

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

SOP# HRP 02.03

Approval Date: 4/10/08

AUDITING SOURCE DOCUMENT CHARTS

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

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Author	Jessica Mendoza		
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Approved	Leslie Katzel, R&D Chair	Approved R&D / Dennis Smith	
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Leslie Katzel, MD, PhD
Chair, R&D Committee

Date

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AUDITING SOURCE DOCUMENT CHARTS

OBJECTIVE:

- To ensure that essential segments of source documentation (accuracy of screening activities, inclusion/exclusion criteria, compliance with dosing regimen of study entity, adverse event reporting) are routinely monitored by Research Service staff who have no active role with the study(ies) in question.
- 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 subjects/studies.
- To educate staff in: good documentation skills, understanding the role of source documents as they apply to good clinical practices (GCP's), organization of source documents charts, etc.
- To document internal quality assurance activities regarding source documents of studies conducted by VAMHCS investigators and staff.

SCOPE:

The Research Service requires that all VAMHCS research units and investigators who conduct research protocols must have measures to assure compliance to research protocols and to subject protection regulations. The Research Service has designated its Office of Research Compliance (ORC) to oversee quality management activities of VAMHCS investigators and programs. The ORC will focus its attention on matters that directly impact human participants' rights and safety (such as informed consent, eligibility criteria and adverse event reporting) and regulatory compliance. In this plan, audits will be triggered by specific circumstances (SOP #HRP 02.02, "Audit Triggers").

One type of audit that can be triggered is a source documents and research chart audit. This type of audit can be undertaken for routine quality management purposes or can be part of a for-cause audit. Source documents/research chart audits are conducted by Research Compliance Specialists (RCS) of the ORC.

RESPONSIBILITIES:

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- 1 The Principal Investigator is responsible for:
 - establishing internal policies and procedures governing source documentation, internal auditing/monitoring, and GCPs;
 - ensuring that his/her staff complies with internal policies and procedures, VAMHCS SOPs, GCPs, and other applicable policies;
 - facilitating the efforts of staff in this process;
 - using their staff, Research Service staff, and external sources as resources for questions;
 - using the chart audit process as a learning tool to improve her/his “good clinical practices”.
- 2 The study coordinator is responsible for:
 - good source documentation,
 - maintaining complete and organized source document charts,
 - resolving errors and/or omissions as outlined in the chart audit report,
 - documenting the resolutions,
 - using their investigators, supervisors, Research Service staff, and external sources as resources for questions,
 - using the chart audit process as a learning tool to improve her/his “good clinical practices”.
- 3 The Research Compliance Specialist (RCS) is responsible for:
 - auditing the research activities of a VAMHCS investigator/staff based on audit triggers and according to the procedures outlined in this SOP;
 - following up on resolutions within approximately 2 weeks of the original chart audit report,
 - following up on these resolutions and giving a final sign-off to the chart,
 - acting as a resource to investigators/staff on GCP’s of source documentation,
 - reporting her/his findings to the Research Compliance Officer (RCO).

DOCUMENTS:

- Sample Audit Notification Letter (Appendix 1)
- Determination of Audit Sample (Appendix 2)
- “Documents Typically Subject to Audit” (Appendix 3)

SEE ALSO:

Research Service Guidance on Source Documentation (HRP 07.03G)

PROCEDURE:

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1. Audit triggers are identified and acted upon according to SOP# HRP 02.02, "Audit Triggers.
2. Routine (scheduled) spot audit
 - 2.1. As time and staffing allows, the RCS may perform one audit per week on a randomly chosen study of a VAMHCS investigator. Most likely, the selection of the investigator or study will be done through the audit triggers listed in HRP 02.02.
 - 2.2. The audit will usually be performed by an RCS, but may also be done by the RCO, delegates of the IRB, or other appropriate agents.
 - 2.3. The auditor will send a letter of notification to the PI and study coordinator informing them that their study has been selected for an audit (Appendix 1). They will be asked to reply to the ORC within three (3) working days to schedule the site visit within the subsequent two (2) week period. Although the auditor will work independently during the audit, it is essential for the PI and study coordinator to be available to answer questions during the audit and to attend the exit interview.
 - 2.4. Once the audit is scheduled, the auditor will contact the PI and study coordinator to obtain a list of subjects enrolled in the study. The auditor will randomly select 2-8 subjects depending on the size of the trial for source documentation review (see Appendix 2).
 - 2.5. The auditor will communicate with the PI/study coordinator finalizing the audit dates and the scope of the audit. This will include the list of subjects selected for source document review as well as a list of study documents that must be available for review during the audit.
 - 2.6. The auditor may conduct chart audits, regulatory document audits, inspections of investigators' internal policies and procedures and SOPs, and audits of compliance with Research Service/VAMHCS policies, procedures and SOPs. Documents subject to audit are listed in Appendix 3. The Research Service reserves the right to audit other documents as necessary for the type & situation of audit being conducted. The Research Service routinely inspects 100% of informed consent forms of any study audited.
 - 2.7. The auditor will use the forms and procedures outlined in #4 below.
 - 2.8. At the conclusion of the audit, an exit interview will be held with the PI, the study coordinator, and other research staff as needed, to review and

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clarify audit observations, answer questions from the research team, and collect feedback on the audit process. .

2.9. Corrective action plans (CAP) (if any are necessary) should be completed within the subsequent two (2) weeks. The auditor will conduct follow-up assessments as needed until the plan is completed and signed off by the RCO/RCS. Further details can be found in the applicable specific audit SOPs.

2.10. Reports will go to the PI, the RCO and, through the RCO, the R&D Committee, the ACOS/R&D, the COS, EPIC, the Medical Center Director, the UMB IRB, and regulatory agencies if necessary. The PI's Division Chair/Section Chief is also made aware of audit results. The PI and the Division Chair/Section Chief, the IRB and other institutional officials will be notified in writing if there is a possibility of inspection by regulatory authorities. See item #5 below for details about the Final Audit Report.

2.11. Original audit sheets, notes and reports are filed in the ORC.

3. For-cause audits

3.1. For-cause audits can be generated by the findings of routine audits (e.g. the audit finds cause for deeper scrutiny and problem-solving) or by audit triggers described in SOP # HRP 02.02, "Audit Triggers".

3.2. There is a possibility that the audit can expand beyond the initial trigger if findings reveal deeper or additional areas of concern.

3.3. The RCS, the RCO, or other appropriate person performs the audit.

3.4. Little prior notice is given to the investigator or study coordinator.

3.5. Based on initial complaints/reports or findings of potential risk of injury to participants, the RCO may recommend to the HRPO that the study be suspended pending the conclusion of the audit. Only the IRB may suspend a study; however, the R&D Committee may decide to suspend the VAMHCS research activities (with notification to the IRB).

3.6. The auditor first assesses the basic problem/complaint. It is possible that an exhaustive root cause analysis will not be necessary if the investigator/staff have already identified and activated remedial actions, if the problem/complaint does not appear to be study/staff related, if the problem/complaint does not appear to be institutionally related, if the problem/complaint does not appear founded in fact, or if there does not

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appear to be noncompliance. The RCO makes this determination and includes it in summary reports to the RDC, the COS and the ACOS/RD.

- 3.7. If there appears to be reason for a thorough audit, an audit plan is specifically designed to examine the area of concern and a root cause analysis is performed. This audit plan may necessitate the development of specific audit tools. Risk Management may be included as an audit agent or as a second prong in the audit approach.
 - 3.8. Up to 100% of charts may be subject to audit.
 - 3.9. The RCS may conduct chart audits, regulatory document audits, inspections of investigators' internal policies and procedures and SOPs, and audits of compliance with Research Service/VAMHCS policies, procedures and SOPs. Documents subject to audit are listed in Appendix 3. The Research Service reserves the right to audit other documents as necessary for the type & situation of audit being conducted.
 - 3.10. At the conclusion of the audit, an exit interview will be held with the PI, the study coordinator, and other research staff as needed, to review and clarify audit observations, answer questions from the research team, and collect feedback on the audit process. If necessary, the PI will be required to develop corrective action plan(s) (CAP), will work with the auditor or ORC to develop a CAP, or will be mandated to comply with the CAP developed by the HRPO (if applicable).
 - 3.11. The Resolution Plan should be completed within the subsequent two (2) weeks. The RCS will conduct follow-up assessments as needed until the Plan is signed off. Further details can be found in the applicable specific audit SOPs.
 - 3.12. Reports will go to the PI, the RCO and, through the RCO, the R&D Committee, the ACOS/R&D, EPIC, the Medical Center Director, the IRB, and regulatory agencies if necessary. The PI's Division Chair is also made aware of audit results. The PI and the Division Chair will be notified in writing if there is a possibility of inspection by regulatory authorities. See item #5 below for details about the Final Audit Report.
 - 3.13. Original audit sheets, notes and reports are filed in the ORC.
4. The audit process is outlined below. The process is similar whether for a "spot audit" or a "for cause audit".

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- 4.1. The RCS obtains selected charts from the PI/study coordinator and initiates a source documents audit. (audit tools are available at the Office of Research Compliance).
- 4.2. The RCS examines the source document chart and completes any sections of the source documents audit tools that apply.
- 4.3. The RCS examines the following documents and compares them against each other in order to detect errors, inconsistencies and omissions:
 - Time-Event Sheets (or similar document) for completeness, notations, inconsistencies with other source documents.
 - Progress Note detailing the informed consent process, the state of mind of the subject (competency), and the timing of the consent (prior to any study procedures).
 - Signed informed consent form
 - Lab reports, medical history, documentation of other measurements or test results necessary for inclusion/exclusion determinations.
 - Medication orders, medication records, progress notes or other documentation of compliance with study drug schedule.
 - Adverse Event (AE) report sheets, progress notes or other documentation of AE's (especially SAE's), interventions and sequelae.
 - Progress notes, internal comments sheets or other documentation of study events, subject compliance, reasons for protocol deviations, unexpected events, and relevant communications with sponsor/PI, etc.
 - Deviation Sheets or other lists of exceptions to the study protocol
 - Internal communications sheets
- 4.4. If a document is misfiled within the source documents chart or takes more than several minutes of the auditor's time to locate within the source documents chart, the auditor may list it as missing. If a particular document needs to be filed in an unusual place, the study coordinator informs the auditor of where the document may be found and files a memo documenting the location.
- 4.5. If a problem is identified, the auditor lists it in the audit report template or in QA notes. Preliminary audit findings are shared with the investigator or staff so that corrective action plans can be initiated as necessary. The auditor schedules a follow-up review of the CAP for approximately two weeks from the date the CAP is developed.
- 4.6. The auditor retains the original audit tools and QA notes.
- 4.7. A draft audit report is written and processed as in section 5 below.

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5. Formal reports will be processed as follows:
 - 5.1. Observations will be listed in the audit report by category (e.g. Informed Consent Process, inclusion/exclusion criteria, UPR reporting, regulatory documentation, etc.) in order of decreasing significance, such that the most significant category of observations will be listed first, and within each category, the most significant observation will be listed first.
 - 5.2. The audit report will also describe any resolution plan(s) and the compliance with or results of implementation of those plans.
 - 5.3. The draft report and all other audit documentation will be forwarded to the RCO for review and approval.
 - 5.4. The final audit report will be presented to the R&D Committee, the ACOS/R&D, the COS, EPIC and the IRB. The report will also be forwarded to the PI/study coordinator and the Division Chair/Section Chief with the addition of comments from the oversight committees. If applicable, the PI will be asked to respond to issues raised by the committees.
 - 5.5. Follow-up discussions, documentation, reports and letters will occur as necessary until the issue(s) are resolved to the greatest extent possible.
 - 5.6. The Full Audit report will summarize all of these developments and will be forwarded to the entities listed in 2.10 and 3.12 above.
 - 5.7. If necessary, regulatory agencies such as ORO, OHRP, the FDA, etc., will be notified (see HRP 01.08). The PI and the Division Chair/Section Chief will be notified in writing if regulatory authorities have been notified.

APPROVAL

This SOP entitled "Overview of QA Activities" has been approved by the Medical Center Director, effective 4/10/08.

Appendix 1

Template of “Audit Notification Letter”

This is a SAMPLE and is subject to change

VAMHCS HUMAN RESEARCH PROTECTION
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VAMHCS Research Service
Office of Research Compliance

[Date]

Dear [Investigator name]:

Your protocol entitled [protocol title] has been selected for a quality control audit for the following reason(s):

- _____
- _____
- _____

Please contact me at [phone number / email address] by [date, within 3 days of receipt of notification] in order to schedule a site visit to occur within 2 weeks of your receipt of this letter.

Although I will work independently during the audit, it will be necessary for you and/or your study coordinator to be available to answer questions during the visit and to attend the exit interview.

I will need to look at the [following documents / attached list of documents]:

- study files of the following subjects: _____
- regulatory documents files
- SAE reports
- protocol exception/deviation reports
- DSMP reports
- study drug disposition documents (inventory, dispensing log, RMAF, _____)
- device or equipment logs and disposition documents
- training files of research staff
- _____
- _____

The Research Service reserves the right to have access to other documents as necessary.

Thank you for your cooperation.

[signature]

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Appendix 2

Determination of Sample Size for Random Audit

Study Size	# Subjects Enrolled	Audit Sample
Small	0-10	1-2
Medium	11-25	3-4
Large	26-40	5-6
Very Large	40-100	7-8

For studies involving >100 subjects, the auditor will use discretion as to how many subjects to audit.

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Appendix 3

Research Documents That 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