The William S. Middleton Memorial Veterans Hospital (Madison VA) has a Human Research Protection Program (HRPP) designed to ensure the rights and welfare of Veterans and other subjects who participate in VA research. The HRPP consists of a comprehensive system of rules, documents, processes, and personnel, including the hospital director; the affiliated Institutional Review Boards (IRBs); the VA Research Service and its Research and Development Committee (R&DC); the Privacy Officer (PO); Information Security Officer (ISO); Research Compliance Officer (RCO); and research study team members.

The Madison VA hospital director is the institutional official for the HRPP. The hospital director is ultimately responsible for the overall conduct of the HRPP.

The Madison VA human HRPP is affiliated with the University of Wisconsin-Madison (UW) Health Sciences IRBs. Some multi-site VA research may need to be reviewed by the VA Central IRB (CIRB) in lieu of a UW IRB (as determined by the CIRB).

The R&DC, in cooperation with the Research Service, reviews and monitors all Madison VA human subjects research, including clinical trials research, medical records reviews, and human tissue studies. The research service and the R&DC provide overall direction and oversight for the Madison VA HRPP. The R&DC is responsible for maintaining high standards for the conduct of research, for ensuring the scientific merit of research protocols, and for ensuring the welfare of all human research participants and research staff.
RESPONSIBILITIES OF VA INVESTIGATORS

VA Principal Investigators:
• Must have an active VA appointment
• Must take an active role in design & conduct of their study
• In short – the project must be their study

Investigators are:
• Responsible for ensuring the protection of human subjects participating in VA-approved research
• Expected to abide by the highest ethical standards
• Expected to conduct all research in accordance with IRB/R&DC approved protocols
• Responsible for overseeing all aspects of research, including supervision of research team members, residents and other staff involved in conducting the research
• Expected to ensure that the informed consent process approved by the IRB is followed
• Responsible for establishing and maintaining open lines of communication with research subjects throughout their participation in the research
• Expected to comply with VA regulations, and institutional policies and administrative requirements, including those of the IRB, for conducting research.
**WHAT MAKES A PROJECT “VA RESEARCH?”**

If a research involves one or more of the following, it may be considered VA research and therefore would require VA R&DC review and approval in addition to IRB review:

1. The project intentionally focuses on, recruits, or enrolls veterans.
2. The project involves the use of medical records, specimens, or tissue collected from veterans.
3. The protocol is funded by the VA.
4. The protocol uses VA facilities not specifically rented or otherwise covered by an agreement for the use of VA space or equipment by a non-VA entity. or
5. The project is being conducted by study personnel during their VA time.

**NOTE:** a UW study with a subject who is a veteran but who was not recruited due to his/her veteran status is not necessarily considered a VA research study. Contact the VA Research office if there is a question regarding VA status of research.

**WHAT CANNOT BE VA RESEARCH?**

Research on the following vulnerable populations cannot be conducted by Madison VA investigators while on official duty or at VA facilities:

- Pregnant women
- Fetuses and/or fetal tissue
- Children
- Prisoners

Also not allowed at the VA: Classified research; planned emergency research; international research; research involving In vitro fertilization.
COMBINING VA AND UW RESEARCH

Studies cannot be opened as combined VA and the UW protocols. If a study team intends to do research at both facilities, they will need to create separate protocols within the IRB’s ARROW system. Only the study designated as VA-only will be reviewed by the VA R&DC. The protocol opened at the UW (including any other non-VA sites) will not be considered a VA study.

WHAT IF NON-VETERANS ARE ENROLLED IN A VA STUDY?

If a research project is considered a VA study, but needs to enroll non-veterans:

1. The study team will need to document justification for enrolling non-veterans in the study.
2. All subjects would be treated as veterans while participating in the study
3. If the study requires flagging of medical records, electronic files will be required to be created for the non-veterans in the VA electronic system (in survey or non-interventional research studies VA medical record may not be required)
4. All research regulations pertaining to veterans would apply to the non-veterans when participating in VA research
5. Only VA consent forms will be used for all subjects
EXEMPT RESEARCH AT THE VA

- Exempt from further IRB review does NOT mean exempt from R&DC review
- All protocols determined to be research but exempted by the IRB which involve VA staff or facilities still require review by R&DC regardless of reason for exemption
- Exemption category 4 (Research involving the collection/study of existing data or documents) cannot be used at VA due to requirements related to the retention of research data
- Research determined to be exempt by the IRB may still require R&DC annual review

PAYMENT OF SUBJECTS IN VA RESEARCH

In general, VA policy prohibits paying subjects when research makes no special demands beyond those of usual medical care. However, payment may be permitted if:
- There is no direct subject benefit involved
- Other subjects are being paid
- Subjects are being paid in comparable situations (i.e., at the affiliate in similar research situations)
- The payment can be considered transportation expenses

If a study plans to pay participants, such justification should be included in the IRB’s ARROW application.
New VA human subjects research projects require submission to both an IRB and to the VA R&DC.

The UW Health Sciences IRBs (HS-IRBs) use an electronic submission system called ARROW. For questions regarding how to use ARROW to initiate a study, and information regarding IRB submission see the IRB website or contact the IRB office.

The VA R&DC submission may include all or some of the following:

1. Copy of IRB ARROW submission
2. Request to Review form including abstract
3. Protocol outline sheet
4. Budget/funding sheet
5. VA Conflict of Interest (COI) form
6. Research Safety Survey

and if applicable:

1. Investigational Drug Information Sheet
2. VA consent form
3. VA HIPAA authorization or waiver
4. Sponsor protocol
5. ISO/PO Checklist and Certification for PIs
6. Investigator Data Sheet (if first VA submission)
Major steps in application process (illustrated in the protocol review flow chart that follows):

- Study team fills out an IRB application in ARROW and submission to the IRB electronically.
- The IRB staff conduct a prereview of the submission to identify areas requiring additional information or clarification.
- Once prereview is complete, application is sent the IRB to the VA R&DC for review and endorsement. [applications cannot be reviewed by R&DC until IRB prereview is complete]
- Once the R&DC endorses the study, the application is forwarded via ARROW for review by the convened IRB.
- IRB reviews and approves with an administrative hold and forwards the application to the R&DC via ARROW.
- Final approval is granted by the VA R&DC and the application is returned to the IRB for release of the administrative hold and any consent forms.

**NOTE:**

- The above steps may involve requests from relevant committees for application modifications. Modifications must be responded to before final approval can be granted.
VA PO and ISO Review

- In addition to the IRB and R&DC, the VA Privacy Officer (PO) and VA Information Security Officer (ISO) are required to review all VA projects.
- It is important to have PO and ISO involved in the process early – ISO/PO review is required before final committee approvals.
- Study teams should contact the ISO or PO to receive a copy of the ISO/PO checklist prior for completing IRB and R&DC applications.

IRB/R&D Committee Meeting Schedules

- IRB generally meets multiple times per month
  - HS-IRB meets weekly
  - MR-IRB meets every other week

- R&DC meets monthly, usually on the first Tuesday of each month (meetings are usually not scheduled in August).
ANY CHANGES to an approved protocol (e.g., exclusionary criteria, endpoints, study population, newly identified risks, recruitment numbers, informed consent, HIPAA information, or study procedures) must be reviewed and approved by the IRB and often the R&DC, prior to their implementation. Changes in study staff also must be reported to the IRB.

If you are not sure if a documented change of protocol is required for a particular amendment, contact the IRB office. Minor changes may involve approval of the change by the IRB-only, but major changes also require R&DC review and approval.

Protocol changes cannot be implemented until documentation of appropriate approvals have been sent to the protocol’s Principal Investigator.
Informed consent is a **PROCESS**, not a signature on a piece of paper. The consent form and discussion needs to be in lay language, avoiding medical, professional, or legal wording where possible.

**Both consent** to participate in a research study and authorization to use protected health information (i.e., **HIPAA Authorization**) are required unless the requirements are waived or altered by the IRB. HIPAA Authorization must be a separate document from consent forms. The VA PO will review HIPAA forms for consistency with VA requirements prior to final approval being granted by the IRB and R&DC.

If someone other than the investigator conducts the interview and obtains consent from a potential subject, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. **Study staff delegated to consent subjects must be knowledgeable about the research to be conducted and the consent process, and must be able to answer questions about the study.** Approved protocols must clearly state who will obtain consent from potential subjects.

If **Surrogate Consent** or **Oral Consent** is needed to conduct a study, there additional requirements that apply.

**Know your population** and **anticipate your needs**. Alteration of the consent process, consent forms, or HIPAA documentation can only be done with committee approvals. If changes are needed, this may significantly slow the recruitment of subjects.

**NOTE:** The VA requires that copies of all signed research-related consent forms be sent to the RCO for auditing. Forms should be sent to the Research Office quarterly or more often if there are a high number of consents involved.
INFORMED CONSENT DOCUMENTATION HINTS

• Be careful to NOT use an informed consent form that has an EXPIRED IRB approval.

• When appropriate, be sure that the CPRS record is flagged promptly upon entering subjects into a study (see below).

• Whoever recruits/obtains consent from subjects must have these roles clearly stated in the approved protocol.

• Subject must sign AND date for him/herself both consent and HIPAA forms unless the IRB has approved a surrogate consent process.

• If the IRB determines that a study requires a witness to the subject signature, be sure that the witness signs and dates the consent form in the appropriate space.

• The date the subject signs the consent must match the date of the “Person Obtaining Consent” and “Witness” signatures.

• Dates on consent forms cannot be altered once a subject signs the form.
A study may be required to flag the Computerized Patient Record System (CPRS), i.e. mark patient records to indicate participation in research. The need to flag records is determined by the IRB as part of their review (e.g., where there are no research-related interventions that could affect medical care the IRB may not require flagging).

Patient health records must be flagged if participation involves:

- Invasive research procedures (e.g., muscle biopsy, bronchoscopy)
- Interventions that may affect a subject’s medical care, or which could interfere with other care a subject may receive (e.g., use of investigational device, administration of medication, treatment)
- Clinical services that will be used in the medical care of subjects (e.g., orders for laboratory tests or x-rays ordered as a part of study), or which could interfere with other care subject is receiving or may receive
- The use of a survey or questionnaire that may provoke undue stress or anxiety unless IRB determines that mandatory flagging is not in best interests of subjects (e.g., an interview study of victims of sexual assault).

Flags should remain active in the CPRS record until active participation in the study is completed or until the IRB determines flagging is no longer required

*(NOTE: “Flagging” here refers to marking patient health records to protect subject safety by indicating participation in research. This is not to be confused with the process used to identify dangerous or disruptive patients)*
CPRS flagging entries should contain:
- Project title (including IRB number)
- Investigator’s name & research team contact information
- Brief outline of the research incl. information required for subject safety or where this information is available
- Date of subject enrollment and when consent was obtained (may be the same)
- Name of the person who obtained consent
- Statement that the subject (or surrogate) was capable of understanding the consent process and was given the opportunity to ask questions
- Dates of any subsequent study visits after enrollment/consent
- Description of study related interventions
- Date the subject's participation was terminated

Scanning Consent Forms

All signed informed consent forms and HIPAA authorizations must be scanned into the Computerized Patient Record System (CPRS) unless the IRB decides otherwise.

Exemptions to the consent form scanning requirement may include:
- The study involves only a single visit / one encounter
- The study involves only the use of a questionnaire
- The study involves only previously collected biological specimens
- Identification as a participant in an otherwise Minimal Risk study would place the participant at greater than minimal risk (to be determined by IRB).
For some VA studies, it may be necessary or desirable to send data to the UW OnCore database. As this would constitute sending VA data to a non-VA facility for storage and possible future research use, there are special language requirements that must be followed.

**Consent Forms** must include the following language:

*Information about you and your participation in this study may be entered into an electronic database at the University of Wisconsin-Madison. This database, known as OnCore, will be used to track information about this study. Information stored in OnCore may be used by OnCore data management staff or for other research activities. Only individuals with appropriate permission can look at identifiable information about you in OnCore. **Data entered into OnCore will no longer be owned by the VA and will not be under VA control.***

**HIPAA Authorizations** must include the following language:

*The research team may also need to disclose the information to others as part of the study process … Identifying information may also be entered into the UW Institute for Clinical and Translational Research (ICTR) OnCore data-base for use in data management. This information may be stored there and used by OnCore data management staff until termination of the database. **The copy of the data entered into OnCore is no longer owned by the VA and is no longer under VA control.***
For VA research studies, special requirements are involved when subject tissue is to be banked for future research:

The following information must be included on consent forms:

- The kind of future research planned
- Whether genetic information will be sought
- Whether the specimens will be deidentified
- If the results will be conveyed to the subject and/or their health care provider
- The disposition of the tissue at the end of the banking period
- Whether specimens & links will be destroyed upon a subject’s request
- Whether the subject will be re-contacted
- Any potential conflict of interest issues

In general, any tissue that is kept for future research must be banked within the Madison VA.

➔ If the study intends to store the tissue outside the Madison VA it can only be banked at:

1. a VA-Sponsored tissue bank (i.e., a VA site)
2. a VA-Approved off-site tissue bank (e.g., ECOG)

NOTE: Tissue may be stored at a non-profit or academic institution if a waiver is obtained from the Office of Research and Development (VA Central Office) before specimens are banked. Tissue cannot be stored at, or on behalf of, a for-profit institution.
• VA investigators must fill out a VA Conflict of Interest (COI) form for each study that they are an investigator for.

• Only those who are considered Principal Investigators, Co-Principal Investigators, or Investigators are required to submit a COI form with their VA application.

• As of August 2012, only the form shown below will be accepted, the form is available at the research office.
Unanticipated problems involving risks to subjects or others, and unanticipated local SAEs, whether related or unrelated to the research, must be reported to the IRB.

**Potential Serious Adverse Events (SAEs)** include:

- the death of a subject
- a life threatening experience
- the hospitalization of a subject, or the prolongation of their hospitalization
- a persistent or significant disability or incapacity
- the manifestation of a congenital anomaly or birth defect
- an AE is also considered serious when medical, surgical, behavioral, social or other intervention is needed to prevent such an outcome

**Within 5 business days** of becoming aware of any local (i.e., occurring in the reporting individual’s own facility) unanticipated SAE in VA research, members of the VA research community are required to ensure that the SAE has been reported in writing to the IRB.

Reports should have complete information, fully explaining the event and how it was dealt with. The IRB will review the information to determine whether the incident is to be considered serious, and related to the research.
The IRB must conduct a re-review of approved studies on at least an annual basis. A shorter approval period may be necessary for a particular study, depending on the degree of risk, or for other reasons at the discretion of the IRB. This process is called **Continuing Review**. The Principal Investigator (PI) is responsible for submitting the required information PRIOR to the expiration of approval in order to keep the study active. The IRB has no authority to extend a study’s period without undergoing the continuing review process.

The continuing review protocol progress report should be provided to the IRB two months before a study expires. Failure to submit a completed continuing review application by the appropriate deadline may result in a lapse of approval of the project and notification of the Chief of Staff, Section Chief, and other appropriate parties.

**Once study approval has lapsed, all research procedures (incl. data analysis) must cease.** Contact the VA Research Office and the IRB immediately if there are subjects on a study drug or undergoing research procedures.

Prolonged lapsed study approval may result in the data being sequestered and a prevention of study resumption.

Studies that were found to be exempt by the IRB must still undergo a continuing review process by the R&DC.

**Research Compliance Officers (RCO) are required by VA Central Office to perform a full regulatory audit of each study’s documentation once every three years.** The RCO will also audit on an annual basis all signed consent forms and HIPAA authorizations (or waivers), verify that research notes are entered were required, confirm enrollment numbers, and verify other protocol-related documentation.
When a study has come to an end and all study activities are complete, study teams must formally inform the IRB of study closure.

If you are completing data analysis and your study involves identifiable data (as defined by the IRB) then you must keep studies OPEN with the IRB and R&DC until data analysis is complete.

You may need to close a study if it turns out that there is an insufficient number of subjects, there is a lack of funds, the sponsor decides to close the study, there are unanticipated increased risks to subjects, or other technical factors.

The VA Research office should be informed of any publications resulting from VA research. Copies of publications may be requested as well.
1. All study personnel need to be current with mandatory training and credentialing, including appropriate Scopes of Practice.

2. Be sure that all committee approvals are received where required (R&DC, IRB, Safety, Radiation Safety) prior to initiating any research procedures.

3. If applicable, complete VA Investigational Drugs form 10-1012 for each study drug used.

4. Obtain ISO and PO review and approval prior to final R&DC review.

5. Maintain current, approved, stamped consent forms, information letters, and other documentation in an organized fashion with the idea of what an external auditor might want to see.

6. Be sure that informed consent is obtained PRIOR to any research activity, unless waived by the IRB.

7. Be sure that current approved HIPAA authorization is obtained, or the appropriate waiver of HIPAA authorization is in place to use protected health information.

8. If the study involves photos, video, or audio recordings, have subjects sign a VA Consent for Picture or Voice (Form 10-3203) in addition to research consent forms.
9. Dual Enrollment – VA subjects may only participate in one study at a time unless prior written approval is obtained. Investigators are responsible for verifying whether subject is in another study. Ask the question at time of enrollment and check for research flags in CPRS.

10. For database or medical records studies, the number of individual subject records reviewed must be reported at the time of continuing review.

11. Be sure to report all local unanticipated SAEs or unanticipated problems the IRB within five (5) days of the study team becoming aware of an incident.

12. Remember to seek prior approval from the IRB for any changes (including changes in study personnel), unless the change is necessary to reduce immediate hazard.

13. Inform subjects of any significant changes or increased risks relevant to their participation.

14. Have any sponsor monitors sign in and report any significant findings to the VA Research Office.

15. Keep in mind any data security issues that may be involved in the research, including storage and transport of Protected Health Information (PHI).
16. Retain all research data/documentation must be indefinitely. If there are storage issues, contact the PO.

17. The Principal Investigator is responsible to for submitting continuing review progress reports to the IRB in a timely manner to ensure IRB approval does not lapse.

18. R&DC continuing review via a protocol progress report is required for open studies that are considered exempt from further IRB review.

19. Contact the VA Research Office or the IRB office with questions regarding the review process or other protocol-related questions.

20. Contact the RCO, PO or ISO with questions related to regulatory issues, privacy issues, or information security issues.
Madison VA Director’s Office:
  Hospital Director          Judy McKee
  Chief of Staff (COS)       Dr. Alan Bridges

Madison VA Research Office (Rm. C3127):
  ACOS/R&D                   Dr. Nasia Safdar
  AO/R&D                     Marvin Rupp
  R&D contact person         Bev Birdsall
  to call the Research Office: 608 256-1901 ext. 17007

Other VA Research Contacts:
  Research Compliance Officer John Hudson (in Res. Office)
  Privacy Officer            Lynn Tarpey
  Information Security Officer Brian Rothermel

UW Health Sciences Institutional Review Boards:
  University Bay Office Building, Suite 105
  800 University Bay Drive
  Madison, WI 53705
  Campus Mailcode: UBOB-9425
  Main Line: (608) 263-2362
  Fax: (608) 265-5811
  https://kb.wisc.edu/hsirbs/

Additional Madison VA research information, including consent
form and HIPAA templates, meeting dates, and more detailed
policy and guidance, can be found on the UW Health Sciences IRB
website:
  https://kb.wisc.edu/hsirbs/18470