

Department of Veterans Affairs  
Harry S. Truman Memorial Veterans' Hospital  
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### **ASSURANCE OF COMPLIANCE AND QUALITY IMPROVEMENT FOR HUMAN RESEARCH PROTECTION PROGRAM**

1. **PURPOSE:** To closely monitor compliance with all requirements of the comprehensive Human Research Protection Program (HRPP) at the Harry S. Truman Memorial Veterans' Hospital (HSTMVH).
2. **POLICY:** To conduct an ongoing, continuous Quality Improvement program and to ensure compliance with policies, regulations, and laws which pertain to human research protections.
3. **DEFINITIONS:**
  - a. **Research Non-compliance.** Failure to follow institutional policies, procedures, stipulations, decisions, state or federal law, or VHA Handbook 1200.5.
  - b. **Serious Non-compliance.** All non-compliance substantially affecting participants' rights and/or welfare, or impacting upon the risks or benefits is serious non-compliance.
  - c. **Continuing Non-compliance.** The systematic and habitual disregard of restrictions, procedures, stipulations, or decisions of the University of Missouri-Columbia Health Sciences Institutional Review Board (HS-IRB).
  - d. **Adverse Event.** Recognized harmful or unfavorable outcome occurring to a participant in a research study. **NOTE:** It is important to remember that adverse events can be injuries other than physical injuries. Events such as emotional distress, employment/insurance consequences, or familial relationship consequences may also be classified as adverse events. It is also important to remember that misplaced records leading to a possible breach in confidentiality also constitutes as an adverse event.
  - e. **Serious Adverse Event.** An event resulting in one of the following outcomes or requiring treatment to prevent one of the following outcomes: death, a life-threatening experience, requires or prolongs hospitalization, persistent or significant disability or incapacity, congenital anomaly and/or birth defect, cancer (secondary or other new cancer in individuals with pre-existing cancer), or drug overdoses. Examples of non-medical events that are classified as serious include, but are not limited to the following: suicide, confidentiality breach, loss of employment, loss of insurance, or severe emotional distress requiring treatment.
  - f. **Expected Adverse Event.** An event that has been documented in the informed consent as a possible side effect/consequence of participation in the study.

g. **Imminent Threat of an Adverse Event.** In the context of research, an imminent threat of an adverse event refers to any situation (determined by an IRB, an investigator, or a clinician) in which an adverse event has not yet occurred, but is likely to occur without preventative measures.

h. **Unanticipated Problems Involving Risk to Participant or Others.** Any event or information that (a) was unforeseen and (b) indicates that the research procedures caused harm to participants or others or indicates that participants or others are at increased risk of harm. Note that expected adverse events cannot meet the first criterion and unrelated adverse events cannot meet the second.

i. **Allegation.** An allegation is an assumption made by a party that must be proved or supported with evidence.

j. **Confirmed Report.** In the context of HRPP, a confirmed report refers to non-compliance that is supported by incontrovertible factual information.

k. **Administrative Hold.** An action taken by the Institutional Review Board (IRB), IRB Chair, IRB designee, or Research and Development (R&D) Committee to temporarily or permanently stop some or all approved research activities. Administrative holds are used when the IRB or R&D Committee is requesting additional information from an investigator and/or is asking for follow-up on the completion of IRB or R&D Committee directed actions. Administrative holds are not suspensions or terminations.

l. **Research (scientific) misconduct.** Fabrication, falsification, plagiarism or other practices that seriously deviate from those that are commonly accepted within the academic community for proposing, performing, or reviewing research, or reporting research results. Misconduct does not include honest error or honest differences in interpretations or judgments of data.

m. **Suspension.** A temporary withdrawal of approval of some or all research, or a permanent withdrawal of approval of some research activities.

n. **Termination.** A permanent withdrawal of approval of all research activities.

4. **RESPONSIBILITIES:** The responsibilities for ensuring compliance and for overseeing quality improvement activities for the HRPP are as follows:

a. **Hospital Director.** The Hospital Director is responsible for the overall assurance of protections for human participants within the HSTMVH. As the designated Institutional Official, the Hospital Director can exercise the authority to suspend or terminate research as deemed necessary, including for the protection of human participants.

b. **Associate Chief of Staff/R&D (ACOS/R&D).** The ACOS/R&D is delegated the responsibility for the implementation, conceptual oversight, and administrative leadership with regard to ensuring compliance and quality improvement for the HRPP.

c. Human Research Compliance Officer (HRCO). The HRCO is responsible for the day-to-day monitoring of the HRPP, including the ongoing Quality Improvement activities, the implementation of needed improvements, and the follow-up of corrective actions. The

HRCO also is responsible for the review and evaluation of reports, audits, compliance assessments, and quality improvement activities as related to human research protections.

d. Administrative Officer/R&D (AO/R&D). The AO/R&D is responsible for the organizational support and deployment of resources that are required to maintain compliance with HRPP activities, including compliance audits.

5. **PROCEDURES FOR COMPLIANCE AUDITS:** The compliance audits for the HRPP are conducted in a coordinated manner with the HS-IRB in conjunction with Continuing Research Reviews (CRRs) and include the following:

a. Compliance Audits of Project Files. The HRCO will audit a minimum of three (3) human research project files per quarter to ensure completeness of records, including original applications, Health Sciences Institutional Review Board (HS-IRB) documentation, investigator communications, and synchronization with computerized tracking systems. Specifically, the audit will ensure that accurate and complete records are maintained as follows: (1) date of original HS-IRB approval, (2) date of original R&D Committee approval, (3) date of most recent HS-IRB approval, and (4) date by which next HS-IRB continuing review must occur.

b. Compliance Audits of VA Training Records. The VA database which documents the training required for human researchers ("Overview of Good Clinical Practices" and "HIPAA Privacy Training") will be audited by the HRCO for training compliance on a quarterly basis.

c. Compliance Audit of HS-IRB Training Records. The HS-IRB training website will be audited by the HRCO for compliance with required biannual HS-IRB web-based training; an audit of the training records will be conducted on a quarterly basis.

d. Compliance Audit of HS-IRB Continuing Review Reports. The HS-IRB website will be audited by the HRCO to ensure that all human research protocols operating within the HSTMVH are compliant with HS-IRB continuing review reports; a minimum of three (3) randomly selected projects will be audited on a quarterly basis.

e. Compliance Audit of Informed Consent Documentation. The placement of consent documents within the medical records of human research participants at the HSTMVH will be audited by the HRCO on a quarterly basis.

f. Compliance Audit of Investigator Records and Practices. Human research investigators at the HSTMVH will receive personal visits by the HRCO to ensure adequacy of records security, data management, operational procedures, consent documentation, reporting of adverse events, adequacy of consent forms, compliance with inclusion/exclusion criteria, and management of deviations from protocol. A minimum of three (3) human research investigators will be visited (audited) personally on a quarterly basis.

**6. PROCEDURES FOR RESPONDING TO ALLEGATIONS OR REPORTS OF NON-COMPLIANCE WITH HRPP REQUIREMENTS:** The HSTMVH defers to the HS-IRB policies and procedures for the review of situations involving allegations or reports of non-compliance and the handling of problems determined by the HS-IRB to be unanticipated problems involving risks to participants and others. In addition to retrospective audits of compliance with the HRPP, any allegation or report of noncompliance which arises will receive responsive examination as follows:

a. Any employee of the HSTMVH or member of a research team (including Without Compensation Employees) who becomes aware of a violation, or who believes there may be a violation, of HS-IRB or HRPP regulations, requirements, or determinations is required to provide a prompt report to the HRCO or to other senior institutional officials (i.e., ACOS/R&D, Chief of Staff, Hospital Director) at the HSTMVH. In addition, participants in human research studies, their designated representatives, or members of their community are also encouraged to report any activities or behaviors that they believe may be non-compliant or inappropriate. The HRCO will be responsible for providing immediate notification to the ACOS/R&D and the Hospital Director.

b. Regardless of the source of the complaint, all allegations and reports of all non-compliance (whether minor, serious, or continuing) will be reported to the HS-IRB Office.

c. The HS-IRB Office will communicate back to the VA Research Office whether allegations of non-compliance are confirmed, whether reports of non-compliance are serious or continuing, and whether additional information is needed.

d. If the HS-IRB Office responds that an allegation of non-compliance had no basis in fact, no further action will be taken.

e. If the HS-IRB Office responds that an allegation of non-compliance was confirmed, but was neither serious nor continuing or that a report of non-compliance was neither serious nor continuing, the Research Office staff will report the finding and the actions taken by the HS-IRB to the ACOS/R&D. The ACOS/R&D will take corrective actions as required to remedy the non-compliance and will report these corrective actions back to the HS-IRB.

f. If the HS-IRB responds that an allegation of non-compliance was confirmed and was either serious or continuing or that a report of non-compliance was either serious or continuing, the Research Office staff will report this finding to the Hospital Director with a copy of the letter sent by the HS-IRB to regulatory agencies and institutional officials.

(1) The Hospital Director may take additional corrective actions, including suspension or termination of protocols, restrictions on privileges to conduct research, or potential disciplinary actions against perpetrators of violations. The Hospital Director will report corrective actions to the HS-IRB.

(2) The Hospital Director will follow all required VA policies, including VHA 1200.5, for reporting to regulatory agencies.

**7. PROCEDURES FOR RESPONDING TO UNANTICIPATED PROBLEMS:**

- a. Principal Investigators are required to follow HS-IRB policies and procedures regarding the problems that require prompt reporting to the HS-IRB.
- b. The HS-IRB Office will communicate back to the Research Office when a problem is determined to represent an unanticipated problem involving risks to participants or others.
- c. If the HS-IRB determines that a problem was determined to be an unanticipated problem involving risks to participants or others, the Research Office staff will report this finding to the Hospital Director with a copy of the letter sent by the HS-IRB to regulatory agencies and institutional officials.
- d. The Hospital Director will follow all required VA policies, including VHA 1200.5, for reporting to regulatory agencies.

**8. ASSURANCE OF APPROPRIATE OVERSIGHT OF IRB:** A key procedure for ensuring compliance and quality improvement for the HRPP is careful oversight of HS-IRB activities. Specific oversight is accomplished as follows:

- a. The HRCO maintains electronic access to HS-IRB data pertaining to VA-related projects.
- b. A VA representative attends a minimum of 75% of HS-IRB meetings in order to monitor appropriate review and oversight of VA-related projects.
- c. A representative of the affiliated HS-IRB attends a minimum of 75% of VA R&D Committee meetings.
- d. The minutes of all HS-IRB meetings are presented for review at R&D Committee meetings.
- e. The HRCO monitors specific HS-IRB activities from a compliance standpoint as follows: (a) qualifications and experience of new HS-IRB chairpersons, (b) appropriateness of HS-IRB membership and experience in the context of research under review, (c) participation of representatives and/or advocates for vulnerable populations, (d) adequacy of HS-IRB policies and procedures, (e) appropriate monitoring of adverse events, (f) timeliness of review process, (g) appropriateness of number of HS-IRBs in relation to workload volume, and (h) the thoroughness of the review process. The HRCO completes the HRPP HS-IRB Performance and Oversight Form on an annual basis (4<sup>th</sup> quarter) and submits the results for review by the R&D Committee.
- f. Quarterly meetings are held between VA and HS-IRB officials (convened by the HRCO) in order to maximize communication, facilitate collaboration, and ensure compliance with all HRPP requirements.

**9. PROCEDURES FOR REPORTING TO REGULATORY AGENCIES:**

a. The Hospital Director will prepare a letter with the following information when not included in the HS-IRB letter to regulatory agencies:

- (1) The nature of the event (unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of approval of research).
- (2) Name of the institution conducting the research.
- (3) Title of the research project or grant proposal in which the problem occurred.
- (4) Name of the principal investigator on a protocol.
- (5) Identification number of the research project as assigned by the HS-IRB and the identification number of any applicable federal award(s), grant, contract, or cooperative agreement.
- (6) A detailed description of the problem including the findings of the organization and the reasons for the HS-IRB's decision.
- (7) Actions that the HS-IRB has taken or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects).
- (8) Additional actions VA has taken or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects).
- (9) Plans, if any, for the HS-IRB to send a follow-up or final report by the earlier of (a) a specific date, or (b) when an investigation has been completed or a corrective action plan has been implemented.
- (10) Plans, if any, for the VA to send an additional follow-up or final report by the earlier of (a) a specific date, or (b) when an investigation has been completed or a corrective action plan has been implemented.

b. The Hospital Director will attach the letter to the HS-IRB letter and send the letter to the following:

- (1) Chief Executive Officer, Veterans Integrated Service Network 15.
- (2) Regional VA Office of Research Oversight.

- (3) VA Office of Research and Development.
- (4) Privacy Officer of an organization, if the report involves unauthorized use, loss, or disclosure of individually-identifiable patient information from that covered entity.
- (5) Information Security Officer of an organization, if the report involves violations of information security requirements of that organization.
- (6) Foundation Director, if applicable.
- (7) VA Service Line Director responsible for the investigator.

10. **COMPLIANCE AUDIT AND MONITORING DOCUMENTATION:** On at least a quarterly basis, the HRCO will provide a written summary of compliance audits and monitoring activities to the Research & Development (R&D) Committee. Results of compliance audit activities pertaining to the HRPP will be maintained on file for a minimum of seven (7) years.

11. **COMPLIANCE WITH CHANGES IN HRPP POLICIES AND REGULATIONS:** Officials delegated as responsible for the HRPP (i.e., ACOS/R&D, HRCO, AO/R&D) will closely monitor all policies and regulations which pertain to HRPP compliance requirements. Strategies for effective monitoring will be as follows:

a. The HRCO and other officials, as appropriate, will participate in recurring training in order to remain cognizant of all changes in HRPP policies and regulations. When changes are identified, they will be promptly reflected in local policies and procedures at the HSTMVH and quickly disseminated to institutional officials, members of research review committees, and human research personnel via the HRPP Investigator Handbook and through ongoing educational activities.

b. Communications from the VA Office of Research and Development, the VA Office of Research Oversight (ORO), and the VA Center on Advice and Compliance Help (COACH) will be closely monitored in order to maintain a keen awareness of changes in HRPP policies and regulations so that compliance can be maintained

12. **REFERENCES:**

a. VHA Handbook 1200.5 "Requirements for the Protection of Human Subjects in Research" dated July 15, 2003.

b. "What to Report to ORO: Action" Memorandum dated September 8, 2005.

13. **REVISIONS:** HPM 589A4-340, dated October 6, 2006.

APPROVED:

*Sallie Houser-Hanfelder, FACHE*

SALLIE HOUSER-HANFELDER, FACHE  
Director

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