



**Department of Veterans Affairs
Jesse Brown VA Medical Center
820 S. Damen Avenue
Chicago, IL. 60612**

R&D 537/151
June 28, 2011
Version 1.3

Research Compliance Officer Auditing SOP

INTRODUCTION

This Research Compliance Officer (RCO) SOP describes how compliance with the regulations and policies governing human subjects research, animal research, lab security and safety, research information security, research misconduct, and debarment for research impropriety for the Jesse Brown VA Medical Center will be measured, reported, and remediated, as needed.

It is critical that the RCO function independently of the Research Service or the Chief of Staff. RCO activities may not be directed or prioritized by Research Service leadership or personnel. Each Facility Director has a responsibility to ensure the functional independence of the Facility's RCO(s).

The RCO function is not part of the business compliance functions. The RCO and Compliance and Business Integrity (CBI) Officer are separate and distinct positions and should not be combined.

Questions regarding the Jesse Brown VA Medical Center Research Compliance Program including standard operating procedures, may be directed to the Research Compliance Officer (RCO) at 312-569-7426.

PURPOSE

To assure highest level of human subject's research protection program at Jesse Brown VA Medical Center. The RCO assures compliance with applicable laws, regulations, and policies according to VHA Directive 2008-0064 October 16, 2008.

POLICY

It is a VHA policy that each Director of a VHA facility conducting Human Subjects Research must appoint an individual as RCO who is responsible for auditing the program at that VA facility.

BACKGROUND

As a public agency, 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 VA must exercise prudent stewardship of public resources, including public funds that support research programs. Appropriate mechanisms must be in place to evaluate the functioning of the Human Subjects Protection Program (HSPP) and the safeguards in place to protect human research subjects in VA research. There must also be appropriately trained staff available at each VA facility conducting human subjects research to audit each research project involving human subjects. Regular audits by the RCO will be conducted to evaluate the functioning of the HSPP and the safeguards in place to protect human research subjects at Jesse Brown VA human research. The RCO at Jesse Brown VAMC is responsible for conducting audits for each research project involving human subjects. Auditing is a mechanism to evaluate VA's human subject research program and, when appropriate, identify areas for corrective action. An active auditing program should provide reasonable assurance of the integrity of the research program and that adequate protections for research subjects are in place. To provide this reasonable assurance the RCO conducting the audits must be *independent of the research program and the research study*. VHA Handbook 1200.05 currently requires that the Institutional Review Board (IRB) develop written procedures for conducting audits of protocols and other IRB activities. This Directive requires that specific policies are in place for periodic and random audits of human subject research protocols and HSPP processes, and require appropriate and timely corrective actions when deficiencies are identified. The SOP for auditing of human subjects protocols has been standardized for VISN 12. Please refer to "Research Compliance Officer (RCO) Auditing of VHA Human Subjects Research VISN 12 Standard Operating Procedure". Auditing of animal and safety protocols will also be standardized, though the SOP has not been issued.

DEFINITIONS

(1) **Institutional Review Board (IRB).** The IRB is a board established in accordance with, and for the purposes expressed in, the Federal Policy (Common Rule) for the Protection of Human Subjects (Title 38 Code of Federal Regulations (CFR) 16.102(g)). It is responsible for the review of, approval or disapproval of, and continuing oversight of research involving human

(2) **Human Subjects Research.** Human subjects research is research that involves human subjects.

(a) As defined in the Common Rule (38 CFR 16) and VHA Handbook 1200.05:
A human subject is a living individual about whom an investigator conducting research obtains:

1. Data through intervention or interaction with the individual, or
2. Identifiable private information.

(b) An intervention includes both physical procedures by which data are gathered and all manipulations (physical, psychological, or environmental) of the human subject, or the subject's environment that are performed for research purposes.

(c) Interaction includes communication or interpersonal contact between the investigator and the human subject.

(3) **Research.** As defined by the Common Rule (38 CFR 16.102(d)) research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

RESPONSIBILITIES

I. The Medical Center Director is responsible for appointing an individual as full-time RCO for the HSPP and ensuring that adequate resources and personnel are available for oversight and auditing of the research. The RCO must report directly to the Medical Center Director. The RCO must have appropriate skills and knowledge to fulfill their duties. The Medical Center Director is also responsible for ensuring that each VA-approved human research study is completely audited at a minimum of every 3 years, that each study is audited for compliance with the regulations and policies on informed consent once a year after the recruiting process begins, and for ensuring that the compliance audits assess compliance with all applicable laws, statutes, regulations, and policies including those related to privacy, confidentiality, and information security. The Medical Center Director is responsible for certifying annually that each VA-approved research study is audited in accordance with requirements by Office of Research Oversight (ORO) and reviewing at least annually the effectiveness of the Research Compliance Program. The medical center director must report any appointment, resignation, or change in status of the research compliance officer to the Office of Research Oversight VHA Central Office, with a copy to the relevant ORO research officer, within 10 business days after the appointment, resignation, or change takes effect.

II. The RCO is responsible for the development and implementation of the JBVAMC Research Auditing Program. This includes:

A) **Developing the policies** and the accompanying standard operating procedures (SOPs) for the auditing program.

B) **Areas to be audited** include, but are not limited to: Regulatory compliance, Adverse event reporting, Inclusion and exclusion criteria, Documentation of informed consent, Waiver of informed consent, Health Insurance Portability & Accountability Act of 1996 (HIPAA) compliant authorization, waiver of HIPAA compliant authorization and the required documentation by the IRB or Privacy Board, Compliance with all data security and data use requirements, and Compliance with all privacy and confidentiality requirements. Any protocol is subject to audit at any time. Audits are conducted with the relevant audit tools

posted on the ORO website (<http://www1.va.gov/oro/>).

i) Types of audits

“Not-for-Cause,” Routine, Random, or Spot Audits:

The RCO will choose the protocol to audit and then notify the Principal Investigator (PI) and the coordinator (if applicable) via email. This notification will explain that their protocol has been selected for a routine regulatory audit and will provide an option of audit dates. If the RCO does not receive a response within 3 business days, the RCO will then make a phone call to the PI. Once the date and time is determined, the RCO will send a confirmation letter stating the date, time, expected length of time needed for the visit and the list of items the RCO expects to review. Investigators may request to reschedule for appropriate reasons. Except in extreme circumstances, audits will not be postponed for more than 45 days after initial notification. If a response is not received within 30 days of the initial contact attempt, notification will be forwarded to the IRB.

“For Cause” Audits:

“For cause” audits will be scheduled within a few days of the audit request. Notification to PI and the coordinator (if applicable) will be via e-mail (phone when required) to confirm a date and time for the audit. The Investigators must comply with the agreed upon date and time of the audit or notification will be forwarded to the IRB. The PI must be present during the audit process. In instances where the PI chooses not to be present, a selected designee or someone associated with the project must be available to answer questions and that may arise during the audit.

Unannounced Audits:

The RCO reserves the right to conduct unannounced audits at any time to evaluate a specific item(s).

ii) Frequency of audits

Informed Consent Audits:

Once recruiting has begun in a human research study, the RCO must complete an audit for compliance with the applicable regulations and policies related to research Informed Consents or Waiver of Consent at least once every year.

Informed Consent Audit Overview:

Research activities monitored may include, but are not limited to, the following: Adhering to HSPP policies; Using only IRB approved

advertisements and participant recruitment materials; Obtaining informed consent prior to initiating any research related procedures; Consent obtained only by trained and authorized individuals; Using only the most current IRB-approved informed consent form; Ensuring the informed consent form is appropriately signed and dated; Verifying documentation of the informed consent in the progress notes; and Verifying documentation that a copy of the signed informed consent forms has been provided to the participant or legally authorized representative.

Triennial Regulatory Audits:

The RCO must review every human subjects research study every three years or more frequently. If a study is less than three years in duration, the RCO must audit the study at least once during the life of the study. All research protocols (human and basic science) initiated after January 1, 2008, will have a regulatory audit at least every 3 years. Studies completed within the June 1 through May 31 reporting period receive a regulatory audit at closure or within 36 months preceding closure. The RCO may plan for protocols to be audited sooner if: (1) they will expire and have not been previously audited; (2) they involve greater than minimal risk; (3) their investigators have a previous history of serious noncompliance; etc. In any case, careful planning will be needed to ensure that all research protocols initiated after January 1, 2008, receive a regulatory audit at least every 3 years.

The IRB, the study sponsor, the PI, VHA administration (ORD, ORO), Medical Center Director, ACOS/R, or the RCO may require more frequent audits. They can also require focused audits of one or more aspects of the study. The requirement to increase the frequency of audits or to audit specific aspects of the study can be based on such considerations as: Involvement of vulnerable populations; Level of risk; Phase I or Phase II studies; Involvement of FDA approved drugs for which there has been a safety warning, or change in the labeling that indicates increased risks; Issues of noncompliance; or Data breach.

Triennial Regulatory Audit Overview:

The RCO will review items including, but not limited to, the following during the Triennial Audits: Initial IRB approval of the protocol, consent form, and any other documents e.g., advertisement, participant recruitment material, grant application, etc., initially reviewed by the IRB; Adherence to IRB-approved protocols and conditions; Using only IRB approved advertisements and participant recruitment materials; Adherence to institutional HSPP policies and procedures, state and federal regulations will be evaluated;

Adherence to policies regarding storage, security and dispensing of investigational drugs and devices; Reconciling adverse events between the PI and R&D Office study files; Required IRB Notifications (i.e., SAE's, unanticipated problems, adverse events, deviations from the protocol, etc.); Annual R&D Committee and all relevant subcommittees continuing review approvals appropriate to the schedule; and IRB approval(s), for any modifications to the research project during the period from initial review to continuing review, e.g., protocol amendments, consent form revisions, etc.

IRB Exempt Studies Audit:

The annual informed consent audit requirement includes human studies determined to be exempt from IRB review. The audit requirement is fulfilled by completing the "Protocol Information" section and the "Protocol Exempt" checkbox on the ORO informed consent audit template (or equivalent) for any active IRB exempt study.

VA Pharmacy Audit:

The RCO will randomly complete pharmacy audits to ensure that the proper procedures are being followed. During the audit the RCO will ensure that there are copies of the subject's consent form are on file prior to pharmacy dispensing study medications, that the drug logs are filled out appropriately, that there is a current VA form 10-9012 on file, and a current FDA 1572 is on file, if applicable. Clinical investigations involving controlled substances must meet the same storage and accountability requirements in accordance with applicable laws, regulations, and VA policy outlined for routine patient care.

iii) During the Audit

The RCO will meet with the PI and/or study staff at the beginning of the visit to introduce himself/herself and explain the audit process. Once the RCO has completed the review of the records, he/she will meet with the study staff and PI (if available) to review any preliminary findings or recommendations, or ask for any clarifications regarding the research records.

iv) After the Audit

Following the visit, the RCO will write up a report, which will be sent to the PI. If remedial actions are necessary the PI will have four weeks to respond, unless there are extenuating circumstances. The report, and the PI's response if received, will go to the IRB for review. Any noncompliance noted in an audit will be reported within 5 working days to the R&DC and IRB Chairs, ACOS/R&D, and the Medical Center Director.

C) Corrective actions

The IRB, with input from the RCO, will determine appropriate corrective actions when regulatory deficiencies or procedural lapses are reported. Consideration will be given to the nature of the deficiency or lapse, its impact on the safety of the human subjects, and the investigator's compliance history. Corrective actions may include, but are not limited to:

- Study termination
- Study suspension
- Suspend enrollment and/or all or specific research procedures in the protocol in question
- Mandated education for the PI and/or the research staff
- A change in the reporting requirements (AEs, re-approvals, amendments, etc.). This change in reporting requirements may involve all studies under the direction of the PI, or only the particular study in which the deficiencies were identified
- The establishment, by the PI, of a corrective action plan to ensure that deficiencies or lapses are corrected and do not re-occur.
- Further monitoring of the research or consent process
- Notification of current and past participants

The evaluation of Corrective Actions (required by the IRB, R&D Committee, or other appropriate entities based on the findings) may be conducted through informal follow-up and formal follow-up audits. Reporting of the formal follow-up audits will be made to the IRB and R&D Committees.

Implementation of Corrective Actions

The IRB is responsible for determining the appropriate remedial action(s) in response to identified noncompliance and for verifying that the remediation is implemented as required. Except in extraordinary circumstances, remedial actions related to specific research projects must be completed within 90-120 days (or sooner if the IRB so determines) of the IRB's determination of noncompliance (or of such a determination by ORO). 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 (or sooner if the IRB so determines) of the noncompliance determination. Where completion of remedial actions extends beyond the periods described above, the facility will provide ORO with a written justification for the delay and an acceptable timeline for completion.

- D) Reporting Procedures:** The RCO must report apparent serious or continuing non-compliance found in audits of protocols and in informed consent audits to the Medical Center Director, ACOS/R, R&D Committee and the IRB Chair within 5

business days of identifying it. The Medical Center Director has an additional 5 business days to report the apparent serious or continuing non-compliance to the ORO regional office, and VISN 12 Director. Annual Certification of JBVAMC audits of VHA Research, first Reporting Period covers annual reporting of informed consent audits & regulatory audits for all protocols of all types.

- Refer to the following UIC HSPP policies and procedures for reporting requirements for the investigator, IRB, RCO, ACOS, and R&D Office:
 - *Unanticipated Problems and Other Events Requiring Prompt Reporting*,
 - *Administrative Hold, Suspension or Termination of IRB Approval*, and
 - *Handling Complaints and Allegations of Potential Non-Compliance with Human Subject Protection Regulations*.
 - Initial Annual Reporting: This report was due July 1, 2009, and covered all regulatory audits accomplished for a portion of studies active (open to enrollment or closed in enrollment but still with data collection or data analysis) during January 1, 2009 through May 31, 2009.
 - Subsequent Annual Reports: In subsequent years, annual reports will cover all regulatory audits for a portion (approximately 33%) of studies active from June 1 of previous year to May 31 of the current year.
 - RCO will determine which protocol to audit during the reporting period. Protocols are to be audited sooner if
 - i) they will expire & have not been previously audited
 - ii) they involve greater than minimal risk
 - iii) their investigators have a previous history of serious non-compliance.
 - RCO will provide copies of the audit reports, including deficiencies, to the Medical Center Director. The Medical Center Director will forward these audit reports to ACOS/R&D, who in turn will ensure that the appropriate subcommittees (i.e., JBVAMC Audit Subcommittee, IRB, R&D Committee, etc.), for corrective action and implementation. The ACOS/R&D will report back to the Medical Center Director in writing regarding type of corrective action(s). The Medical Center Director will report back to the RCO to update his or her record. It is the responsibility of ACOS/R&D to use JBVAMC Audit Subcommittee, R&D Committee or IRB to review these audit reports for corrective action(s). Once corrective action(s) will be suggested, it is the responsibility of ACOS/R&D to implement these recommendations by communicating involved parties including PI, and all regulatory agencies.
- E) **RCO Role as Non-Voting Consultant to Review Committees:** The RCO will serve as a non-voting consultant, as needed, to the Collaborative IRB (human subject subcommittee), R&D Committee, Research Audit Subcommittee, Institutional Animal Care and Use Subcommittee, and Subcommittee on Research Safety. The RCO may attend these meetings when requested by the committee.
- F) Concerns related to **conflict of interest** or possible conflicts of interest between the role of the RCO on the review committees and the role of the RCO in auditing

and reviewing research for compliance with applicable regulations/ requirements: If the RCO has a conflict of interest in auditing research protocol(s) related to regulatory and consent audits, the Medical Center Director will appoint an alternate RCO to conduct these audits. The Administrative Officer for the R&D and Assistant to the Medical Center Director will process an official request to arrange for an alternate RCO from another VA.

- G) The RCO is responsible for preparation of Section III (Annual Summary of Informed Consent Audits), Section IV (Summary of Triennial Regulatory Audits), and Section V (Certification and Signature) of the Facility Director's Certification of Research Oversight Annual Report.
- H) The RCO is responsible for sending any monitoring reports of external auditing (FDA, sponsors) and accrediting (AAHRPP, AAALAC, and Joint Commission) bodies and including pertinent findings into the research compliance program to the Medical Center Director, who will forward the applicable documents to ORO.
- I) **Audit Worksheets Records Retention & Maintenance of Documentation:**
These audit worksheets should be retained in JBVAMC R&D Office for an indefinite period of time after the completion of the study according to the VHA record retention schedules.

The RCO office is located in the Research Service area. In the RCO's office there is a locked filing cabinet, key available to only the RCO. In addition, the RCO has a secure drive to store write protected documents including policies, audits, and the RCO Database. This Research Compliance Officer Auditing Standard Operating Procedure (SOP) will remain current and in compliance with all applicable regulations. To remain current, this SOP will be reviewed and periodically updated. In general, this review will occur at least annually or as needed to comply with VA policies and regulations. The RCO will review these policies and procedures for compliance with the most recent VA and federal regulations. Proposed changes will be presented to the Medical Center Director or ACOS/R&D as appropriate for their input. Revisions will be implemented upon review. Notifications of changes and an updated RCO SOP manual will be distributed as appropriate and available upon request.

J) RCO TRAINING AND GUIDANCE

RCO training resources in addition to the numerous written resources available from the ORO and ORD web pages include: ORO provides mentoring and guidance and provides up-to-date information on recently issued memos and publications, as well as ORO Offices contact information and an RCO FAQ for RCO activities through:

- Research Compliance Officer Education webpage
<http://vawww.vha.vaco.portal.va.gov/sites/ORO/RCO/default.aspx>

- Active RCO list serve providing inter-VISN peer advice and support as well as prompting timely clarifications from ORO regarding major concerns and questions expressed by the national RCO community.
- Monthly conference calls with VISN 12 Research Compliance Officer.
- RCOs also complete VA, VHA, and job-specific required training, including HSPP/GCP and other research-related training as required for research staff and R&DC members.
- RCO knowledge of regulations and their application is also enhanced and continually refreshed by their attendance at the IRB and R&D committees, as well as their participation in other research-related facility activities such as AAHRPP accreditation processes.

K) Other duties as assigned by the Medical Center Director.

According to recent memo dated July 26, 2010 from Chief Research & Development Officer (12) and Chief Officer, Office of Research Oversight (ORO-10 R) entitled: "Role & Authority of the VISN & Medical Center Research Compliance Officer (RCO) and Office of Research Oversight (ORO) with regard to a VA-affiliated Nonprofit Research & Education Corporation (NPC), should the situation arise where a RCO or ORO Reviewer seeks review of an NPC's documents, has communicated a valid oversight purpose to the NPC and the NPC refuses to provide the records, the RCO or ORO Reviewer should contact the Administrator of VA's Nonprofit Program Office (NPPO) at 816-922-2043. The Administrator will work with the RCO or ORO Reviewer and the NPC to find a solution.

REFERENCES

VHA Directive 2008-0064 (October 16, 2008) Research Compliance Officers and the Auditing of VHA Human Subjects Research to Determine Compliance with Applicable Laws, Regulations, and Policies

VHA Handbook 1200.05 (October 15, 2010) Requirements for the Protection of Human Subjects in Research

VHA Handbook 1200.01 (June 16, 2009) Research & Development Committee

VHA Handbook 1605.1 Privacy and Release of Information

VHA Handbook 1058.01(May 21, 2010) Requirements for Reporting Research Events to Facility Oversight Committees and the Office of Research Oversight

FOLLOW-UP RESPONSIBILITIES

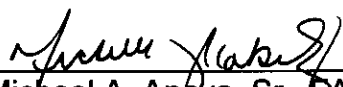
The Research Compliance Officer at the Jesse Brown VA Medical Center is responsible for updating this SOP according to the ORO recommendation(s).

RESCISSION This SOP dated January 26, 2011 is rescinded.

REVISION LOG:

Version (#, date)	Replaces (#, date)	Summary of changes
v1.1date 1/26/11	v 1.0 April 30, 2009	According to revised VHA handbook 1058.01, 1200.01 & 1200.05.
v1.2date 4/13/11	v1.1date 1/26/11	Administrative changes made to ensure consistency throughout SOP and with other SOPs
v1.3date 6/28/11	v1.2date 4/13/11	Add statement to the policy on page 3 under "Responsibilities" item I: The medical center director must report any appointment, resignation, or change in status of the research compliance officer to the Office of Research Oversight VHA Central Office, with a copy to the relevant ORO research officer, within 10 business days after the appointment, resignation, or change takes effect.

Approve / Disapprove


 Michael A. Anaya, Sr., DACHE
 Medical Center Director