IOWA CITY DEPARTMENT OF VETERANS AFFAIRS (VA) HEALTH CARE SYSTEM
Iowa City, Iowa

Medical Center Memorandum February 21, 2013
Number 13-034 151

RESEARCH INVOLVING HUMAN SUBJECTS AND INVESTIGATIONAL DRUGS AND/OR PROCEDURES

1. PURPOSE. To state the policy and procedure for the protection of human subjects in research studies conducted at the Iowa City Department of Veterans Affairs (VA) Health Care System.

2. POLICY.

a. All research conducted at the Iowa City VAHCS must have a review and approval by the Research and Development (R&D) Committee prior to being initiated. The VA HCS has an agreement with the University of Iowa (UI) for Institutional Review Board (IRB) review of all human subject protocols. Hence, all research involving human subjects must first be reviewed and approved by the University of Iowa IRB on Human Studies before full R&D approval will be granted.

b. The R&D Committee cannot reverse a negative decision made by the IRB, but may disapprove an IRB-approved study that has been requested to be opened at the VA HCS. Such disapproval would be based on concerns for the welfare of VA study subjects. The IRB has the latitude to determine that some studies are exempt from full review if the study meets specific criteria (see Attachment C). The IRB may also determine that some studies are eligible for expedited review if they meet criteria found in VHA Handbook 1200.05 and the University of Iowa IRB Standard Operating Procedures. Such determinations will be made in writing and can only be made by the IRB Chair or his/her designee.

c. The R&D Committee requires the full consent form (VAF10-1086), if applicable, along with the IRB approval for submission with the VA R&D Committee packet. Guidelines for submission of research proposals to the R&D Committee along with the necessary forms are located in the VA Research Office.

d. VA Subjects may not be enrolled into research protocols until both full IRB approval and full VA R&D Committee approval has been received by the principal investigator in writing from the VA Research Office.

e. The Chief, Diagnostic Imaging and Radioisotope Therapy Service, will be responsible for the custody and dispensing of radioactive drugs in clinical stages of evaluation that have been authorized for use by the Pharmacy and Therapeutics (P&T) Committee, by VA Headquarters, or the Research and Development (R&D) Committee. Unused radioactive drugs will be disposed of as dictated by the research protocol. All other investigational drugs will be stored in the Pharmacy where they will be dispensed as called for in the protocol.

f. Any investigator desiring to use investigational drugs and/or procedures for investigational purposes will submit the proposal to the University of Iowa Institutional Review Board (IRB) as outlined in the IRB "Investigator's Guide to Human Subjects Research" online at http://research.uiowa.edu/hso/index.php?get=inv_guide_toc. Once the IRB has the approval of the appropriate subcommittees the necessary documents will be sent to the VA Research Office.

g. The costs associated with studies involving human subjects will be considered in approving studies to be opened. Studies involving medications dispensed through the Investigational Drug Service (ISD) incur a flat fee for service initially and then annually during the active recruitment phase (see Attachment D). These costs are dependent upon available funds and are negotiated based on the complexity of the study. Other costs for VA services are to be negotiated when the R&D Committee has approved the study.

h. Approval relating to the use of investigational drugs and/or procedures for investigational purposes, unless otherwise stated, will ordinarily be for a period of one year. The IRB will notify the investigator when an ongoing review of the project must be accomplished. Investigators will maintain an up-to-date list of patients or subjects who participate in such studies.

i. It will be the responsibility of the principal investigator using the drug to furnish to the IDS Pharmacist, a copy of the protocol and pertinent information about the drug. The Principal Investigator (PI) must inform the IDS Pharmacist, and the VA R&D Committee when a study involving investigational drug has been terminated.

j. Additional protections will be provided to vulnerable populations (pregnant women and fetuses, prisoners, mentally disabled and those with impaired decision-making capacity, children, and economically and educationally disadvantaged persons) participating in VA-approved research projects. These additional protections will be considered during the review process by the IRB and VA R&D Committee and will be in accordance with VHA Handbook 1200.05 and the University of Iowa IRB Standard Operating Procedures.

k. Non-veterans may be entered into VA-approved research studies only when there are insufficient veterans available to complete the study. All regulations pertaining to the participation of veterans as research subjects, including requirements for indemnification, in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research.

3. RESPONSIBILITY. The responsibility, procedures, and references related specifically to research involving human subjects and for investigational drugs and/or procedures are noted in the attachments.

4. PROCEDURES. See paragraph 3, Responsibility.

5. REFERENCES. See paragraph 3, Responsibility.

6. RESCISSIONS. Medical Center Memorandum 12-034, Research Involving Human Subjects and Investigational Drugs and/or Procedures, dated January 9, 2012.

/s/
BARRY D. SHARP
Director

Attachments

RESEARCH INVOLVING HUMAN SUBJECTS

3. RESPONSIBILITIES.

a. Investigator Responsibilities.

(1) The principal investigator (PI) is responsible for the submission of all documents required for review by the University of Iowa (UI) IRB and the VA R&D Committee. The principal investigator must assure that, prior to recruitment, the VA R&D Committee has approved all studies involving VA patients.

(2) The PI is responsible for adhering to all policies and requirements of the UI IRB as well as VA HCS policies with regard to approved protocols. This includes timely submission of continuing and ongoing reviews. The PI is expected to know the date of the continuing review and to be aware that the project is automatically suspended when the continuing review does not occur on schedule. All amendments to, or modification of, the research proposal, including the consent form, must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent, immediate hazards to the subject.

(3) The PI is responsible for obtaining a legally effective informed consent of the subject or the subject's legally authorized representative and a legally effective authorization for the use and disclosure of the subject's protected health information (PHI). The process of consent should ensure that the potential subject, or legally authorized representative, is provided with information about the research project that is understandable and permits the subject to make an informed and voluntary decision about whether or not to participate. If someone other than the investigator conducts the interview and obtains consent, the PI should formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The Department of Veterans Affairs (VA) Form 10-1086, Research Consent Form, must be used as the consent form, and all required elements must be completed. The most recently IRB-approved consent form must be used when consenting the subject. The consent process may be observed by IRB members, UI Human Subjects Office staff (acting on behalf of the IRB), the VA Research Compliance Officer (RCO), and/or members of the VA Research Office or their designees. PIs are responsible for providing a copy of the IRB-approved and signed informed consent document to each subject at the time of consent, unless the IRB has specifically waived this requirement. All signed consent documents are to be retained in a manner approved by the Research Office.

(4) The PI is responsible for reporting any unanticipated problems that involve risk to research subjects or others to the IRB and any other required entities. This may involve, but is not limited to, a Serious Adverse Event (SAE) or an Unexpected Adverse Event (UAE). SAEs and UAEs are defined in VHA Handbook 1200.5 and the University of Iowa's Investigator's Guide.

(5) The PI is responsible for the timely submission of all annual reports regarding the approved studies to the VA R&D Committee, or, the VA Research Office. This includes the annual review of project data, copies of IRB approvals of continuing review, consent forms of subjects enrolled in the study, and any other ad hoc reporting requirements.

(6) The PI is responsible for fulfilling all VA-directed human subjects educational requirements and for providing documentation of that training to the VA Research Office.

(7) The PI must be credentialed by the Iowa City Veterans Affairs Health Care System (VA HCS) to conduct research involving human subjects and is responsible for providing all necessary information in a timely manner so the credentialing process may be completed.

(8) The PI must provide the names of all individuals who will be working on the research project at the VA HCS to the Research Office. This information will be used to ensure individuals fulfill VA-directed human subjects education requirements and that credentialing requirements are met. The PI is responsible for notifying the Research Office anytime a change in research project staff occurs.

(9) The PI will comply with ICVAHCS conflict of interest policies involving human subjects' protocols.

b. VA Research Office and R&D Committee Responsibilities.

(1) The VA Research Office will ensure that all research protocols submitted to the R&D Committee include all required documents and have been approved by the appropriate R&D subcommittees and/or the UI IRB.

(2) The VA Research Office will verify that credentialing and VA-directed human subjects education requirements have been completed on the PI and all individuals listed as research project staff.

(3) The VA Research Office will notify investigators of the status of submitted protocols (including written approval notifications) and convey any information requested from the investigator by the R&D Committee.

(4) The VA Research Office will notify investigators of VA annual reporting requirements and due dates of VA annual reports of project data and requirements for information concerning human subjects. The University of Iowa's Human Subjects Office (UI HSO) notifies investigators when a research project is due for IRB continuing review.

4. PROCEDURES.

a. Project Monitoring.

(1) The Research Office will receive and record VA Annual Updates of Project Data for each research project that is active at the VA HCS. Data provided by the PI on the VA Annual Update of Project Data will be imported into the research database and transmitted electronically to VA Central Office.

b. Human Use Monitoring.

(1) When a research study is initiated at the VA HCS and it involves the use of human subjects, a human use file will be established in the Research Office. This file will contain all relevant information pertaining to the use of human subjects in a particular project.

(2) The VA Research Office will have live query access to the UI HSO database that can be used to verify IRB approval dates, renewal dates, etc., on human subject protocols submitted and/or opened at the VA HCS.

(3) The UI HSO will forward all IRB minutes to the VA Research Office for VA R&D Committee review. The UI Human Subjects Office will also send all approvals (initial, modification, and continuing review) on projects that involve VA to the VA Research Office. The VA R&D Committee will approve all initial protocols before IRB-approved documents are released to the PI or member of the research team.

(4) The consent process may be observed by IRB members, UI HSO staff (acting on behalf of the IRB and the VA HCS), RCO, and/or members of the VA Research Office or their designees.

(5) The PIs are required to keep complete and accurate records regarding projects involving human subjects and make those files available for periodic audits to be conducted by the RCO, VA Research Office, UI HSO, etc.

(6) The principal investigator is required to retain all research documents/data until disposition instructions are approved by the National Archives and Records Administration and are published in the VHAs Record Control Schedule (RCS 10-1). .

(7) The RCO will monitor compliance with all requirements by conducting periodic audits. The VA Research Office will review reports regarding audits conducted by the RCO and other entities (i.e., UI HSO, VA Cooperative Studies Program) on VA-approved research projects. Action will be recommended to the R&D Committee and other entities, as required, in cases of noncompliance.

(8) The VA R&D Committeecoordinates annual reviews of UI IRB activities to ensure that responsibilities are performed properly, that membership is appropriate for research being reviewed, that chairs have appropriate qualifications and experience, that adequate IRB conflict-of-interest policies are in place for members and investigators, and that policies and procedures are adequate.

5. REFERENCES. VHA Handbook 1200.5; 38 USC 4131; 38 CFR 17.34; M-2, Part 1, Chapter 23; University of Iowa IRB Standard Operating Procedures Manual.

RESEARCH INVOLVING INVESTIGATIONAL DRUGS AND/OR PROCEDURE

An investigational drug for clinical research use is one for which the PI or a sponsor has filed an Investigational New Drug Application (IND) with the Food and Drug Administration (FDA). An investigational drug is also defined as an approved drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial. The use of an investigational drug in clinical research must be conducted according to a protocol approved by the Pharmacy and Therapeutics (P&T), IRB and the VA R&D Committee. Research involving human subjects is the use of investigational materials, devices, or procedures that directly influence a subject's functions. Investigational devices include transitional devices that are objects of investigations. An investigational device may also be an approved device that is being studied for an unapproved use or efficacy.

3. RESPONSIBILITIES AND PROCEDURES.

a. Principal Investigators.

(1) On approval of the proposal by the VA R&D Committee, an R&D Committee approval letter will be prepared and forwarded to the investigators with instructions to fully inform the patient about the study and planned use of drugs and/or procedures, including possible adverse reactions. This should be done orally and in writing. The patient should then sign the VA Form 10-1086, VA Research Consent Form, which includes a written narrative incorporating the basic elements of informed consent (and additional elements of informed consent when appropriate) as found in VHA Handbook 1200.5 and the University of Iowa's Investigator's Guide.

(2) It will be the responsibility of the PI using the drug to furnish to the Chief, Pharmacy Service, a copy of the protocol and pertinent information about the drug. The PI must inform the Chief, Pharmacy Service, and the VA R&D Committee when a study involving an investigational drug has been terminated.

(3) An Investigational Drug Information Record (VAF 10-9012) will be completed by the PI. The original of this form will be kept in Pharmacy Service as a part of the study protocol.

(4) An authorized prescriber for the study will complete a VA prescription on Form VAF 10-2577f, Security Prescription Form, or electronic equivalent for the investigational agent and indicate the study the drug is being prescribed for on the face of the prescription. The properly completed prescription form, along with a copy of the completed VAF 10-1086, Consent Form, will be presented to the Pharmacy for filling. Subsequent requests to fill the same investigational agent for the same patient do not require a VAF 10-1086.

b. Nurses

(1) Nurses who are called upon to administer investigational drugs must have available to them basic written information concerning such drugs including dosage forms, strengths available, actions and uses, side effects, and symptoms of toxicity from the investigating physicians or pharmacists.

(2) All information regarding drug administration and patient reaction to drugs will be recorded using existing medical center policies and procedures related to medication administration.

c. Pharmacy. The Chief, Pharmacy Service, has responsibility for custody, dispensing, and control of investigational drugs authorized for use by the Pharmacy and Therapeutic (P&T) Committee and the R&D Committee.

d. With respect to studies that involve the use of investigational drugs and/or procedures for investigational purposes, the RCO will be responsible for:

(1) Periodically determining whether the above-noted consent forms, including narrative and pertinent statements, are present in patients' medical records or outpatient treatment folders.

(2) Periodically apprising the R&D Committee about the status of previously approved studies and the results of the determinations noted in the preceding paragraph.

5. REFERENCES. VHA Handbook 1200.5; 38 USC 4131; 38 CFR 17.34; M-2, Part 1, Chapter 23.

RESEARCH ACTIVITIES EXEMPT FROM REVIEW
BY SUBCOMMITTEE ON HUMAN SUBJECTS

Research activities in which the only involvement of human subjects will be in one or more of the following categories may be exempt from full review by the Institutional Review Board (IRB). Such determinations will be made in writing and can only be made by the IRB Chair or his/her designee.

1. Research conducted in established or commonly accepted educational settings involving normal educational practices such as:

- Research on regular and special education instructional strategies.
- Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:

- Information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects.
- Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. NOTE: Loss of insurability is also included in this category.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:

- The human subjects are elected or appointed public officials or candidates for public office.
- Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information must be maintained throughout the course of research and thereafter.

4. Research involving the use or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects that are conducted by or subject to the approval of department or agency heads and are designed to study, evaluate, or otherwise examine:

- Public benefit or service programs.
- Procedures for obtaining benefits or services under such programs.
- Possible changes in or alternatives to such programs or procedures.
- Possible changes in methods or levels of payment for benefits or services under such programs.

NOTE: The determination of exempt status for these research and demonstration projects must be made by the Under Secretary for Health on behalf of the Secretary of Veterans Affairs, after consultation with the Office of Research and Development, the Office of Research Oversight, the Office of General Counsel, and other experts, as appropriate.

6. Taste and food quality evaluation and consumer acceptance studies:

- If wholesome foods without chemical additives are consumed.
- If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or an agricultural chemical or environmental contaminant at or below a level found to be safe by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Investigational Drug Service Fee Schedule†

Start-up/Maintenance/Closing Fee*: For industry sponsored studies For non-profit organizations (CALGB,SWOG,NCI, NIH)/Non-funded studies For VA Co-operative studies	 **$600.00** **$300.00** **$100.00**
Includes: Protocol review and notebook setup Pharmacy package update – addition of new drug. Drug receipt and inventory Perpetual inventory Inventory storage Administrative overhead In-services to pharmacy staff Drug preparation and dispensing Prepare drug return reports and shipment Closing of the study	
Annual Renewal Fee: For industry sponsored studies For non-profit organizations (CALGB,SWOG,NCI, NIH)/Non-funded studies For VA Co-operative studies	 **$200.00** **$100.00** **No Charge**
Miscellaneous fees**	**Negotiable**
* One-time non-refundable fee, even if no patients are enrolled. ** Medications that are not supplied by the sponsor: there would be an additional charge for the cost of the medications depending on standard of care.	
†**A request for Fee Wavier or Request for Fee Reduction is available on a case by case basis.**	