RESEARCH COMPLIANCE AUDITS

IRB Education Meeting
May 20, 2014
Research Education

• To protect the rights and welfare of human subjects and research animals
• To promote regulatory compliance and scientific integrity
• To ensure that staff are well trained, managed and supported

Research Compliance

• To identify high-risk areas and to see that appropriate corrective actions are taken
• To confirm program adherence to all applicable laws, regulations, and policies
• To ensure that employee actions are consistent with applicable laws and policies

...To support the development of effective health care innovations for veterans
Types of Audits

• Informed Consent & HIPAA Authorization Audits
  • 100% of all documents submitted to the IRB

• Triennial Regulatory Audits for:
  • Human Research Protection Program
  • Research Safety
  • Animal Research

• “For Cause” Audits
  • May be requested by any of the research oversight committees, the ACOS/Research, and/or the Facility Director
  • May be a full audit or focused on specific areas

• Unscheduled Audits
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- **Unscheduled Audits**
HRPP Regulatory Audit

- **Purpose:** To ensure compliance with all VA and other federal requirements for the conduct of human research
- **An audit must be performed every three years** for all studies that are still *interacting with subjects* and/or *collecting data*
- **This audit will be coordinated with the Research Safety Audit** if hazards have been identified by SRS.

* More frequent audits may be required, 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 a change in the labeling that indicates increased risks
  - Issues of noncompliance
  - Data breach
Preparing for the Audit

The Research Compliance Officer (RCO) will:

- E-mail the PI and Study Coordinator to schedule the audit and provide a list of documents that should be available for review.

- Review the Protocol History in IRB/SRS records.

- Review the study protocol and the most recent abstract for information regarding the objectives, study design, and progress to date.

- Document training completion dates and Scopes of Practice for study personnel who are currently listed in IRB record.
# REGULATORY AUDIT PREPARATION TOOL

<table>
<thead>
<tr>
<th>Document – Investigator Regulatory Files</th>
<th>Present and Reviewed Y/N/NA</th>
<th>Comments</th>
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<th>Comments</th>
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<tbody>
<tr>
<td>Protocol &amp; Amendments</td>
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<td>R&amp;D Correspondence</td>
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<td>Case Report Forms</td>
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<td>Notes-to-File</td>
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<tr>
<td>IRB Approved Consent Forms</td>
<td></td>
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<td>Site-Sponsor Correspondence</td>
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<tr>
<td>-Information Provided to Subjects</td>
<td></td>
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<td>-Conference call minutes</td>
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<td>-HIPAA Forms</td>
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<td>-E-mails</td>
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<td>-Advertisements</td>
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<td>-Newsletters</td>
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<td>-Record of Approved Consent Form Versions</td>
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<td>-Conference calls</td>
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<td></td>
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<td>-Letters, memos, faxes</td>
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<tr>
<td>Subject Log (current/accurate)</td>
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<td>Study Site Personnel</td>
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<tr>
<td></td>
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<td>Signatures, Qualifications, Training, Scope of Practice, CVs, Delegation</td>
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<tr>
<td>IRB Correspondence</td>
<td></td>
<td>Signed Attestation or Investigator’s Agreement (Sponsor, Institution, FDA)</td>
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<tr>
<td>IRB Submissions, Notifications, Approvals</td>
<td></td>
<td>Official Documents</td>
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<td>Letters, Memos, etc.</td>
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<tr>
<td>Serious Adverse Events/Safety Reports</td>
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<td>Signed PI Conflict of Interest/Disclosure Statement</td>
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<tr>
<td>Investigator Brochure/VA Form 10-9012</td>
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<td>Investigational Products</td>
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<tr>
<td></td>
<td></td>
<td>Accountability, Handling, Pharmacy, Elsewhere</td>
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</table>
Conducting the Audit

The RCO will:

• Describe the audit plan to PI/SC and ask about:
  • The Informed Consent process
  • Confidentiality protections
  • Protocol-required activities
  • Current study personnel and their roles

• Review all communications and required documents in the study file and reconcile with IRB/SRS records.

• Review all SAE/UP Reports and match to IRB records.

• Select and review 10-30 subject files.
### ADMINISTRATIVE INFORMATION

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Protocol Title:</th>
</tr>
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<tbody>
<tr>
<td>Protocol Number:</td>
<td>Sponsor / Source of Funding:</td>
</tr>
</tbody>
</table>

**Study Site(s):**
- [ ] VA Facility
- [ ] Academic Affiliate
- [ ] Other

**VHA Central IRB?**
- [ ] Y
- [ ] N

**Initial IRB Approval Obtained?**
- [ ] Y
- [ ] N

**Initial R&DC Approval?**
- [ ] Y
- [ ] N

**ACOS/R Letter Obtained?**
- [ ] Y
- [ ] N

**Date Protocol was first approved by IRB:**

**Study Type:**
- [ ] International Study
- [ ] Study involves children
- [ ] Study involves prisoners

**ORD/CRADO approval on file?**
- [ ] Y
- [ ] N

**Study Site(s):**
- [ ] VA Facility
- [ ] Academic Affiliate
- [ ] Other

**Date of Current Audit:**

**Auditor(s):**

**Status at time of Current Audit**
- [ ] Actively enrolling new subjects
- [ ] Active only for long-term observation
- [ ] Active only for long-term data analysis
- [ ] New enrolments temporarily suspended
- [ ] Closed to enrolments
- [ ] Closed / Terminated Date:

### CONTINUING REVIEWS

<table>
<thead>
<tr>
<th>Did required Continuing Review(s) occur as scheduled per policy by the IRB?</th>
<th>Y</th>
<th>N</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>If NO, did any Research occur during the lapse?</td>
<td></td>
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</table>

**NOTE:** If a human protocol is opened and closed without enrolling human subjects at this site, completing the audit tool to this point satisfies the requirement for the HRPP audit.
Reconcile IRB documents with the PI’s study records:

- Have all protocol amendments been reported to the IRB?
- Are original IRB approval documents in the PI’s study file?
- Are all required signatures, dates, and stamps present?
- Were actions completed within required timeframes?
Note Consent/HIPAA Authorization versions and approval periods:

- Are there any gaps in ICF approval dates?
- Are IRB date stamps on all forms that are (or were) in use?
- Were ICF/HIPAA documents revised when necessary?
- Were appropriate subjects re-consented if required by IRB?
Reconcile IRB documents with the PI’s study records:

- Have SAEs/UPs been reported to the IRB as required?
- Are IRB-stamped original documents in the PI’s study file?
- Were actions completed within required timeframes?
<table>
<thead>
<tr>
<th>Site Personnel</th>
<th>All Training Current Y/N</th>
<th>No Evidence of Training Ever Being Completed Y/N</th>
<th>SCOPE OF PRACTICE OR EQUIVALENT DOCUMENTED* Y/N/NA</th>
<th>Current WOC? Y/N</th>
<th>Role in Study PI/SC/SI</th>
<th>Comments</th>
</tr>
</thead>
</table>

- Are all members of the study team listed in the IRB files?
- If not, should an amendment or notification be submitted?
- Which individuals are exposed to hazards (for Safety Audit)?
- Is training current and appropriate for their study responsibilities?
- Are all Scopes of Practice on file in the Research Office?
<table>
<thead>
<tr>
<th>SUBJECT STUDY ID</th>
<th>DOCUMENTATION THAT CONSENT OBTAINED PRIOR TO INITIATION OF STUDY PROCEDURES[^2]</th>
<th>INCLUSION/EXCLUSION CRITERIA CORRECTLY APPLIED[^3]</th>
<th>SUBJECT INCLUDED IN RESEARCH IN PRESENCE OF DOCUMENTATION THAT INCL/EXCL CRITERIA WERE NOT MET</th>
<th>Other issues found, specify on line below</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y/N/NA</td>
<td>Y/N/NA</td>
<td>Y/N/NA</td>
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</tbody>
</table>

- How many subjects did the IRB approve for enrollment?
- How many subjects have been enrolled to date?
- Is the Master Subject Log complete and securely maintained?
- Is the screening/consenting process consistent with the protocol?
- Have signed ICFs/HIPAA Authorizations been audited by the RCO?
Audit Follow-Up

- The RCO gives a verbal report of preliminary findings to the PI/SC at the time of the audit and sends an email update after all required information has been reviewed.

- A written report is submitted to the IRB within two weeks of the audit, and the PI receives a copy from the IRB within one month of the subcommittee review.

- The RCO provides a monthly summary of all audit results to the R&D Committee.

- An annual summary of the RCO’s research audit activities is reported to the Facility Director in person and in writing.

- The Director submits an “Annual Facility Director Certification of Research Oversight” report to the Office of Research Oversight.
Common Audit Findings

- Master Subject Log is missing or out-of-date.
- Data sets described as “de-identified” contained PHI.
- Study personnel have expired CITI training.
- A Scope of Practice is not on file for study personnel.
- An IRB-required consenting note is not in CPRS.
- Informed Consents have missing or incorrect dates.
- IRB has not been notified of changes in study personnel.
Significant Audit Findings

If “APPARENT Serious or Continuing Noncompliance” is identified by the RCO during an audit:

• An investigation must be conducted and a written report must be submitted within five business days to the Facility Director, ACOS/R, R&DC Chair, and the IRB.

• At its next convened meeting, the IRB must review the report and determine whether “Serious or Continuing Noncompliance” has occurred.

• Remedial actions involving a specific study or research team must be completed within 90-120 days of the IRB’s determination (except in extraordinary circumstances).
Serious or Continuing Noncompliance…

- Involves substantive harm or genuine risk of harm to the safety, rights, or welfare of human subjects, staff, or others.
  - Study procedures were performed before obtaining the subject’s informed consent.
  - PHI was sent to an individual who was not listed on the HIPAA Authorization.
  - The wrong study drug was dispensed to a subject.

- Substantively compromises the effectiveness of our human subject protection or human research oversight programs.
  - Research was initiated without written notification from the ACOS for Research that the project may begin.
  - Substantive protocol changes were implemented without IRB approval.
  - Study Coordinator performed tasks outside of the approved scope of practice.

- Reflects a persistent failure to adhere to the laws, regulations, or policies governing human research.
  - Failure to maintain documentation required by the IRB or by the IRB-approved protocol for ten or more subjects
  - Repeatedly late submissions of continuing reviews or reportable events
  - Failure to implement remedial actions within the required timeframes
Research Compliance Officers

Nancy Flemmons, RN, MS  x3563
Lead RCO for VISN 23

Deanna Rohde, RN, CCRC  x5858
Facility RCO

The Research Compliance Office is located across from the IRB Office in Room 3N-103.