RESEARCH COMPLIANCE AUDIT PLAN

South Texas Veterans Health Care System
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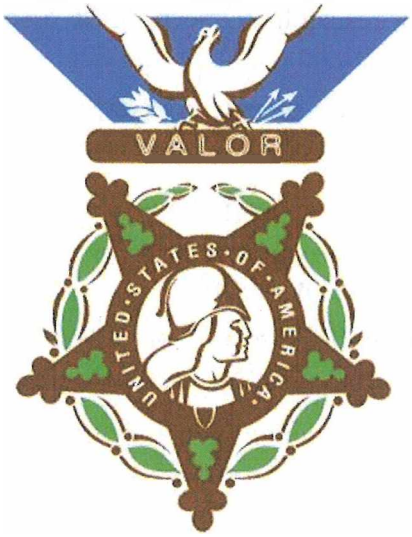
South Texas Veterans Health Care System

Department of Veterans Affairs



STANDARD OPERATING PROCEDURES

MARCH 1, 2015

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As a public agency, Veterans Health Administration (VHA) has an obligation to preserve public trust in the integrity and quality of research carried out by its investigators, involving subjects in VA research, and in its facilities. The Research Compliance Program is an integral part of the South Texas Veterans Health Care System's (STVHCS) commitment to the improvement of the quality and integrity of research activities. Compliance monitoring will provide internal oversight on quality and compliance issues relating to the performance of human, animal, and science-safety research through observing trends and providing educational activities to all individuals involved in research.

PURPOSE

To establish auditing and reporting policies and procedures governed by the VHA Office of Research Oversight (ORO) and the VHA Office of Research and Development (ORD) and administered by the STVHCS Office of Research Compliance. For purposes of this Audit Plan, the administration of the Research Compliance Program shall be known as the Office of Research Compliance (ORC).

This Audit Plan defines the procedures and audit tools utilized in research compliance monitoring as a mechanism to provide internal oversight on quality and compliance issues with regards to the performance of research activities relative to the protection of human subjects, laboratory animal welfare, research safety, research laboratory security, research information protection, and other areas under the jurisdiction of the VHA Office of Research Oversight.

RESEARCH COMPLIANCE PROGRAM OVERVIEW

The ORC is charged with the oversight of all research compliance issues identified through its auditing activities and allegations of non-compliance within Human Research Protection Program (HRPP). Research compliance activities are reported to the Research and Development Committee (R&DC) and relevant subcommittees that include: the Institutional Review Board (IRB), the Institute of Animal Care and Use Committee (IACUC), and the Subcommittee Research Safety Committee (SRS).

The ORO provides guidance on VA policies and regulations, and auditing tools regarding ORC's audit requirements. These documents are issued prior to each new auditing cycle and set forth the requirements for ORC auditing each year. These documents include definitions, type and frequency of audits to be completed within a specified timeframe.

The Research Compliance Officer (RCO) is responsible for the development, implementation and activities of the Research Compliance Program at STVHCS. The RCO reports directly to the Medical Center Director (MCD) and holds a permanent, full-time position. The ORC activities are independent of the Research and Development Service and the research studies under its purview.

PRINCIPAL INVESTIGATOR RESPONSIBILITIES

1. Conduct the study according to the most recently approved version of the protocol.

2. Ensure research staff is qualified to perform procedures assigned to them during the study (current training, WOC/IPA, credentialing, scope of practice).

3. Use the most recently approved version of the ICD and HIPAA Authorization.
4. Maintain all copies of submissions to oversight committees.
5. Maintain approval letters and emails, from all applicable oversight committees.
6. Initiate study after receiving a written notification from the ACOS/R&D and the R&DC Chair that the study has been approved by all relevant oversight committees.
7. Document inclusion/exclusion criteria eligibility.
8. Obtain consent prior to initiating study procedures.
9. Document study consent process in CPRS (unless instructed otherwise by IRB).
10. Maintain a Master List or subject log of all subjects, if applicable (unless waived by IRB)
11. Maintain copies of drug logs, if applicable.
12. Document and report SAEs, if applicable.
13. Respond in a timely manner to requests from ORC for auditing or minor corrections.

AUDIT PROCESS

Auditing is one of the primary functions of the ORC and is a mechanism to evaluate VA's research program and, when appropriate, identify areas for corrective action. STVHCS' research compliance auditing shall provide reasonable assurance of the integrity of the research program; and that adequate protections of human subjects in research, safety of personnel conducting laboratory and clinical studies, laboratory security research information protection, and laboratory animal welfare are in place. Please refer to the following appendices for specific process details.

1. Appendix A – Informed Consent Audits
2. Appendix B – Triennial Regulatory Audits
3. Appendix C – Animal Welfare Audits
4. Appendix D – Research Safety Audits

INFORMED CONSENT AUDITS

Informed consent audits of all **active human** research studies must be performed **each year** (i.e., annually, during the June 1st – May 31st reporting period) and require in every case a confirmation of the administrative data on the ORO informed consent audit tool, the most recent continuing review by the IRB or R&DC, as well as a review of subjects' signed VA informed consent documents, where applicable, and HIPAA authorization documents, where applicable.

1. **Studies to be audited.**
   All human research studies **active at any time** during the reporting period must receive an informed consent audit, whether or not any ICDs were required or signed during the reporting period.

2. **IRB-exempt studies.**
   The annual informed consent audit requirement includes human studies determined to be exempt from IRB review. The audit requirement for exempt human research is fulfilled by completing or re-confirming the administrative data section of the ORO informed consent audit tool (or locally-modified equivalent). The box for "Exempt" will be checked and the auditor will confirm that the R&DC has performed initial and/or continuing reviews as required by VA policy for any active study that is not followed by any other research oversight committee.

3. **Studies overseen by the IRB with no Informed Consent Documents signed during the audit period.**

   If an active human study has no informed consent documents signed during the period being audited, the audit requirement will be fulfilled by completing or re-confirming the administrative data section of the ORO informed consent audit tool. The reason there are no informed consent documents to audit will be noted. This may be because informed consent was waived by the IRB, or the documentation of the informed consent was waived by the IRB, or because informed consent documents were approved but no subjects were accrued or re-consented during the period being audited. The auditor will also note whether continuing review of the study occurred as required by VA policy.

4. **Informed Consent Documents to be audited.**

   a. Initial audits of studies must include all informed consent documents and HIPAA authorizations obtained since study initiation. Studies initiated during this period will have an informed consent audit during this period even if no subjects have yet been consented.

   b. Audits of studies that **were** audited previously will include all informed consent documents and HIPAA authorizations obtained since the **previous** audit. This includes re-consents, if any.

   c. If either documentation of informed consent or documentation of HIPAA authorization but not both has been waived by the IRB, all documentation that is not waived will be audited.

5. **Studies completed during the reporting period.**
   A final informed consent audit will be conducted for any study that is active for any part of the audit period, even if it becomes completed during the current period. A study audited during the reporting period will require a supplemental audit if the study is completed before the end of the reporting period and additional informed consent documents are obtained after the audit. If no additional informed consent documents are obtained, then the study audit already performed during the period is sufficient.

6. **Million Veteran Program (MVP).**
The MVP process includes extensive control measures to detect and correct deviations from the expected outcomes for informed consent and HIPAA documents. These processes are similar to the manual auditing review that is performed for the informed consent forms for all other VA human subjects research.

    a. ORO requires auditing 10% of informed consent documents and HIPAA authorizations each month of enrolled Veterans in the local MVP. MVP informed consent documents and HIPAA authorizations will be audited during a recurring monthly meeting with the study coordinator.

        i. In preparation for the monthly audit the auditor will obtain a list of Veterans enrolled in the MVP each month since the last audit session.

        ii. Subjects will be randomly identified prior to initiating the audit.

        iii. The auditor will not record any PHI at any step of the auditing process. Only protocol subject numbers will be recorded for the audit.

        iv. **Deficiencies identified**. If any deficiencies are identified, a repeat audit of that Veteran's documents will be performed 2 weeks later to determine whether the deficiency has been corrected by the MVP quality control process.

    b. The RCO or designee shall prepare and submit a quarterly MVP report to ORO that will include data from the preceding quarter of the auditing period. ORO will send an email reminder with the attached MVP report form for submission.

REGULATORY AUDITS

1. **Regulatory audits required for research overseen by the IRB using ORO's Human Research Protection Program (HRPP) audit tool.**

    Regulatory audits of human research studies will be performed at least **every 3 years** (i.e., triennially). Initial audits with the HRPP tool must be no later than 3 years from initial approval as VA research by the R&D Committee. Subsequent audits with the HRPP tool must be completed no later than 3 years from the previous HRPP audit.

    a. **HRPP audits required.**
    All active human research studies overseen by the IRB will receive at least one HRPP audit using ORO's HRPP audit tool, to include completion of an informed consent audit (as described in the aforementioned Informed Consent section of this document).

    b. **Human research followed by the IRB but initiated (i.e. approved for implementation by the R&DC as a VA study) prior to January 1, 2008.**

Regulatory HRPP audits are required for studies that involve interaction or intervention with human subjects that were initially approved prior to January 1, 2008 **and** remain open to enrollment as of May 31, 2014.

2. **Circumstances where HRPP audits are not required.**
   Regulatory HRPP audits of the following studies overseen by the IRB are not required, even at study closure:

   a. **Closure HRPP audits are not required after an initial HRPP audit.** Any human research protocol that has already had at least one HRPP regulatory audit and is completed and/or closed to oversight by the IRB less than 3 years after an HRPP audit does not require a final HRPP audit at closure. However, any research followed by the IRB that is closed to oversight by the IRB within less than 3 years will have at least one HRPP audit. If no HRPP audit has been done prior to closure by the IRB, then an HRPP audit will be done within the reporting period in which IRB oversight is completed.

   b. **Repeat HRPP audits for previously-audited research not required for certain studies.** Once a protocol has had at least one HRPP regulatory audit, additional HRPP regulatory audits are not required, even at study closure, for the following types of studies determined by the IRB to involve no more than minimal risk:

      i. **Chart Review studies.** Once a protocol has had at least one HRPP regulatory audit, additional HRPP regulatory audits are not required for studies solely involving chart reviews.

      ii. **Studies in Data Analysis and/or Long-Term Follow Up.** Once a protocol has had at least one HRPP regulatory audit, additional HRPP regulatory audits are not required for studies **that satisfy 1 or 2 below:**

         1. Where 1) the research is permanently closed to the enrollment of new subjects; and 2) all subjects have completed all research-related interventions; and 3) the research remains active only for long-term follow-up of subjects; or

         2. The remaining research activities are limited to data analysis.

      iii. **Abbreviated HRPP audits.** If a human research study is opened and completed at a VA research facility without enrolling any subjects locally and before an HRPP audit is done, then the requirement for an HRPP audit may be satisfied in an abbreviated fashion by review and completing the administrative data only on the first page of the HRPP audit tool.

3. **Regulatory audits required for Animal Research overseen by the IACUC using ORO's Animal Welfare audit tool.**
   a. All active animal research studies overseen by the IACUC must be audited using ORO's Animal Welfare audit tool within 3 years of each triennial review. The

audit will include a review of the approved protocol submitted at the most recent triennial review.

b. **Closure audits are not required after an initial Animal Welfare audit.** Closure audits are not required for animal studies that have been audited at least once in the last 3 years. This is true even if the previous Animal Welfare regulatory audit occurred prior to the most recent triennial review.

4. **Regulatory Audits required for research overseen by the SRS using ORO's Research Safety audit tool.**
   a. Research studies overseen and reviewed annually by the SRS must have a regulatory audit with ORO's Research Safety audit tool at least every 3 years (i.e., triennially). Initial audit with the SRS tool must be no later than 3 years from initial approval as VA research by the R&DC. Except for certain animal research studies, subsequent audits with the SRS tool must be completed no later than 3 years from the previous SRS audit.

   b. VA research followed by the SRS generally falls into one or more of 3 categories: 1) Animal research also followed by the SRS; 2) certain human subjects research that involves exposure to blood or body fluids, human tissues, or other hazards; or 3) bench or laboratory research that involves hazards or safety concerns. For animal research that is also followed by the SRS the auditor may elect to perform the Research Safety audits in combination with the Animal Welfare audits and on the same schedule, i.e. within 3 years of each triennial IACUC review, even if this occasionally results in more than 3 years between the dates of consecutive Animal Welfare/Research Safety audits. All research overseen by the SRS should have Research Safety audits no less frequently than every 3 years, whether the Research Safety audits are combined with an HRPP audit or separate.

   c. The Research Safety audit should include review of the approved protocol and the identified hazards and safety concerns, as well as SRS actions and reported events occurring since initiation or the previous audit. When performing a Research Safety study, it is NOT necessary to record the same information (e.g., research staff training) on both audit tools.

   d. **Closure audits are not required after an initial Research Safety audit.** Closure audits are not required for studies that have been audited with the research safety tool at least once in the previous 3 years.

5. **No regulatory audits required for VA research overseen by the Research and Development Committee only.**
   a. Any VA research study that is overseen by the R&DC only and is not overseen by the IRB, IACUC, or SRS does not require a regulatory audit. VA research followed by the R&DC only may include human research exempt from IRB oversight, and also any study that does not involve human subjects, live animals, or any hazards or safety concerns. Any VA research that is overseen by the IRB,

the IACUC or the SRS will be audited with the relevant ORO regulatory audit tool.

b. Any **human** study determined to be **exempt** from IRB review and followed only by the R&DC does not require a regulatory. However, **informed consent** audits of IRB-exempt studies are required annually as described in paragraphs 1 and 2 of Informed Consent Audits.

FOR CAUSE AUDITS

"For Cause" audits are generally requested by the R&DC, any subcommittees, MCD, and/or ORO.

1. Criteria to determine if a "for cause" audit is warranted. The requirement to increase the frequency of audits or to audit specific aspects of the study can be based on such considerations as:

    a. Involvement of vulnerable populations

    b. Level of risk

    c. Phase I or Phase II studies

    d. Involvement of FDA approved drugs for which there has been a safety warning, or label change that indicates increased risk

    e. Issues of non-compliance

    f. Data breach

2. **When to do a For Cause audit**. For Cause audits are upon request and on a one-time basis. However, it may be deemed more frequent by the individual(s) noted in paragraph 1 of this section, (i.e. every 6 months).

3. **Timeframe for Performing a For Cause audit**. For Cause audits will be scheduled in accordance to a timeframe determined by the requesting authorized individual(s); or if no time is specified, within 2 weeks of the audit request, if possible.

AREAS TO BE AUDITED

The areas that may be audited include but are not limited to:

1. Informed Consent Document – each approved version, individuals authorized to obtain consent, completeness and compliance with federal and VA regulations

2. Documentation of informed consent in CPRS

3. Protocol Compliance

4. Compliance with applicable local, state and federal laws, regulations, and guidelines

5. Adverse event reporting
6. Inclusion and exclusion criteria
7. Waiver of informed consent
8. HIPAA compliant authorization
9. Waiver of a compliant HIPAA authorization and the required documentation by the IRB in the research file
10. Compliance with all data security and data use requirements
11. Compliance with all privacy and confidentiality requirements
12. Research subject's dispensing file in Research Pharmacy
13. Scope of practice and training requirements
14. Completeness of the study's regulatory binder
15. Adequacy of processes such as effectiveness of communication with all applicable committees, persons, and officials

IDENTIFYING AND SCHEDULING PROTOCOL AUDITS

1. At the beginning of each new audit cycle the Research Compliance Coordinator (RCC) will query ePromise and the local Research and Development (R&D) databases to identify all current active research protocols at that time. The RCO will independently query ePromise and the local R&D databases, and will identify all active protocols for the audit period that are due for a regulatory audit. A comparison of the queried reports of the RCO and RCC will ensure all protocols are captured accurately and appropriately. The RCO will identify all active protocols that require a regulatory audit and will disseminate accordingly. The RCC will apply updates accordingly to the Office of Research Compliance (ORC) database. A detailed report is generated reflecting a breakdown of each active protocol type, to include dates of when the last audit (by type) was completed and when the next (by type) audit is due.

2. The RCO will ensure that not less than one-third of all active protocols are audited every year. The list of research protocols identified for mandatory audits are provided to the Research Compliance Auditor (RCA) for scheduling and conducting. Typically all other mandatory audits are handled by the RCC; and the RCO as needed. Additional mandatory audits are identified throughout the audit cycle and assigned by the RCO or designee.

3. The RCA will review the report and will contact the PI or his or her designee to schedule time to coordinate and conduct an on-sight regulatory audit. Regulatory audits are generally scheduled at least 2 months prior to the protocol's continuing review due date

(reference requirements in Regulatory Audits section for all human and animal regulatory audits and Appendix B).

NEW INVESTIGATORS AND THEIR PROTOCOLS

1. At the beginning of each new audit cycle and throughout the year new protocols are identified. Specific focus is on protocols identifying studies where the principal investigator is new to the VA system and very likely does not have a project coordinator to assist him or her with the administrative requirements to conduct VA research. The goal is intended to be proactive in providing assistance to new investigators to help guide them through the plethora of required research documentation and to mitigate or eliminate any possible noncompliance issues that may arise.

2. The RCO will contact the new PI to discuss VA research compliance requirements and answer any questions or concerns that he or she may have. Follow-up meetings will be scheduled as needed.

MONITORING PROTOCOLS

1. Each month the Research Compliance Coordinator (RCC) compares the ORC database to the R&DC minutes to identify new and inactivated protocols; and updates to the database are made accordingly. Any protocols identified that require an audit, e.g. protocol closures, are added to the list of required audits and scheduled to be conducted.

2. Each month the RCC will monitor and review the minutes of the R&DC to identify studies that are new, closed, approved for continuing review, etc. to ensure accuracy of the ORC database. Closed studies are reviewed to identify whether any regulatory audit is needed if no regulatory audit was completed.

3. On a daily basis the RCC receives various documents via email from the IRB. Each document is reviewed and compared to the R&D files. Documents that are identified as a new protocol are printed and placed in a pending file until the new protocol is reflected in the R&D database and is matched to an existing R&D file. Documents that are identified and matched to an existing protocol are verified with the R&D file, but are not printed.

AUDIT REPORTING

1. At the completion of every audit, a written audit report is provided to the PI, to include if any findings (or no findings) were identified; along with a copy of the completed audit tool(s) used. Copies of the audit report are also provided to the chairs of the IRB, R&DC, IACUC and SRS committees and the ACOS-R.

2. On a monthly basis a written summary of all completed audits for the previous month is provided to the R&DC for inclusion into the committee minutes. The summary includes a list of each protocol audited for the reported month. The RCO regularly attends the R&DC monthly meeting and provides an oral report of the previous month's auditing activities.

3. The RCO will annually provide a written summary report to the R&DC of all auditing activities performed for the entire audit period.

4. **Apparent non-compliance.**
   Reports or allegations of apparent non-compliance identified through or reported to the ORC will be investigated, and if confirmed, appropriate corrective actions will be taken. Corrective actions will be appropriate to the nature and the degree of non-compliance. All apparent non-compliance issues will be reported to the MCD, IRB, R&DC and ORO within 5 business days of discovery and in accordance with VHA Handbook 1058.01.

REMEDIAL ACTION

1. The relevant research review committee is responsible for determining the appropriate remedial action(s) in response to identified noncompliance and for verifying that the remediation is implemented as required.

   a. Except in extraordinary circumstances, remedial actions related to specific research projects will be completed within 90-120 days of the research subcommittee's determination of noncompliance.

   b. Except where remediation requires substantial renovation, fiscal expenditure, hiring, legal negotiations, or other extenuating circumstances, remedial actions related to programmatic noncompliance must be completed within 120-180 days of the research subcommittee's determination.

2. The PI is responsible for implementing the required corrective action(s) as determined by the relevant research review committee.

   a. Reports or allegations of apparent non-compliance identified through or reported to the ORC will be reported by and followed through by the ORC.

   b. Reports or allegations of apparent non-compliance identified through or reported to the Research and Development Office (R&D Office) will be reported by and followed through the R&D Office.

FACILITY DIRECTOR'S ANNUAL CERTIFICATION

The Veterans Health Administration (VHA) requires that each Facility Director annually certify oversight of the facility's research program.

1. The RCO will collaborate with R&D Office, Privacy Officer and Research Information Security Officer for completing the Facility Director's Annual Certification.

2. The RCC will pull the data required to respond to the questions relevant to Research Compliance on the certification. The RCO and RCC will review the data to ensure accuracy prior to completing and submitting the research compliance section of the certification.

REFERENCES

VHA Handbooks:

- 1058.01 Research Compliance Reporting Requirements
- 1058.02 Research Misconduct
- 1100.19 Credentialing and Privileging
- 1200.01 The Research and Development Committee
- 1200.05 Requirements for the Protection of Human Subjects in Research
- 1200.06 Control of Hazardous Agents in VA Research Labs
- 1200.07 Use of Animals in Research
- 1200.08 Safety of Personnel Engaged in Research
- 1605.1 Privacy and Release of Information

VHA Directives:

- 2008-072 Research Personnel Notification of Pharmacy Benefits Management
- 2012-030 Credentialing of Health Care Professionals

Code of Federal Regulations (CFRs):

HUMAN SUBJECTS PROTECTION

- Title 38 CRF, Parts 16 and 17;
- Title 45 CFR, Parts 46 and 164

FDA

- 21 CFR, Parts 50, 54, 56, 312, 809 and 812

Other Policies:

SOUTH TEXAS VETERANS HEALTH CARE SYSTEM

- R&D SOPs
- IACUC SOPs
- SRS SOPs

RESCISSION: Office of Research Compliance Audit Plan, June 1, 2013 – May 31, 2014

Celeste Burton, MSA
Research Compliance Officer

3/25/2015
Date

Marcos I. Restrepo, MD, MSc
per Dr. Clark

Robert Clark, M.D.
Research and Development Committee Chair

3/25/2015
Date

Julianne Flynn, M.D.
Acting Director

MAR 30 2015
Date

APPENDIX A: INFORMED CONSENT AUDITS

1. Informed consent audits are performed once annually for each study. Audits will occur within twelve months after the previous audit or concurrently with a regulatory audit. All informed consent documents and HIPAA authorizations signed since the previous audit will be reviewed.

2. Upon notification of selection for audit, the PI will be asked to submit their Master List of consented subjects.

3. The auditor will:

    a. Meet with the PI and/or designee and review the original signed informed consent document and HIPAA authorization; or

    b. Review the scanned informed consent documents and HIPAA authorizations in CPRS.

4. Elements to be audited will include:

    a. Approved version(s) of the informed consent document, or a copy;

    b. Signed informed consent document;

    c. Correct informed consent document used;

    d. Subject signature present;

    e. Correct date of subject signature present;

    f. Date and signature of person obtaining consent present;

    g. Person obtaining consent is authorized by the IRB;

    h. Informed consent document contain IRB approval stamp;

    i. HIPAA authorization required;

    j. HIPAA authorization obtained, if required;

    k. Informed consent document contains required sponsor information, when applicable;

    l. Informed consent document includes language about research-related injury (greater than minimal risk studies only);

    m. Informed consent document contains statement on ClinicalTrials.gov website (FDA-regulated research only);

n. The auditor will review the consent note in CPRS to determine if the consent process is adequately documented.

o. The auditor will verify whether a required continuing review occurred as scheduled.

5. **Waiver of Documentation of Informed Consent and HIPAA.** If documentation of informed consent and HIPAA authorization signature is waived in accordance with 38 CFR 16.117(c), annotate evidence that the waiver criteria was met and documented in IRB records. The date of the IRB determination shall be noted.

6. **Waiver of Informed Consent.** If informed consent is waived in accordance with 38 CFR 16.116(c) or (d), annotate evidence that the waiver criteria was met and documented in IRB records. The date of the IRB determination shall be noted.

APPENDIX B: HUMAN RESEARCH REGULATORY AUDITS

1. Prior to the audit, the auditor will review, as applicable, the protocol history, all approved amendments, informed consent documents, HIPAA authorization, applicable waivers and other information available in the Research protocol files located on the Shared drive. This information will be used to become familiar with the study and to populate the HRPP audit tool.

2. On the specified date and time of the audit the auditor will meet with the PI and/or designee to answer any questions concerning the audit. The PI or his/her designee will make themselves available during the audit should a question arise.

3. The PI (or designee) will make the following documents, if applicable, available for review the auditor and will assist the auditor in completing the audit.

    a. Protocol(s) and amendment(s);

    b. Subject case report forms;

    c. Consent form(s) and approval(s);

    d. HIPAA authorization(s);

    e. Consent waiver(s), if applicable;

    f. HIPAA authorization waiver(s), if applicable;

    g. Advertisements (including letters, surveys) and approvals;

    h. Subject log;

    i. Subject case histories;

    j. R&DC and subcommittee correspondence;

    k. R&DC and subcommittee submissions, notifications, approvals;

    l. Serious adverse event and/or safety reports;

    m. Investigator brochure(s);

    n. VA Form 10-9012;

    o. Sponsor correspondence;

    p. Study personnel signatures, qualifications, training records, research scopes of practice, CVs, and documentation of delegation of authorization;

    q. Signed investigator agreement or attestation;

r. Signed FDA Form 1572

s. Signed conflict of interest/disclosure statements;

t. Investigational product handling records; and/or

u. Any other official/unofficial documents related to the study.

4. The auditor may also review additional records pertaining to the study, including:

   a. VA R&D Office records;

   b. R&D Committee files and minutes;

   c. Subcommittee files and minutes; and/or

   d. Subject progress notes/CPRS documentation.

5. The HRPP Audit Tool will be populated as follows:

   a. **Administrative information.** This information identifies and describes each protocol.

   b. **Subject accrual.** The number of subjects who were entered into the study since initiation.

      i. For studies with intervention or interaction with living individuals, this is the number of subjects enrolled.

      ii. For studies only obtaining identifiable private information, this is the number of subjects who passed screening and were included for analysis.

   c. **Documentation of actions of the IRB & R&DC related to the study.** This will include initial review/approval, amendments, continuing review/approval, changes in staff and any other action taken by the research committees. The protocol file should include documentation of the submission of the request for an action and a letter communicating the action to the PI by either the IRB, R&DC, ACOS/R&D, or as designated by policy. The auditor will note any lapses in continuing review approval and will determine whether any research occurred during the lapse. The auditor will review the date for every IRB action. This will allow the auditor to determine, as relevant, the timeliness of the action and the timeliness of any further actions that may be required by regulation.

   d. **Documentation of Informed Consent.** The auditor will record sequentially the versions of the informed consent document that have been approved by the IRB for the protocol, the date of approval, and whether re-consent was required. The auditor will verify that the appropriate IRB stamp was used. The RCO will ascertain that all enrolled subjects received the version of the informed consent

document that was appropriate on the date of their enrollment in the research. The auditor will verify that re-consent occurred, when required.

e. **Local Unanticipated SAEs, UPRs and Significant Safety Reports.** The auditor will record all such events and notices for each audited human subject protocol to ascertain that required review and determinations occurred in the manner and time specified by VA policy.

f. **Study Staff Qualifications and Training.**

   i. **Training.** The auditor will audit training that is specific to the research program (e.g., CITI, research-specific safety training, etc.). The auditor will determine if the research-specific training is current at the time of the audit. There will be no look-back for training/training lapses. The auditor will note, however, if there is evidence that research began without all required research-specific training. The auditor will verify that the research-specific training is current by reviewing the training database maintained by the R&D Office.

   ii. **Scope of Practice.** The auditor will ascertain the presence of a research scope of practice at the time of audit. This is completed through verification of the training database or through a review of the hard copy documents maintained in the R&D Office. There will be no look-back for credentialing lapses. The auditor will not evaluate the content or appropriateness of the scope of practice.

g. **Subject Record Review.** The RCO will review a sample of the subjects' records to assess:

   i. **Timing of Consent.** The auditor will verify that consent was obtained prior to initiation of study procedures. The date the subject signed the informed consent document will be compared with the documented date that study procedures began for the subject to ascertain whether informed consent preceded research initiation. For research procedures that began on the same date that the subject signed consent, the auditor will look for documentation in CPRS or in the subject's case history indicating that consent occurred before study procedures began. This comparison will be made for all studies requiring a signed informed consent document, including minimal risk studies, such as questionnaire research, and studies involving interventions of more than minimal risk.

   ii. **Compliance with Eligibility Procedures.** For research that involves intervention of more than minimal risk to subjects, the auditor will determine if subjects met inclusion/exclusion criteria by one or more of the following:

      1. PI use of an inclusion/exclusion criteria checklist.

2. Documentation in CPRS that inclusion criteria were met and exclusion criteria were not met.

3. Sponsor monitoring reports stating that the study monitor has verified eligibility criteria.

4. FDA-required documentation.

5. Review of source documents.

NOTE: If no documentation is available, the auditor will seek guidance from the IRB Chair and PI how to best assure that criteria were correctly applied in the subject records reviewed.

h. Investigational Product Accountability

APPENDIX C: ANIMAL RESEARCH REGULATORY AUDITS

1. The auditor will review, as applicable:

    a. Protocol and all approved amendments;

    b. ACORP;

    c. IACUC Annual Renewal Form;

    d. R&DC/subcommittee correspondence;

    e. R&DC/subcommittee submissions, notifications, approvals;

    f. Qualifications, training records, research scopes of practice, CVs;

    g. Veterinary consultation;

    h. Log(s) of inventory and usage of controlled substances; and

    i. Any other official/unofficial documents related to the study.

2. The auditor may also review;

    a. R&DC files and minutes;

    b. Subcommittee files and minutes; and

    c. VA R&D Office records;

3. The audit tool will be populated as follows:

    a. **Administrative Information.** This information identifies and describes each protocol, including whether the required annual approvals occurred as scheduled and documented.

    b. ACORP Contents (Y/N)

        i. For VA-funded studies, an Animal Component of Research Protocol was submitted.

        NOTE: *The auditor will determine whether the correct version was used (version 3 or version 4).*

        ii. Maximum number of animals to be used during the 3-year approval period.

        iii. Scientific justification for not relieving pain or distress, if the study includes a Category E pain and distress level.

iv. Consultation with a veterinarian during the planning stage of the research.

v. Scientific justification or veterinary medical reason to explain why group housing is not being used, if the study states that animals should be individually housed.

vi. Identification of animal and procedure locations (both VA and non-VA).

vii. Endpoint criteria for euthanasia and/or removal of animal(s), when applicable.

viii. Search for alternatives to animal use for procedures involving pain or distress to the animals.

c. Compliance with guidelines for obtaining controlled substances through VA Pharmacy.

d. Involvement of personnel in an approved Occupational Safety and Health Program.

e. Study staff qualifications and training.

i. **Training.** The auditor will audit training that is specific to the research program, rather than additional training required of all VA or VHA employees. The auditor will determine if the research-specific training is current at the time of the audit. There will be no look-back for training/training lapses. The auditor will note, however, if there is evidence that research began without all required research-specific training. The auditor will verify that the research-specific training is current by reviewing the training database maintained in the R&D Office.

ii. **Scope of Practice.** The auditor will ascertain the presence of a research scope of practice at the time of audit. There will be no look-back for credentialing lapses. The auditor will not evaluate the content or appropriateness of the scope of practice.

f. Documentation of Actions of the IACUC and R&DC related to the study. This will include initial review/approval, amendments, annual review/approval, triennial review/approval, changes in staff and any other action taken by the research committees. The protocol file should include documentation of the submission of the request for an action and a letter communicating the action to the PI by either the IACUC, R&DC, ACOS for R&D, or as designated by policy. The auditor will note lapses in annual review approval and will determine whether any research occurred during the lapse.

APPENDIX D: RESEARCH SAFETY REGULATORY AUDITS

1. The auditor will review, as applicable:

    a. Protocol and all approved amendments;

    b. Research Protocol Safety Survey and Supplement;

    c. R&DC/subcommittee (e.g., SRS, IBC) correspondence;

    a. R&DC/subcommittee (e.g., SRS, IBC) submissions, notifications, approvals;

    b. Qualifications, training records, research scopes of practice, CVs;

    c. Log(s) of inventory and usage of controlled substances; and

    d. Any other official/unofficial documents related to the study.

2. The auditor may also review;

    a. R&DC files and minutes;

    b. Subcommittee files and minutes;

    c. VA R&D Office records;

    d. R&DC files and minutes;

    e. Subcommittee files and minutes; and

    f. VA R&D Office records.

3. The Audit Tool will be populated as follows:

    a. Administrative information. This information identifies and describes each protocol, including whether the required annual approvals occurred as scheduled.

    b. Satisfaction of requirements for use of chemical, biological and radiation hazards in research.

    c. Involvement of personnel in an approved Occupational Health and Safety Program.

    d. Study staff qualifications and training.

    e. Training. The auditor will audit training that is specific to the research program (e.g., research-specific safety training, etc.), rather than additional training required of all VA or VHA employees (e.g., environment of care, etc.). The auditor will determine if the research-specific training is current at the time of the

audit. There will be no look-back for training/training lapses. The auditor will note, however, if there is evidence that research began without all required research-specific training. The auditor will verify that the research-specific training is satisfied by reviewing the training database maintained in the R&D Office.

f. Scope of Practice. The auditor will ascertain the presence of a research scope of practice at the time of audit. There will be no look-back for credentialing lapses. The auditor will not evaluate the content or appropriateness of the scope of practice.

g. Documentation of actions of the SRS, IBC and R&DC related to the study. This will include initial review/approval, amendments, annual review/approval, changes in staff and any other action taken by the research committees. The protocol file should include documentation of the submission of the request for an action and a letter communicating the action to the PI by either the SRS, IBC, R&DC, ACOS/R, or as designated by policy. The RCO will note lapses in annual review approval and will determine whether any research occurred during the lapse.