally identifying data. 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 Research and Development (R&D) Committee is ensuring the welfare of all human subjects. Therefore, the Truman VA Director has designated a Research Compliance Officer (RCO), who oversees compliance of all

aspects of the VA human research portfolio. The Associate Chief of Staff for R&D (ACOS/R&D) is responsible for the daily implementation of the HRPP. The RCO's oversight includes verifying that the Research Office has ensured proper credentialing, educational verification, training for human researchers, and investigator compliance with all local research policies, handbooks, and regulatory requirements. 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 (C-IRB), and the Research and Development (R&D) Committee. The R&D Committee serves as the oversight committee for all research conducted at the Truman VA. The Research Office, led by the ACOS/R&D, has developed local policies regarding the conduct of human research in support of the HRPP which are available from the Research Office (on request) or on the Truman VA intranet website 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?

Wade Vlosich, Truman VA Director
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Mr. Vlosich is the Institutional Official for the HRPP. He is ultimately responsible for the overall conduct of the Research and Development Program, including the welfare of human participants. He is responsible for ensuring that adequate resources and facilities are provided for the HRPP. Mr. Vlosich is advised and assisted by the R&D Committee, the RCO, and the Associate Chief of Staff for Research & Development (ACOS/R&D).

Adam Whaley-Connell, DO, Associate Chief of Staff/R&D (ACOS/R&D)
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Email: Adam.Whaley-Connell@va.gov

Dr. Whaley-Connell is responsible for the daily operations of the Research Service and related HRPP by providing leadership, administrative direction, and support related to all applicable local and national research policies, as well implementing the decisions of the R&D Committee and the IRB of record. Truman VA research policies are developed and updated by the ACOS/R&D to comply with federal regulations of topics such as human subject protections, research safety, and animal welfare. The ACOS/R&D provides direction and assistance to investigators on scientific and administrative matters including the conduct of research involving human participants. Dr. Whaley-Connell also serves as the Truman VA Research Integrity Officer and the Conflict of Interest Administrator. He is responsible for all aspects related to Truman VA's compliance with all federal regulations applicable to VHA research. He also is responsible for ensuring that decisions of the R&D Committee are communicated to investigators, and that proper records are maintained and stored per the Record Control

Schedule 10-1. He communicates with investigators new directives pertinent to the investigator's program of research.

Rob Crawford, Administrative Officer/R&D (AO/R&D)
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Email: Robert.Crawford5@va.gov

Mr. Crawford 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, C-IRB, and investigators concerning relevant VHA 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 ensuring compliance with the HRPP policies and procedures, as well as VHA regulations. She monitors compliance with IRB of record policies, investigator compliance, and works closely with 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 advices investigators of relevant VA regulations pertaining to the conduct of human research.

Danielle Field, Pharm.D. BCPS, Clinical Research Pharmacist
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The Clinical Research Pharmacist is responsible for the proper conduct of the research investigational drug program in accordance with Truman VA Policy 589A4-123, VHA Handbook 1108.04 and VHA Handbook 1200.05. She works closely with the MU Investigational Pharmacist, as applicable. The Truman VA Pharmacy will dispense all investigational drugs (unless delegation authority has been granted) to research subjects seen at Truman VA.

Bob Miller Research Secretary
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The Research Secretary initiates the process for new research applications. He coordinates the process of research staff appointments and two-year reappointments. He also oversees staff compliance with training and credentialing requirements,

maintains the training database, and assisting with primary source verification (e.g., verifying the education and certification).

Karen Johnston, AA, Program Assistant
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Ms. Johnston serves as the Research and Development (R&D) Committee, Subcommittee for Research Safety (SRS), and Subcommittee for Animal Studies (SAS) Coordinator/Recording Secretary. Ms. Johnston 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. Ms. Johnston is the facility liaison to the C-IRB (an IRB of record).

What committees or other partner(s) are involved in the HRPP?
There are several committees that must approve all research conducted at the Truman VA. The R&D Committee is the oversight committee for all research conducted at the Truman VA 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 C-IRB (IRBs of record which focus on human subjects protections), the Subcommittee for Research Safety (SRS; which focuses in personnel safety), the Subcommittee for Animal Studies (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 will approve your research during the review by the HS-IRB or C-IRB 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 VA sensitive information (VASI) must stay within the Truman VA, unless there is a valid signed HIPAA authorization and authorization has been obtained from the Hospital Director through the Data Security Plan and Request for an encrypted USB thumb drive. These requests are available through the Research Office and on-line with HPM 391. Through these requests, investigators must explicit indicate what sensitive data can be removed from the Truman VA and where data will be stored outside the Truman VA.

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 research

participants involved in VA-approved research (which means research that has been approved by the R&D Committee). The PI is expected to abide by the highest ethical standards. The Common Rule and VA-specific responsibilities of the investigator and the required protocol content are listed in VHA Handbook 1200.05 (dated November 12, 2014): http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=3052

Some of the expectations and Best Practices of Truman VA PIs 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 VA-approved protocol. Ensuring adequate resources and qualified staff are available to execute the research safely.

4. Submitting required functional statements to the Research Office for all research staff delineating their responsibilities as delegated by a designated PI.

5. Ensuring that research staff involved in human research are credentialed and privileged as required by Truman VA, PRIOR to involvement in the PI's research study.

6. Ensuring that the informed consent process approved by the IRB of record is followed and properly documented, per Section 16 of VHA Handbook 1200.05.

7. Ensuring that written consent is obtained prior to initiation of any study procedures, unless a waiver has been granted by the IRB of record.

8. Ensuring that study team members who consent subjects (without involvement of the PI) have been delegated that responsibility by the PI (e.g. by the use of a delegation letter or in the functional statement) to consent eligible subjects into the research study and that the IRB of record has approved such delegation.

9. Ensuring that the correct version of the informed consent is used in all cases (initial consent and re-consenting).

10. 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.

11. 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 (as approved by the PO and ISO).

12. Establishing and maintaining open lines of communication with research participants throughout their research participation, as part of the consent process.

13. Complying with institutional policies/procedures 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.

14. 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.

15. The PI must also submit all IRB Amendments to SRS for review and approval, although immediately following IRB approval the changes are to be implemented (e.g., using newly-approved version of consent), unless specified otherwise by the IRB.

16. Ensuring the protections of sensitive VA data and the privacy and confidentiality of research participants.

17. Ensuring that all research activities have been approved by IRB of record AND that written notification from the ACOS/R&D in the VA Research Office has been obtained before initiating the conduct of research.

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

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

20. Obtaining the required administrative (Director's approval) and participant approval (HIPAA authorization) for the removal, transport, and storage and of all VASI outside the protected environment of the Truman VA. This can be done by completing the "Data Security Plan for Principle Investigators" and the "Request for USB Thumb Drive" from the Research Office and on-line through HPM 391.

21. Disclosing financial 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.

21. 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. Refer to the IRBs policies and procedures and VHA Handbook 1200.05.

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

24. 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.

25. Ensuring that initial phone contact to prospective subjects was preceded with a letter and that there is no request for SSNs during any phone conversations. Scripts of phone contacts should be submitted and approved by the IRB of record.

26. Ensuring submission of the required paperwork to close a study at IRB of record and by the R&D Committee.

27. Ensuring investigator records are transferred to the VA Research Office for long-term retention and storage by the Truman 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 Truman VA and University of Missouri Office of Research. The PI must appreciate that the investigator does not own the data and research records must be retained be the Truman VA where the research was conducted.

28**.** When applicable and appropriate, communicating the results of the research to the participants.

29. 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 42CFR493 (see VHA Handbook 1106.01).

30. Ensuring that the research protocol is scientifically sound, complies with all applicable local, VA, and other Federal requirements, involves a recruitment plan that is fair and equitable in the selection of subjects; minimizes risks to the subjects and others; and describes a Data and Safety Monitoring Plan (DSMP) consistent with the nature of the study.

31. 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) provide details related to protection of subject’s privacy, confidentiality and data/information security are part of the IRB documentation; and (g) compliant regarding the reuse of data and describes the research data repository in which the data is to be stored (as applicable; see VHA Handbook 1200.12).

32. Ensuring that the Research Service and Pharmacy Service/Clinical Research Pharmacist have received all VA Form 10-9012(s) (if applicable). The VA Form 10-9012 informs authorized prescribers and other clinical personnel of the side effects, disallowed therapies, and any known antidote of the investigational agent as well as who the designated contact person is for un-blinding questions. VA Form 10-9012 is required on all investigational agents where a drug manufacturer’s package insert is not available. If a manufacturer’s package insert is available, it is not necessary to complete VA Form 10-9012 referring to the package insert for information. The investigator must place an electronic version of each VA Form 10-9012 in the subject’s medical record as part of the CO-Research Participant Note, when applicable.

33. The investigator must provide the Pharmacy Service/Clinical Research Pharmacist investigational drug information on each patient receiving an investigational drug through the electronic medical record. This documentation (as part of the 10-9012s) is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements (herbals, nutriceuticals).

34. Ensuring that the Pharmacy Service/Clinical Research Pharmacist 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, such as the sponsor) specific to the investigational drug(s) (if applicable).

35. Informing the IRB of record and when applicable, the Pharmacy Service/Clinical Research Pharmacist, in writing when a study involving investigational drugs has been suspended, terminated, or closed.

36. Provide the Pharmacy/Service/Clinical Research Pharmacist with any sponsor-provided documents relating to the storage, preparation, dispensing, and accountability of the investigational products.

37. Maintaining a list of all subjects for whom informed consent has been obtained whether or not IRB granted a waiver of documentation of informed consent. This list will include 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 will be responsible for securing the list appropriately to meet all VA confidentiality and information security requirements. This list could be maintained as part of an Excel spreadsheet used to collect retrospective data when a waiver of consent was granted by IRB or record.

38. Retaining a list of all heath records that were accessed during the study and a list of who accessed the records for inspection by the Health Information Manager (HIM) and others such as the Privacy Officer who are required to audit or review such information. This file must be maintained with the same level of security as all other sensitive information used for research purposes. (see VHA Handbook 1907.01)

39. Notifying the HIM administrator (in addition to the PO and/or Information Security Officer) when study has been completed or that accessing patient health records is no longer required or that the HIPAA authorization has been revoked. (see VHA Handbook 1907.01)

40. Submitting Incident Reports (from the Truman VA Intranet site) by the first person to first become aware of an issue that may be a close call, potential or actual medication error, or other issue that may be or is a patient safety issue.

41. Ensuring documentation for research is under a no count or non-billing clinic (using CO-ADMIN Research clinic) or is coded as a research credit code (and is differentiated from other clinic visits) to ensure that research subjects are not billed for their participation in research. (see VHA Handbook 1907.01)

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 C-IRB (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 Truman VA Research staff and one of the IRBs of record.

Request to Conduct Research - 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. The R&D Committee generally meets on the third Wednesday of each month. Complete applications must be received at a minimum of four (4) weeks prior to the R&D Committee meeting. Final R&D approval will not be given until approval by all required subcommittees of the R&D Committee have been obtained AND the issuance of a memorandum of approval by the ACOS/R&D. The R&D subcommittees include the IRB of record, MU Institutional Biosafety Committee (IBC), Subcommittee for Animal Studies (SAS), Subcommittee for Research Safety (SRS), and Radiation Safety Committee (RSC). The Privacy Officer (PO) and Information Security Officer (ISO) must review/approve your data security plan, HIPAA authorization, and any transport or storage of sensitive VA data off-site prior to initiation of the study. 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 ACOS/R&D has sent the PI a memorandum indicating approval of the project.

Application Parts

Part I: Research and Development Committee
Part II: Subcommittee for Research Safety (SRS)
Part III: Human Studies Subcommittee (HS-IRB or C-IRB Forms)
Part IV: Subcommittee for 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 (Financial 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]). 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 within the IRB of record materials; the R&D and IRB materials 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 Truman VA 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 the Radiation Safety Officer at (573) 814-6000 extension 52590 regarding the requirements and application to RSC.

5. The PI is responsible for obtaining 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 PI.

7. Submit the original (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 E002 (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 C-IRB?
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 Truman VA 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 of 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, the HS-IRB approval letter, and all related documents, including the HIPAA waiver, IRB-approved consent, recruitment documents, research protocol, and data security plan. The process of applying for HS-IRB approval is electronic and completed

on the e-compliance website (located at https://ecompliance.missouri.edu/login). All submissions to the HS-IRB are electronic and are paperless. Follow the directions on e-compliance and attach one copy of the HS-IRB application and related materials to Part III of the "Application to Conduct Research" and submit via paper to the Truman VA Research Office.

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

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

How do I disclose a Financial COI (FCOI)?
Investigators must submit COI documentation with their R&D application. This includes completion of the "Research Financial Conflict of Interest Statement (OGE Form 450 – Alternative VA)" for each investigator (including PIs, Co-PIs, an investigator including a Co-I or Sub-I along with study chairs); and completion of Part VI of the R&D application ("Conflict of Interest").

The ACOS/R&D is the designated COI Administrator for the Truman VA. The ACOS/R&D reviews all FCOI disclosure statements and determines if there will be a negative impact on the research. Findings from these reviews are sent to the Institutional Official to determine need for outside counsel and then 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 and the research 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.

As the Institutional Official, the Truman VA 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 FCOI. If a FCOI 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 refer to the “Research Financial Conflict of Interest Statement” (OGE Form 450 – Alternative VA) available in the Research Office and on the Truman VA Research webpage http://www.columbiamo.va.gov/services/Research.asp.

Staff Appointments

Who must acquire a VA staff appointment?

All research personnel who perform regular study-related activities at the Truman VA site must be a VA-paid employee OR must obtain WOC status. Individuals who are engaged in VA research who meet at least one of the following criteria must hold a VA VA appointment (Paid or Without Compensation [WOC]). Individuals that; work on research project(s) on-site in Truman VA sites (see definition below), whose research work directly involves recruitment of or interaction with veterans within the Truman VA, or has regular verbal or physical contact with human participants in the Truman VA. These individuals may include, but are not limited to principal investigators, sub-investigators, study coordinators, research assistants, data managers, lab personnel, pharmacy personnel, IRB staff, R&D Committee members, and Research Office staff. These individuals do not include secretarial level support staff. 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.

Note: Research staff or collaborators, whose study-related activities/interactions are entirely off-site, may not need to be VA-paid employees or WOCs. This is further defined as those off-site staff or collaborators who are not interacting with veterans and not accessing veteran protected health information:

- Do not need WOC status.
- Must be adequately trained and licensed, as attested to by the PI.
- Must comply with VA rules with regard to data use and privacy issues.

To determine whether a WOC is needed for an individual please discuss with the ACOS/R&D.

What are the procedures to receive a VA appointment?

1. Notify the Research Secretary **at least four weeks in advance** of the processing date and anticipated date to begin working. Appointments requiring credentialing typically take longer than one month and may take up to three months.

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 for use by contacting the Research Office and 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 the Truman VA Research office.

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?

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

2. **Human Research Training:**

Investigators and staff conducting human research are required to complete "Good Clinical Practices," VA privacy and Information Security," and "Privacy and HIPAA training" Completion of the "Good Clinical Practices" 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/** and must be renewed every three years, specifically within 1095 days after the previous training. "Privacy and HIPAA training" and "VA Privacy and Information Security" are also required annually located at https://www.tms.va.gov/learning/user/login.jsp. Instructions for both CITI and TMS training can be provided by the Research Secretary

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. VA Privacy and Information Security and Rules of Behavior. 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, or if you are a WOC, Resident, Medical Student, etc., the training may be accessed from any computer at www.tms.va.gov. Provide the certificate to the Research Secretary.

5. Privacy and HIPAA Focused Training. Any employee with access to protected health information (PHI) maintained by Veterans Health Administration for administrative and clinical purposes or access to PHI through VA Information technology (IT) systems, such as CPRS, VistAWeb, ASISTS or the Occupational Health Records System MUST also complete **"**Privacy and HIPAA Focused" training annually even if it is not automatically listed on their mandatory training list in TMS.

6. Hospital-wide Safety Training is also required for all VA staff (including WOCs) and is available in TMS.

6. Research Laboratory Specific Safety Training: This annual 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 C-IRB 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. The CITI Human Research Training is acceptable training to meet these 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 have fulfilled their training requirement (up-to-date).

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's e-compliance website at https://ecompliance.missouri.edu/login) must be used to tailor written informed consent documentation or a script for waiver of consent documentation. The VA C-IRB 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 Practices 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 and be easily retrievable. 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), it is best practices that a copy of the signed and dated informed consent form 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 sent to VA Document Scanning via VA sensitive information envelope for scanning purposes.

NOTE: Another Best Practice is that 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, otherwise avoid collecting SSNs.

Add the name of each individual who signed an informed consent document to the list of enrolled subjects maintained by the PI (see PI responsibilities), even if they failed the screening process. Maintaining this list ensures at any time the PI can respond to inquiries as to the exact number of subjects enrolled at a given point in time.

Best Practices: Documentation of the informed consent process is 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.

Typically, there will be 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.

Record Retention Requirements: 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 https://ecompliance.missouri.edu/login . PI's should add study specific information to this template. The C-IRB 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. The consent sent to document scanning will be shredded after being scanned into CPRS.

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 sent to Document Scanning using a secure envelope; best practices involving sending documents pertaining to one patient per envelope (thereby ensuring documents do not get mixed up and scanned incorrectly into the wrong patient's record). Full SSN is required on each page to be scanned into 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 Truman VA.

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 that do not have a commercially available package insert.

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 drugs that are listed on 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-ADMIN RESEARCH CLINIC (NC). 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, add the Clinical Research Pharmacist as a co-signer to alert her/him of enrollment of each subject into the study.
8. Level II flags are required on all significant risk studies involving medications or dietary restrictions. 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 Truman VA as an inpatient, treated as outpatients at the Truman VA, or when research procedures or interventions are used in the medical care of the VA research subject at the Truman VA or at facilities contracted by the Truman VA 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 and IRB #; (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 an OI&T CPRS team member 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 contents of the note that MUST be included are stated in the above paragraph.

4. CO-Research Note or CO-Research Follow-up Note or CO-Research Phone Note(s): A blank "CO-Research Note" or "CO-Research Follow-up" or CO-Research Phone" notes are available as progress notes to document research-related clinical interventions over the course of the study and each research-related participant contact. 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 Level 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. For all studies involving an investigational drug, the Clinical Research Pharmacist MUST also be added as a co-signer to alert her/him of subject termination or study completion.

How do I get consents and HIPAA forms scanned into CPRS?
Signed consents and HIPAA forms are to be sent to “Document Scanning, ProDental Building” via secure envelope 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-ADMIN Research (NC) Clinic as the location since it is a no count clinic and will never generate a bill OR use a regular clinic title that has a “credit code” of 474 for research (PIs must ensure the use of a properly coded clinic to credit research and to alert coders not to bill as a clinical visit). Be sure that CO-ADMIN Research (NC) Clinic or other Research Credit Code clinic appears on the top of the CPRS screen. If not, click on the encounter location and indicate under the "new visit" tab CO-ADMIN Research (NC) 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 Phone Note” or “CO-Research Completion Note.” If you would like to develop a template to ease the study documentation burden, contact the CPRS Support Team (Sarah Fehling (ext. 56712; pager 5767) or Cheryl Meisinger (ext 56537; pager 5765) for assistance.

Pharmacy

What information is maintained by the Clinical Research Pharmacist regarding my research study?
The Clinical Research Pharmacist maintains an up-to-date protocol file for each study, which includes the following information/documentation:

1. A Subject Informed Consent Verification Record where the Clinical Research Pharmacist documents that the IRB of Record approved consent form, dated and signed by both the subject and the individual conducting the consent process was received for each subject, prior to dispensing to the subject for the first time.

2. A copy of the Investigational Drug Information Record (VA Form 10-9012) for each drug (including placebo) used in the study where a drug manufacturer's package insert is not available. If a manufacturer's package insert is available, it is not necessary to complete VA Form 10-9012 referring to the package insert for information. Each 10-9012 will be signed by the IRB of 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 IRB of record approved protocol amendments; IRB of record and R&D Committee approval letters; any sponsor-provided documents relating to the storage, preparation, dispensing, and accountability of the investigational products; updates and changes to authorized prescribers, including updates to VA Form 10-9012, after the IRB of record's approval; documentation of the IRB of record's continuing review approval; and written notice of study suspension, termination/completion, or closure. .

4. A copy of the Investigator Brochure for the study, including all updates.

5. Investigational drug receipt and destruction/disposition records.

6. A valid and updated Investigational Drug Dispensing Log for the protocol.

What information is maintained for my study's Investigational Drug Dispensing Log?
The following information is included in an *Investigational Drug Dispensing Log*:

Name of subject or other subject identifier for individuals receiving the medication

Name of drug

Dosage form
Strength
Source of the drug (manufacturer, sponsor)
Name of PI
Protocol name or number

Amount and date of drug received
Expiration, retest, or repass date of drug
Lot/control number, or other ID number

Serial number and date of prescription dispensed
Quantity dispensed

Inventory balance
Name of prescriber
Initials of dispensing pharmacist

What information must be maintained for my study's Investigational Device Dispensing 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 Clinical Research <u>Pharmacist</u> after <u>initial</u> approval by R&D?

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

1. Provide copies of all IRB of record and SRS approved amendments and updates to the investigator's brochure, protocol, and informed consent document to the VA Pharmacy.

2. Ensure a signed/approved 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 IRB of record and R&D signatures.

3. All medications used at VA are to be dispensed by the Truman 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 and dispensing procedures for all study medications.

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 Program Assistant who will distribute to the Clinical Research Pharmacist and RCO.

3. Updated, signed original VA Form 10-9012 to obtain IRB of record and R&D Committee chair signatures. Once signed, the original VA Form 10-9012 will be maintained by the Research Office 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 https://ecompliance.missouri.edu/login . See the C-IRB website for directions as to how to close a study locally. The R&D Committee will need to review and approve the closure of the study, following closure at the IRB of 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 Clinical Research Pharmacist, of your intent to close an 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 of 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 of 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 the HS-IRB policies on the University of Missouri (MU) Office of Research website. 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 forms for C-IRB reviewed and 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 go to e-compliance for a list of problems that require reporting and the time frame for reporting. Reporting requirements are available for C-IRB studies at http://www.research.va.gov/vacentralirb/forms/default.cfm .

The Truman VA defers to the IRB of record policies and procedures for the review of these problems and the handling of problems determined by the IRB of 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 of 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, privileges, OHSP enrollment, any changes in COI, and study progress. When it is time for this annual review by the ACOS/R&D, the investigator 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 review by the IRB of record and the R&D Committee.

The IRB of record will review all studies at least every 12 months, but could require review more often. For additional information about continuing review procedures see the HS-IRB policies on the MU Office of Research website. 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 C-IRB 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 of record-approved protocol procedures must be reported to the IRB of record in accordance with IRB of record policies and procedures. For additional information, go to the following website the MU Office of Research website and for C-IRB information go to the following website 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 apparent 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 then the Hospital Director will then need to report to all appropriate oversight bodies within 5 days.

What is required when I complete a study?

When all data analysis, publications and patient interaction are completed, follow IRB of record policies and procedures for closing a study. For additional information about HS-IRB policies and procedures go to the MU Office of Research website and for C-IRB information go to the following website 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. Investigators should alert the Research Office of a study closure by the IRB of Record.

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 about the HS-IRB, go

to the MU Office of Research website, and for information regarding the C-IRB go the following website 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.

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 identified. De-identified health information is health information that does not use <u>any</u> of the 18 HIPAA identifiers <u>and</u> there is no reasonable basis to believe that the information can be used to identify an individual.

What are the Dos and Don't's of Privacy?

E-mails	• **Do** use VistA within Veterans' Heath 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	• **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	• **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	• **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	• **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	• **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	• **Do** take reasonable precautions to minimize the inappropriate disclosure of patient information.
Disposal	• **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	• **Do** report privacy violations or concerns immediately. • **Do** contact the 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 <u>any</u> of these identifiers from the Truman VA 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 Truman VA?

The Truman VA requires written permission by the Truman VA Director, Information Security Officer (ISO), ACOS/R&D, and Chief of Office of Information and Technology (OI&T) to waive requirements to maintain all VA sensitive information on site at the Truman VA or off-site. The authorization occurs through completion of the “Data Security Plan for Principle Investigators” which requires a detailed description of all sensitive data being collected and stored. In order to collect and store VASI off-site written permission will need to be obtained through a “Request for USB Thumb Drive.” Through both forms investigators are required to provide a detailed description of VASI that will reside outside the protected environment of the VA facility. These requests are available through the Research Office and on-line with HPM 391. 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 Truman VA Director.

Any transport of VASI will need to have protection of the thumb drive in mind and will need to be either hand-delivered to the intended recipient using protection, mailed using "Special Attention" envelopes (used only within the Truman VA), or via traceable carrier.

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

It is <u>everyone's</u> responsibility to handle VASI 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 Truman VA Local Area Network server (LAN) which is backed up nightly not on your desktop. It is the investigator’s

responsibility to ensure that his/her staff following all procedures outlined in their Data Security Plan and approval to transport PHI (if applicable) through the request for USB thumb drive. Every Truman VA employee that identifies a privacy or information security violation is to report the violation within 1 hour to the Privacy Officer (PO) at (573) 814-6589 or the Information Security Officer (ISO) (573) 814-6319.

What needs to be included in a data security plan?

If VASI will be collected in any form, the investigator must complete the "Data Security Plan for Principle Investigators" available through the Research Office or on-line at HPM 391. In your protocol, investigators must also dedicate specific sections of the protocol to privacy and confidentiality.. This section must be in sufficient detail to appreciate how the PI plans to protect 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 hard copy and electronic form 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.

References and Resources for More Information

Human Subjects Research Policies located on the Truman VA Intranet (ask Research office to provide current copies for your review)

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)

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)

Investigational Drugs (HPM 589A4-123)

VA Central IRB Policies

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