SOP# HRP 02.02
Approval Date: 01/08

AUDIT TRIGGERS

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

Version	2.1	Origin	Version 2.0
Author	Jessica Mendoza		
Reviewed/ Revised by	Jessica Mendoza	Dates Reviewed / Revised	4/16/08
Changes	Changes in Procedures 1, 3.2.3, 3.2.7, 3.2.11, 3.3.5, 3.7, 4.4 New items 3.2.6, 3.3.6.1, 3.6.4	New Version #	2.1
Approved	Leslie Katzel, R&D Chair 5/8/08	Approved R&D / Dennis Smith	5/8/08
File Name	\Audit Triggers (HRP 02.02) 2008.2.1		

This amended version (2.1) was approved by the Chair, R&D Committee, / R&D Committee on 5/8/08.

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

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AUDIT TRIGGERS

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 instigate changes in procedures to prevent problems in future studies/research programs.
- To educate staff in the VAMHCS Quality Management Plan specifically and good clinical practices (GCP's) in general.
- To document internal quality assurance activities of the VAMHCS Research Service.

SCOPE:

The Research Service requires that all VAMHCS research units and investigators must follow measures to assure compliance to the research protocol and to human subject protection regulations. These measures may be the unit's/investigators' own internal policies or may be the Research Service's, UMB's or other agent's policies which are adapted to the unit/investigator as necessary.

The Research Service has designated its Office of Research Compliance (ORC) to oversee quality management activities of VAMHCS investigators and research 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 ORC will not routinely include data integrity as an integral part of 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.

In this spirit, the Research Service has delineated specific "audit triggers" whose goal is to capture potential noncompliance, to remediate when noncompliance, error, or system-wide problems are discovered, and to educate our research community in proactively improving compliance with participant protections and protocol implementation.

RESPONSIBILITIES:

1. The Principal Investigator is responsible for:
    - Establishing internal policies and procedures to ensure compliance with VAMHCS SOPs, IRB SOPs, GCPs, and other human subject protection regulations;
    - Ensuring that his/her staff complies with these internal policies and procedures (P&Ps);
    - Facilitating the efforts of staff in this process;
    - Using staff, Research Service staff, and external sources as resources for questions;
    - Using Research Service SOPs and Standards (listed below) for specific guidance in these areas;
    - Using the chart audit process as a learning tool to improve her/his "good clinical practices".
2. The Office of Research Compliance (ORC)* 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 audit report;
    - Acting as a resource to investigators/staff on GCP's, program development, and internal and campus-wide policies and procedures;
    - Reporting findings to the R&D Committee, the Chief of Staff (COS), the Medical Center Director (MCD) and/or ACOS/R&D, EPIC, the IRB, and regulatory agencies if necessary.

   *Research Compliance Specialists (RCS) within the ORC carry out many of these functions.

DOCUMENTS:

- Sample Audit Notification Letter (Appendix 1)
- Determination of Audit Sample (Appendix 2)
- "Documents Typically Subject to Audit" (Appendix 3)
- Table of Contents of Research Service SOPs and Standards (Appendix 4)

SEE ALSO:

Research Service SOP	Overview of Quality Assurance Activities (HRP 02.01)
Research Service SOP	Auditing Source Document Charts (HRP 02.03)
Research Service SOP	Addressing and Responding to

	Research-Related Complaints, Comments and Suggestions Related to the Human Research Protection Program (HRP 01.07)
Research Service SOP	Addressing and Responding to Research-Related Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program (HRP 01.08)
Research Service SOP	Investigator Responsibilities for Internal Quality Assurance or Their Research Programs (HRP 02.04)
Research Service SOP	Auditing the Investigational Pharmacy (HRP 02.05)
Research Service SOP	Research Personnel Education & Training (Scope of Practice) (HRP 04.02)
Research Service	Human Research Protection Plan (HRP 01.02)
	Investigator Self-Assessments

PROCEDURE:

1. The 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 observer 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/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. The ORC will act upon the following audit triggers. Based upon the circumstances, most of these audits are subject to either routine or ‘for cause’ audits.
    - Routine (scheduled) spot and full audits
    - 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, psychiatric patients, persons with impaired decision-making)
- Reportable events - numerous or of interest
- 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 about the quality of IRB or R&D Submissions
- Ongoing concerns of IRB or R&D about document processing
- ACOS/AO/R&D, Chief of Staff, MCD, RCO, Department Chair, IRB Chair, or other has concerns
- Scheduled follow-ups to Resolution Plans
- Findings of routine or other audits disclose further issues to evaluate
- Systems audits, when audits, institutional reports, participant complaints or other feedback indicate that VAMHCS policies or procedures should be changed.

3. When audit triggers are identified, they are acted upon in the following ways:

3.1. Routine (scheduled) spot or full audit

3.1.1. As time and staffing allows, the RCS will perform several audits per month on randomly chosen studies of VAMHCS investigators. The RCS will aim for 4 spot audits per month and 1 full audit per quarter (30-50 audits per year), however, for-cause audits or other projects may take precedence. Most likely, the selection of the investigator or study will be done through the audit triggers listed above (#2).

3.1.2. 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.

3.1.3. The auditor or RCO 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.

3.1.4. 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 subjects depending on the size of the trial for source documentation review (see Appendix 2).

3.1.5. 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.

3.1.6. 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.

3.1.7. The auditor will adapt audit form templates and tools as needed to capture the information required by the scope of the audit.

3.1.8. 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 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) or will work with the auditor or ORC to develop a CAP.

3.1.9. The CAP should be developed within the subsequent two (2) weeks. The auditor will conduct follow-up assessments as needed until all issues are resolved and signed off by the RCO/RCS. Further details can be found in the applicable specific audit SOPs.

3.1.10. The RCS writes a final report which is sent to the PI, the RCO and, through the RCO, the R&D Committee, the MCD and/or ACOS/R&D, EPIC, the IRB, and regulatory agencies if necessary. The PI's Division Chair may also be 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 #4 below for details about the Final Audit Report.

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

3.2. <u>For-cause audits</u>

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

3.2.2. For-cause audits can be generated by the findings of routine audits (3.1 above), or by several of the audit triggers listed above (#2).

3.2.3. Any egregious or possible investigator/staff misconduct, noncompliance, or incompetence automatically triggers a for-cause audit.

3.2.3.1. A death of a participant that may possibly be study-related or related to noncompliance or incompetence of the investigator/staff, and thus triggers a for-cause audit.

3.2.3.2. Audits that are performed due to a suspicion of or allegation of noncompliance trigger the Research Service procedures delineated in HRP 01.08. As part of that process, the HRPO is immediately notified and proceeds according to applicable IRB policies and procedures.

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

3.2.5. Minimal prior notice is given to the investigator or study coordinator.

3.2.6. 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).,.

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

3.2.8. If there appears to be reason for a full audit, the RCS designs an audit plan that is specific to the area of concern and that attempts to find a root cause for any problems found. This audit plan may necessitate the development of specific audit tools. VAMHCS Risk Management may be included as an audit agent or as a second prong in the audit approach.

3.2.9. Up to 100% of charts may be subject to audit.

3.2.10. The RCS conducts 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.

3.2.11. 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.

3.2.12. The CAP should be developed within the subsequent two (2) weeks. The auditor will conduct follow-up assessments as needed until all issues are resolved and signed off by the RCO/RCS. Further details can be found in the applicable specific audit.

3.2.13. Reports will go to the PI, the RCO and, through the RCO, the R&D Committee, the MCD and/or ACOS/R&D, EPIC, 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 #4 below for details about the Final Audit Report.

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

3.3. <u>Principal Investigator/study personnel request</u>

3.3.1. Principal Investigators (PIs) or their staff may request audits of their studies or program at any time. This may be done as a way for them to assess their programs, as a way to address a perceived problem, or for other reasons.

3.3.2. The actual process of the audit will depend on the reason for the request. For example, a "Routine Audit' would be appropriate for a general assessment of the study or program, but a "For-Cause Audit" might be more appropriate for a perceived problem.

3.3.3. The audit will usually be performed by the RCS, but may also be done by the RCO, delegates of the IRB, or other appropriate agents.

3.3.4. Audits are performed in the spirit of strengthening or improving the research practices of investigators and staff. However, if problems are uncovered, corrective action plans (CAPs) and reporting must occur

3.3.5. Reports will go to the PI, and, through the RCO, the R&D Committee, the COS, the MCD, the ACOS/R&D, EPIC, the 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 will be notified in writing if there is a possibility of inspection by regulatory authorities. See item #4 below for details about the Final Audit Report.

3.3.6. Investigators should not completely depend on this mechanism as their internal quality control, as the ORC cannot guarantee this service if staff is unavailable.

3.3.6.1. HRP 02.04 "Investigator Responsibilities for Internal Quality Assurance or Their Research Programs" describes the expectations and procedures to be followed by investigators and staff.

3.4. Investigator initiated studies

3.4.1. The goal of the audits is to determine whether or not studies are being conducted properly and participants' safety and rights are being protected.

3.4.2. A "Routine Audit' would be appropriate for a general assessment of the study or program, but a "For-Cause Audit" might be more appropriate for a perceived problem. The audit procedure will follow #3.1 or #3.2 above, whichever applies.

3.4.3. The RCS will check for the presence and adequacy of the investigator's internal policies and procedures.

3.4.4. The RCS will pay special attention to the Data Safety Monitoring Plan, and the activities and reports generated by the DSMP (i.e. compliance with the DSMP).

3.4.5. The RCS will audit investigator/staff compliance with their policies and procedures, if they exist.

3.4.6. The RCS may audit charts, regulatory documents, RMAFs, reports, and other documents, as applicable (see Appendix 3 and applicable SOPs).

3.4.7. Resolution plans and audit reports will be done according to #3.1.8-3.1.10 or 3.2.11-3.2.13 above.

3.5. PI's with high numbers of protocols

3.5.1. The goal of the audits is to determine whether or not studies are being conducted properly and participants' safety and rights are being protected.

3.5.2. An assessment will be made of the staffing level of the investigator's research staff (number/size/complexity of protocols per research coordinator, turnover of staff, support services available to staff, etc.) as well as the amount of work expected of staff that is "indirect" to study conduct (IRB submissions/reports/ communications, internal QA activities, developing/enforcing policies & procedures, SOPs, etc.).

3.5.3. Routine audits will usually occur as in #3.1 above unless other triggers are in play or there is reason for for-cause audits (#3.2 above).

3.5.4. Section 3.4 may also apply.

3.5.5. Resolution plans and audit reports will be done according to #3.1.8-3.1.10 or 3.2.11-3.2.13 above.

3.6. PI's with vulnerable populations (elderly, children, psychiatric patients, persons with impaired decision-making capacity)

3.6.1. The goal of the audits is to determine whether or not studies are being conducted properly and participants' safety and rights are being protected.

3.6.2. Routine audits will usually occur as in #3.1 above unless other triggers are in play or there is reason for for-cause audits (#3.2 above).

3.6.3. Section 3.4 may also apply.

3.6.4. Special attention will be paid to recruitment activities and the informed consent process.

3.6.4.1. Only IRB- and RDC-approved recruitment and consent procedures may be used.

3.6.4.2. For decisionally impaired participants, there must be documentation in CPRS by independent medical staff as described in HRP 03.03.

3.6.4.3. The LAR must conform with VA requirements (HRP 03.03).

3.6.5. Resolution plans and audit reports will be done according to #3.1.8-3.1.10 or 3.2.11-3.2.13 above.

3.7. Reportable Events - numerous or interesting

3.7.1. By using their "read-only" status in BRAAN, the RCS/RCO routinely reviews investigator reports to the IRB. The RCO/RCS also regularly attend IRB meetings as non-voting observers. In these ways, internal (VAMHCS protocols/investigators) adverse events and serious adverse events can be monitored on a timely basis.

3.7.2. Using BRAAN, the RCO can obtain prompt, independent expert review of the nature of unanticipated problems involving risk to participants or others (UPR).

3.7.3. Too many, unusual/unexpected, or very serious UPR may initiate routine or for-cause audits.

3.7.4. Particularly egregious or possible investigator/staff misconduct, noncompliance, or incompetence resulting in a UPR triggers a for-cause audit performed and reported as in 3.2 above.

3.7.5. Resolution plans and audit reports will be done according to #3.1.8-3.1.10 or 3.2.11-3.2.13 above.

3.8. Research participant/family member complaint

3.8.1. During the informed consent process, research participants should be told of their recourse for filing complaints about the investigator, staff or conduct of the study. The UMB IRB requires language in the informed consent form (ICF) giving the contact information for the IRB. In addition, VAMHCS studies are required to have a VAMHCS contact and phone number on the ICF. Complaints from research participants, family or research staff are directed to the ORC. If the IRB receives complaints regarding a VAMHCS study or investigator, the IRB forwards the complaint to the ORC. See SOP #01.07, "Addressing Research Subject or Research Personnel Complaints/Concerns", for further details.

3.8.2. Depending on the focus of the complaint, a for-cause audit is generated (see item #3.2).

3.8.3. Resolution plans and audit reports will be done according to #3.2 above. It is possible that the complainant(s) will also be present at resolution meeting(s). If necessary, hospital counsel, the IRB, and others may also be present at resolution meetings and in finalization of reports.

3.8.4. Unless the complainant(s) has withheld his/her contact information, the complainant(s) will receive communication from the ORC describing the outcome of the investigation as outlined in SOP 01.07 or 01.08.

3.9. Participant death

3.9.1. Unexpected death of a participant triggers an assessment by the ORC of the precipitating causes of the death and whether the death is potentially related to the study agent or procedures.

3.9.2. If the death appears to be related to the study or to actions of research or general hospital staff, a for-cause audit is triggered (3.2) and a root cause analysis is conducted.

3.9.3. Resolution plans and audit reports will be done according to #3.2.11-3.2.13 above.

3.10. Appearance of lack of staff support/resources/high staff turnover

3.10.1. See section 3.5.

3.11. Lapses in continuing review/studies administratively closed by IRB

3.11.1. The RCO monitors the IRB status of VAMHCS studies by attending IRB meetings and monitoring VAMHCS activities via BRAAN. Additionally, the IRB notifies the ORC of lapsed or problem studies.

3.11.2. A for-cause assessment will be done as in #3.2.

3.11.3. Resolution plans and audit reports will be done according to #3.2.11-3.2.13 above.

3.12. Ongoing concerns about the quality of IRB or R&D submissions

3.12.1. See 3.11 above.

3.13. Ongoing concerns of IRB or R&D about document processing

3.13.1. See 3.11 above.

3.14. ACOS/AO/R&D, Chief of Staff, VA/Director, VA/Administrator/Department Chair, IRB Chair has concerns

3.14.1. See 3.11 above.

3.15. Scheduled follow-up to routine or other audits

3.15.1. At the end of an audit, the auditor writes an audit report.

3.15.2. Any audits that have resulted in problems needing resolution are revisited approximately two weeks after the report has been delivered to study staff.

3.15.3. Study staff is expected to have resolved the problems according to the resolution plan that was negotiated. Additionally, the PI is expected to have signed off on the audit and resolution.

3.15.4. Prolonged or continued failure to resolve the problems according to the resolution plan will be reported to the RCO.

3.15.5. Ideally, results of the resolution plan will be evident and available for reporting in the Final Audit Report.

4. Reports will be processed as follows:

4.1. Observations will be listed in the audit report by category (e.g. Informed Consent Process, inclusion/exclusion criteria, SAE 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.

4.2. The audit report will also describe any resolution plan(s) and the compliance with or results of implementation of those plans.

4.3. The draft report and all other audit documentation will be forwarded to the RCO for review and approval.

4.4. 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 with the addition of comments from the oversight committees. The Division Chair/Section Chief will also be apprised of audit results. If applicable, the PI will be asked to respond to issues raised by the committees.

4.5. Follow-up discussions, documentation, reports and letters will occur as necessary until the issue(s) are resolved to the greatest extent possible.

4.6. The Full Audit report will summarize all of these developments and will be forwarded to the entities listed in 4.5 above.

4.7. If necessary, regulatory agencies such as ORO, OHRP, the FDA, etc., will be notified. The PI and the Division Chair/Section Chief will be notified in writing if regulatory authorities have been notified.

APPROVAL

This SOP entitled “Audit Triggers” has been approved by the Medical Center Director, effective 1/10/08.

Appendix 1

Template of "Audit Notification Letter"

This is a sample letter. The format is subject to change.

Date
PI
Assistant Professor:
Location:
Bldg.: (if applicable)
VAMHCS or UMMC
Address
City, STATE , zip code

Re: H# -Protocol title

Dear [PI's name],

This letter is to confirm that your site has been selected for a Clinical QA audit by the VA Maryland Health Care System Research Service. The studies to be evaluated include IRB protocols:

The audit has been scheduled to begin on [DATE]. As discussed with the study coordinator,[SC NAME] approximately [TIME]on [DAY/DATE] to begin the audit. The audit will be based on protocol compliance, federal regulations, and ICH GCP guidelines. It will include the following:

- Introductory meeting with you and your research staff to discuss the purpose of the audit and the organizational aspects and conduct of the trial.
- Inspection of the facilities, including storage and availability of all medical/research/study records, special equipment required by the protocol (if applicable), drug/device storage area (e.g. hospital pharmacy), laboratory facilities, and biological sample storage area (if applicable).
- Review of study documentation (see enclosed list).
- Review of original signed informed consent forms for all subjects screened for the study.
- Review of the source documentation vs. case report forms for a random selection of VA study subjects
- Exit interview with you and the research staff to discuss the audit observations.

I plan to work independently during the audit, with as little disruption to you and your research staff as possible. However, it is important that you, the study coordinator(s), and/or another knowledgeable research staff member be available to answer questions during the audit.

Thank you in advance for your time and effort in preparation for the audit, and in accommodating me for this inspection. I look forward to meeting you and your staff. If you have any questions, please do not hesitate to contact me.

Regards,

Research Compliance Specialist

cc: Program Manager, Human Protections Administrator
VAMHCS Research Compliance Officer

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
	40-100	7-8
	>100	10%

Appendix 3: 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

Appendix 4

Table of Contents of Research Service SOPs and Standards

Available on the Research Service website;
www.research.maryland.va.gov