

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

SOP# HRP 02.01

Approval Date: 1/10/08

OVERVIEW OF QUALITY ASSURANCE ACTIVITIES

This SOP, originally approved on 1/10/08, underwent changes on 4/16/08 summarized below:

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Author	Jessica Mendoza		
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Changes	<ul style="list-style-type: none"> • Updates in references and new IRB SOPs • New 6.1 • Wording changes 	New Version #	2.1
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This amended version (2.1) was approved by the Chair, R&D Committee / by the R&D Committee on 5/8/08.

Leslie Katzel, MD, PhD
Chair, R&D Committee

Date

\\Overview of QA Activities (HRP 02.01) 2008.2.1

Prior versions: Version 1.0 (3/11/04)

Version 2.1

Review due: 01/11

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OVERVIEW OF QUALITY ASSURANCE ACTIVITIES

OBJECTIVE:

- To establish an efficient system of quality management audits of research activities at the VAMHCS.
- To ensure that remedial action is taken for any shortfalls found or, if the error cannot be corrected, to initiate changes in procedures to prevent problems in future studies or research programs.
- To educate staff on the VAMHCS quality management program and good clinical practices (GCP's).
- To assess the performance, membership, policies and procedures of the UMB IRB.
- To document internal quality assurance and quality improvement activities of the VAMHCS Research Service.

SCOPE:

The VAMHCS Research & Development (R&D) Service has established a comprehensive, integrated quality management program (QMP) outlined in its Human Research Protection Plan (HRPP) (HRP 01.02).

The provisions of the QMP apply to all research involving human subjects that is conducted completely or partially in VAMHCS facilities, conducted in approved off-site locations/facilities and/or conducted by VAMHCS researchers while on official duty, or involves VAMHCS medical records or VAMHCS databases or otherwise derives data from intervention or interaction with VAMHCS subjects or tissues. The research may be VA funded, funded from extra-VA sources, or conducted without direct funding. No protocol will undergo a "routine audit" more than once within an 18 month period unless the Medical center Director (MCD), ACOS/R&D, Research Compliance Officer (RCO), R&D Committee, the IRB, or the Resolution Plan recommends a re-audit.

Elements of the VAMHCS QMP are:

- Audit processes to evaluate investigators' compliance with the VAMHCS Human Research Protection Plan (HRPP), including but not limited to the informed consent process and documentation, compliance with procedures described in the protocol submission

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processes (IRB and R&D Committee applications), compliance with the protocol (for non-Pharma studies), compliance with procedures for regulatory and source documentation, compliance with VAMHCS, Research Service and IRB policies and procedures, and adequacy of staff education, trainings and scope of practice.

- Audit processes to evaluate investigators' compliance with their own internal SOPs or quality management plans.
- Intake and evaluation of comments, complaints, suggestions, and allegations of non compliance from research participants, their families, research staff, institutional and IRB officials, and external sources.
- Audit processes to evaluate the performance of the VAMHCS Investigational Drug Service (IDS);
- Review processes to evaluate the performance of the R&D Committee and its subcommittees;
- A review process to evaluate the adequacy of IRB policies and procedures and the performance of IRB committees with regard to VAMHCS studies;
- Education of research staff in policies and procedures necessary to protect the rights and safety of human research participants and the scientific integrity of the research project.

The Research Service has designated its Office of Research Compliance (ORC) to oversee quality management activities of VAMHCS investigators and programs. The Research Compliance Officer (RCO) oversees Research Compliance Specialists (RCS) in quality assurance and quality improvement activities such as audits, investigations of complaints or allegations of noncompliance, and evaluations of effectiveness of policies and procedures.

The Research Service requires that all VAMHCS research units and protocols involving the use of human subjects have measures to assure compliance to the research protocol. The ORC will not routinely include data integrity in its quality management program and will instead focus its attention on matters that more directly impact subject rights and safety (such as informed consent, eligibility criteria and adverse event reporting) and regulatory compliance (“audit triggers”).

The Investigational Drug Service (IDS) also falls under the purview of the ORC with regard to handling of study entities (drugs and devices).

The R&D Committee periodically evaluates Research Service and IRB policies and procedures.

This SOP describes the overall quality management program. Details on specific areas can be found in the SOPs listed in the “See Also” section below.

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RESPONSIBILITIES:

1. The Office of Research Compliance (ORC) is responsible for:
 - Proactively educating research staff on the proper and ethical conduct of research;
 - Acting as a resource to investigators and research staff on issues of practice and compliance, including investigators' internal quality management plans (HRP 02.04);
 - Auditing the research activities of VAMHCS investigators and research staff based on audit triggers (HRP 02.02);
 - Assisting investigators with developing corrective action plans (CAPs) and following up on the resolution of audit findings;
 - Reporting findings to the R&D Committee, the ACOS/R&D, the COS, the MCD, the Executive Performance Improvement Committee (EPIC), and the IRB.
2. The Principal Investigator is responsible for:
 - Being knowledgeable about institutional and regulatory policies and procedures regarding conduct of research involving human subject participants;
 - Establishing internal policies and procedures to ensure compliance with VAMHCS SOPs, IRB policies and procedures, study protocols, GCPs, and other regulations;
 - Ensuring that his/her staff complies with these internal policies and procedures and facilitating their efforts in this area;
 - Using the Research Service staff, and external sources as resources ;
 - Using this process as a learning tool to improve her/his "good clinical practices".

DOCUMENTS (ATTACHMENTS):

"Documents Typically Subject to Audit"
Sources for SOPs and Audit Tools

Appendix 1
Appendix 2

SEE ALSO:

The following Research Service documents describe the quality management plan in detail:

Research Service Human Research Protection Plan (HRPP) (HRP 01.02)
Research Service SOPs

- Audit Triggers (HRP 02.02)
- Auditing Source Documents Charts (HRP 02.03)

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- Investigator Responsibilities for Internal Quality Assurance or Their Research Programs (HRP 02.04)
- Auditing the Investigational Pharmacy (HRP 02.05)
- Addressing and Responding to Comments, Complaints and Suggestions Related to the Human Research Protection Program (HRP 01.07)
- Addressing and Responding to Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program (HRP 01.08)

Research Service Guidelines

- Informed Consent Guidebook (HRP 03.01G)
- Guidelines for Setting Up a Study Binder and Regulatory Documents Binder (HRP 07.02G)
- Guideline on Source Documents (HRP 07.03G)
- Writing Standard Operating Procedures (HRP 07.05G)
- Study-Specific SOPs (HRP 07.06G)

Research Service auditing and self-assessment forms

PROCEDURE:

1. The Office of Research Compliance (ORC) (specifically, the Research Compliance Officer [RCO]), is aware of VAMHCS research activities through the following mechanisms:
 - The RCO (or RCS) attends IRB meetings as a non-voting observers and thus becomes aware of VAMHCS protocol approvals, terminations, and other actions/reports.
 - The RCO attends VAMHCS R&D Committee meetings as a non-voting member and thus becomes aware of protocol approvals, terminations, and other actions or reports.
 - The RCO has read-only access to all VAMHCS protocols in the BRAAN system and can thus keep abreast of reportable events.
 - The IRB forwards to the RCO any IRB audit reports pertaining to VAMHCS protocols or investigators.
 - The IRB notifies the RCO of allegations of investigator noncompliance or misconduct involving VAMHCS protocols or investigators.
 - Research participant, family or research staff comments, complaints, suggestions or allegations of noncompliance are directed to the ORC.

2. Based on this, the following areas of study conduct and VAMHCS and UMB policies may be evaluated through QA activities:
 - Source documentation and regulatory documents files
 - Informed consent process and documentation
 - Investigator compliance with the materials submitted in BRAAN and to the R&D Committee and approved by the IRB and R&D Committee

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- DSMP conduct, reports and actions
 - Investigational pharmacy
 - Unanticipated problems involving risks to participants or others
 - Complaints
 - Allegations of regulatory noncompliance
 - Routine audits with the goal of quality assessment and education & training of staff
 - Credentialing, training and qualifications of study staff (scope of practice)
 - Investigator management of investigational devices and study related procedures
3. The ORC will act upon the following **audit triggers** which apply to any of the areas above:
- Routine (scheduled) spot or full audit
 - For-cause audits
 - Principal Investigator/study personnel request
 - Studies without identified oversight
 - Investigator initiated studies
 - Scheduled follow-up to routine audits
 - PI's with high numbers of protocols
 - PI's with vulnerable populations (elderly/children/psych/impaired decision-making)
 - Reportable Events - numerous or of interest (may be 'for cause')
 - Research participant/family member complaint
 - Participant death
 - Appearance of lack of staff support/resources/high staff turnover
 - Lapses in continuing review/studies administratively closed by IRB
 - Ongoing concerns of quality IRB or R&D Submissions
 - Ongoing concerns of IRB or R&D about document processing
 - ACOS/AO/R&D, Chief of Staff, VA/Director, VA/Administrator/Department Chair, IRB Chair has concerns
 - Scheduled follow-ups to Resolution Plans
 - Systems audits, when audits, institutional reports, participant complaints or other feedback indicate that VAMHCS policies or procedures should be changed.
4. Documents that are typically reviewed during audits are listed in Appendix 1. The Research Service reserves the right to audit other documents as necessary for the type & situation of audit being conducted.
5. Descriptions of some audit processes are detailed in Research Service SOPs, "Audit Triggers" (HRP 02.02), "Auditing Source Documents Charts" (HRP 02.03), "Auditing the Investigational Pharmacy" (HRP 02.05).

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Additional types of audits/evaluations are undertaken as needed; for example, an observation of an informed consent discussion between an investigator and a patient.

6. All audit activities done by the RCS staff will be reported to the RCO through written reports and meetings. The RCO makes summary reports to the R&D Committee, the ACOS/R&D, the COS, the MCD, EPIC and the IRB.
 - 6.1. In the case of findings of possible or actual noncompliance, the RCO proceeds according to HRP 01.08. As part of that process, the HRPO is immediately notified and proceeds according to applicable IRB policies and procedures.

APPROVAL

This SOP entitled “Overview of QA Activities” has been approved by the Medical Center Director, effective 1/10/08.

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Appendix 1

Research Documents Which Are Subject to Audits by the ORC

1. All original informed consent forms signed by all subjects enrolled in the study.
2. Presence of the following in CPRS:
 - Enrollment note (informed consent note)
 - Scanned signed informed consent form
 - Research Subject Clinical Warning (if applicable)
3. All source documents (e.g. hospital/medical records, clinic/outpatient charts, research/study charts) for all subjects selected for audit.
4. Subject visit log, sign-in record, and/or office appointment book, if applicable.
5. Records of payment to subjects, if applicable.
6. Drug accountability records
 - Shipping and receipt records
 - Dispensing records
 - Final disposition records
 - 10-9012s
 - Documentation of compliance with the Research Methods Accountability Form
7. Device accountability records
 - Shipping and receipt records
 - Maintenance and storage records
 - Dispensing records
 - Final disposition records
 - Documentation of compliance with the ---- Attestation Form
8. Records of staff licensure, credentialing, education and training
9. Regulatory/Study Binder – Essential Documents
 - Protocol and all signed amendments
 - BRAAN protocol and supporting documents
 - Investigator's Brochure and/or package inserts
 - FDA Form 1571/1572 – original and all versions
 - Investigator/sub-investigator curricula vitae
 - Financial disclosure forms
 - Study personnel identification and delegation log
 - Subject screening and enrollment log
 - Subject identification roster
 - Informed consent form – original and all versions
 - CRF completion guidelines, if applicable
 - Study aids (e.g. exclusionary concomitant medications), if applicable
 - Advertisements, if applicable
 - IRB documentation (e.g. submissions, correspondence, approvals for protocols, amendments, informed consent forms, advertisements; SAE notifications; continuing reviews; membership lists)
 - Laboratory licenses
 - Laboratory normal values
 - Monitor sign-in log
 - Correspondence
 - SAE reports
 - Reports of protocol deviations/exceptions
 - DSMP plans and reports

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Appendix 2

Research Service SOPs

Available at the Research Service website:

www.maryland.research.va.gov

Research Service Audit Tools

Available through the Office of Research Compliance
X6512