

HUMAN RESEARCH PROTECTION PROGRAM GUIDE AND PROCEDURES

JAMES H. QUILLEN VA MEDICAL CENTER (MOUNTAIN HOME, TENNESSEE)

February 2008

1. Definition:

The Human Research Protection Program (HRPP) is a systematic and comprehensive program, with dedicated resources, to ensure the rights, safety and well being of human research subjects in relation to their participation in research activities.

2. Statement of Principles Concerning Protection of Human Research Subjects:

a. The Belmont Report of April 18, 1979 contains the principles upon which the HRPP is based. These principles are:

(1) Respect

(2) Beneficence

(3) Justice

b. The principles of the Belmont Report are addressed in the annual Institutional Review Board (IRB) training and on the IRB website (www.etsu.edu/irb.htm) as a reference, and shall be applied to the review and conduct of all human subject research at this facility.

3. Institutional Official Accountable for the HRPP: The Medical Center Director (MCD) is the institutional official (IO) accountable for the James H. Quillen (Mountain Home) VAMC's HRPP. The MCD signs all assurances. The Associate Chief of Staff for Research (ACOS-R) has delegated authority for implementation of the HRPP.

4. Assurances:

a. The James H. Quillen VAMC (JHQVAMC) is operating under Federalwide Assurance #00002117 issued by DHHS (OHRP) on March 7, 2002, updated on January 25, 2006, expires on January 25, 2009.

b. The VA Medical Center Director is the responsible official.

c. The Chief Officer for the VA Office of Research Compliance and Assurance (ORCA – now Office of Research Oversight or ORO) approved the FWA on February 22, 2002.

d. The Medical Campus ETSU/VA IRB is operating under Federalwide Assurance #00002703 issued by OHRP.

5. Organizational Structure:

a. The operating relationships of the HRPP are shown on the chart on the last page. For the James H. Quillen VAMC the key individuals are the MCD, Chief of Staff (COS), ACOS-R, the Chairs of the VA Research & Development (R&D) Committee and the Medical Campus ETSU/VA IRB. The key entities are the R&D Committee and the Medical Campus ETSU/VA IRB. The policy-making process occurs through the deliberations of both entities, with interaction between them being facilitated by cross-membership. Review of these policies is done using the same mechanism. Additionally, the HRPP will consist of the Administrative Officer for Research and Development (AO-R), Subcommittee on Research Safety (SRS), Privacy Officer, Research Pharmacist and HRPP Director.

b. VA R&D Committee oversees all research activities at the James H. Quillen VA Medical Center. The R&D Committee reviews the membership of the IRB to ensure appropriate VA representation and qualifications, (and the scientific and non-scientific skills of its members). The VA R & D Committee provides oversight and is responsible for reviewing all actions taken by the subcommittees pertaining to VA research to include but not limited to such areas as: conflict of interest, scientific merit reviews, and training.

c. Medical Campus ETSU/VA IRB functions as the human subjects subcommittee of the R&D Committee. The IRB reviews and approves, requires modifications to, or disapproves all human subject research activities in order to assure that the rights and welfare of individuals involved as research subjects are being protected in accordance with federal regulations.

6. Roles and Responsibilities of the R&D Committee in Protecting Human Subjects

a. Operational Principle: The R&D Committee represents the institution, the IRB represents human research subjects.

- IRB members are human research specialists. The R&D Committee members include specialists who represent services that interface with research activities. There is cross-membership between the two committees. The IRB meets the first Tuesday of the month. The R&D Committee meets the last Wednesday of the month and reviews the IRB's detailed minutes. The R&D Committee has full authority to disapprove items approved by the IRB but cannot approve items disapproved by the IRB. The R&D Committee minutes are forwarded to the R&D Committee Chair, ACOS-R, COS and MCD for review and approval.

b. The R&D Committee is Responsible for the Scientific Quality and Appropriateness of all Research Involving Human Subjects.

- The R&D Committee is responsible, through the COS, to the MCD, for oversight of the VA research program and ensuring the highest standards of scientific and ethical quality of all research projects. The review for scientific merit is a vital part of ethical review and the JHQVAMC R&D Committee. The R&D Committee is responsible for and provides oversight on all IRB actions as they pertain to human subjects research protection. The R&D Committee Chairperson in concert with the ACOS-R will assign a Primary Reviewer to review both the IRB-required and approved documentation and all VA-required documentation. The R&D Committee, in consultation with the ACOS-R and COS, reviews the membership of the IRB to ensure members are qualified to conduct scientific and ethical review, makes recommendations to the Director for membership approval and ensures there is cross-membership between the R&D Committee and the IRB.

c. The R&D Committee re-evaluates, at least annually, the scientific quality of all research studies involving human subjects to assure protection of human subjects.

- The R&D Committee re-evaluates all IRB-approved human research studies at least annually. The timing of the re-evaluation is set by the timing of the IRB continuation review. This process is accomplished by the interaction of members on both committees, and by the review of detailed IRB minutes by the R&D Committee.

7. Implementation of HRPP:

a. Responsibility: The ACOS-R is the individual responsible for ensuring that the HRPP is operational and for monitoring changes in VA and federal regulations as they relate to human subject research.

b. Review and evaluation of the reports and results of compliance assessment and quality improvement activities.

- The ACOS-R, R&D Committee, and IRB reviews actions, reports and compliance assessments.

c. Implementation of needed improvements and follow-up actions as appropriate

- Through quality assessment audits conducted by the R & D Office which are accomplished during the year and no less than annually, areas of needed improvement will be identified.

Corrective plans will be developed Corrective plans will be developed and implemented as appropriate. To ensure corrective action is taken each area identified will be revisited

and re-evaluated, by the R & D Office and/or other staff as delegated by the R & D Committee, at least monthly until all corrections have taken place. All actions will be reported to the ACOS-R, the R&D Committee and the IRB.

8. HRPP Budgeting Process:

a. In accordance with VHA Directive 2003-031 dated June 13, 2003, as of July 1, 2003 our VAMC will not accept industry grants (including those administered through the James H. Quillen Veterans Administration Medical Center Biomedical Research Corporation) that do not allow for support of the HRPP.

- The ACOS-R will notify, in writing, the entity administering the study about the implementation of the HRPP policy.
- The ACOS-R will ensure that any grant accepted by the VA (or Corporation) includes an amount equal to 22% of the direct cost of the study, or a flat fee of \$1200 (whichever is greater) to be applied to the costs of the HRPP incurred by the VAMC. These funds will be used in support of the HRPP. (i.e., personnel, supplies, equipment, training & education).
- The ACOS-R will obtain an annual accounting of the total amount of direct costs of industry-funded studies conducted at the JHQVAMC, as well as the amount of funds that were made available from the Corporation for support of HRPP costs.
- The Research and Development Office will forward this report to the Director of Finance at the Office of Research and Development (ORD) along with an accounting of all expenditures in support of compliance-related activities.

9. Institutional Oversight of the IRB:

a. The IRB is evaluated at regular intervals basis by the R&D Committee, the ACOS-R, COS and MCD through auditing, reports and minutes. Communication between the AO-R and the HRPP Director is done on a "as needed basis". VA and R&D Committee membership on the IRB also facilitates oversight/evaluation. Additionally, the AO-R is an ex-officio member of the IRB and monitors its function for compliance with VA and federal guidelines.

b. IRB Membership:

(1) The membership of the IRB is reviewed/evaluated annually by both Institutional Officers accountable for the HRPP.

(2) The R&D Committee will annually review the membership of the IRB by the October meeting to assure its appropriateness, given the research being reviewed, and

to evaluate the presence of representatives having experience with vulnerable populations (either as members or ad hoc consultants).

c. IRB Chair:

(1) Both institutions represented on the IRB assess the knowledge and qualifications of candidates before recommending them for appointment to the Institutional Officers. When a new candidate is considered for the IRB Chair, both the IRB and the R&D Committee will assess their knowledge and qualifications as presented via a current CV/Resume.

(2) IRB Function:

(a) Evaluation of IRB performance occurs on a monthly basis by careful review of the IRB minutes and by review of proposals approved by IRB. Evaluation includes the following areas:

- (1) Content and accuracy of informed consent document (all elements included).
- (2) IRB analysis of risks and benefits including designation of minimal risk.
- (3) Special considerations and protections for vulnerable population.
- (4) Privacy and confidentiality protections.
- (5) Continuation review of approved research.
- (6) Ongoing review of previously approved research (i.e., mods, AEs).
- (7) Use of expedited review.
- (8) Granting of exemption from Federal requirements for IRB review.
- (9) Granting of waivers for documentation of informed consent.
- (10) Granting of waivers of any elements of informed consent.

(b) IRB deliberations are meticulously documented. The IRB minutes are a stand-alone document that demonstrates all performance elements. The R&D Committee, ACOS-R, COS and MCD receive a complete set of IRB minutes monthly for review and evaluation.

10. Conflict of Interest Policies:

a. Based on guidance from ORD, all studies shall submit financial information to the IRB and R&D Committee for review.

b. Investigators:

(1) Investigators will be required to include a financial Conflict of Interest Statement with each proposal submitted to the IRB. The IRB will report the findings to the R & D Committee through the AO – R.

c. R & D and IRB Committee:

(1) R&D and IRB Committee members do not participate in the deliberation or vote of any protocol for which a potential conflict of interest exists (this will be documented in the minutes). At the beginning of each meeting the Chair will poll the committee for any conflicts of interest. R & D and IRB members are considered to have a conflicting interest whenever any one of the following are true:

- 1) The R & D and IRB Committee Member, Consultant, R & D and IRB staff or a member of their immediate family has a significant financial interest as defined in Policy 17a.
- 2) The R & D and IRB Committee Member, Consultant, R & D and IRB staff or a member of their immediate family is a member of the research team designing, conducting, or reporting the research presented in the protocol, or has an immediate family members involved in the design, conducting or reporting the research presented in the protocol.
- 3) The R & D and IRB Committee Member, Consultant, R & D and IRB staff, or a member of their immediate family has any other interest of any kind that the individual believes conflicts with his or her ability to objectively review a protocol.

d. The Institution:

(1) The ACOS-R has been delegated by the MCD to be the Conflict of Interest Administrator who will be responsible for the day-to-day activities related to conflicts of interest in the research program. If the institution or an institutional official has a potential conflict of interest that is determined to be problematic, then the committee will review the institution's financial relationship with the sponsor. If the institution/official stands to benefit from the successful outcome of the trial, then it could directly influence the conduct of the trial (i.e., design/reporting).

(2) In such cases, having the study conducted and evaluated at a different site may best protect the integrity of the research, as well as the institution.

11. Questions, Concerns, Complaints and Allegations of Noncompliance:

a. A standard element of the Informed Consent Document (ICD) is entitled "Contact for Questions." This paragraph states "If you have any questions, problems, or research-related medical problems at any time you may contact (PI) at (ph#) or (name

of PI appointed second or co PI) at (ph#). You may call the Chair of the Institutional Review Board at (ph#) for any questions you may have about your rights as a research subject.” Each ICD must contain this statement in order to be approved. All issues will be addressed by the IRB and reported to the VA (see Memorandum of Understanding (MOU) dated February 1, 2004). The process by which complaints and non-compliance issues are managed are addressed in the East Tennessee State University/James H. Quillen VAMC Policy Statement Procedures for Managing Noncompliance/Complaints. Additionally, posters are hung in patient areas soliciting feedback from research subjects with the phone numbers of the IRB Office.

12. Investigational Devices: The JHQVAMC does not conduct studies using investigational devices at this time.

13. Investigational Drugs: The JHQVAMC does conduct studies using investigational drugs and does so In Accordance With (IAW) VHA Handbook 1108.4, VHA Handbook 1200.5 and Medical Center Memorandum 119-06-04 "Investigational Drugs in Research"..

14. Monitoring, Evaluation and Quality Improvement:

a. Primary monitoring of investigator performance occurs at the IRB level (both administrative and board). The following are evaluated:

- (1) Adherence to IRB-approved protocols
- (2) Reporting all unanticipated problems involving risks to subjects
- (3) Reporting all protocol deviations
- (4) Obtaining IRB approval prior to initiating changes in the protocol or consent
- (5) Using only IRB-approved advertisements and subject recruitment materials
- (6) Obtaining consent prior to initiating any research related procedures
- (7) Using only IRB-approved consent form VA Form 10-1086 (except in cases where the documentation of informed consent is waived by the IRB) to include:
 - (a) description of expected benefits
 - (b) description of potential discomforts
 - (c) description of alternative procedures
 - (d) full explanation of procedures to be followed

(e) assurance of the right to refuse to participate

(f) dating and signing of Informed Consent form by:

- Subject or the subjects legally authorized representative,
- Witness to the subject signing, and
- The person obtaining the Informed Consent

(g) Providing a copy of the consent form to the subject (or legally authorized representative).

(h) Interview person obtaining consent to determine if consent was adequately reviewed with subject (questions/concerns answered).

(i) The institution monitors the performance of investigators to ensure compliance with HRPP and IRB requirements. The institution evaluates the following

(1) Adherence to HRPP policies.

(2) Adherence to electronic record entry policy.

(3) VA Form 10-1086 scanned into medical record.

(4) Monitoring adherence to “Stand Down” policies regarding verification of licensure, education, background checks.

b. Quality Improvement Program for Human Subjects Research (QIP) has a charge as follows:

(1) Determine if investigators implement protocols as approved

(2) Evaluate whether the IRB adequately addresses applicable ethical and compliance issues.

(3) Determine if written documentation comply with institutional, industrial, federal, state, local and VA regulatory requirements.

(4) Identify issues to be addressed in IRB educational/training initiatives.

(5) Examine/evaluate the informed consent process to determine areas in need of improvement.

(6) Monitor/evaluate responsiveness and reporting regarding participant questions, concerns, withdrawals and complaints.

(7) Identify areas for improvement.

15. Mandatory Training:

a. All Principal Investigators, Co-Principal Investigators, co-investigators, key personnel, VAMC R&D Committee members, and VAMC representatives serving on the IRB are required to complete annual mandatory HRPP training. Overview of required courses can be reviewed at the following web;

<http://www.research.va.gov/programs/pride/training/all-staff.cfm> The following is a list of training requirements:

- VA Cyber Security Awareness Training Course
- VHA Privacy Policy Training Course
- VA Research Data Security & Privacy Training Course
- Ethical Principles of Human Subjects Protection and Good Clinical Practices (CITI)

All training is available on the IRB website at www.etsu.edu/irb.htm. This VA mandated course may also be found at <http://vaww.ees.aac.va.gov>. No study using human subjects in research will be given approval until all required personnel involved in the study have completed the mandatory training. Training records are maintained by the R & D Office .

16. The following HRPP Overview, Guidelines and Regulations can be found on the IRB website:

- (1) History of the IRB and Ethical Guidelines
- (2) Policies of the Medical Campus ETSU/VA IRB
- (3) Standard Operating Procedures (IRB & R&D)
 - (a) VA Research Guidelines/Forms/Samples
 - (b) Federal Regulations
 - (c) References (Belmont, FWA, etc.)
 - (d) Appendices (Samples/Forms, etc.)
 - (e) Supplements (Websites, Glossary, Case Reports, etc.)
 - (f) VA Handbooks
 - (g) Training Guidelines/Links
 - (h) Available Reference Materials (i.e., videos, CDs, etc.)

(i) Submission Dates & Guidelines

(j) Contact Information

(k) Informed Consent Guidelines

Expiration Date: September 2009