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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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.

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

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.

VHA Triennial Regulatory Compliance Audit

Human Research Protection Program Audit Tool

Auditing period June 1, 2013- May 31, 2014

ADMINISTRATIVE INFORMATION[1]			
Principal Investigator:		**Protocol Title:**	
Protocol Number:		**Sponsor / Source of Funding:**	
Study Site(s): (check all that apply):	☐ 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: (check all that apply)	☐ **International Study**[2] **ORD/CRADO approval on file?** ☐Y ☐N ☐ **Study involves children**[3] **ORD/CRADO approval on file?** ☐Y ☐N ☐ **Study involves prisoners**[4] **ORD/CRADO approval on file?** ☐Y ☐N		
Date of Current Audit:	**Auditor(s):**		
Status at time of Current Audit (check all that apply)	☐ **Actively enrolling new subjects** ☐ **Active only for long-term observation** ☐ **Active only for long-term data analysis**	☐ **New enrollments temporarily suspended** ☐ **Closed to enrollments** ☐ **Closed / Terminated Date:**	

CONTINUING REVIEWS				
	Y	**N**	**NA**	***COMMENTS***
Did required Continuing Review(s) occur as scheduled per policy by the IRB?	☐	☐	☐	
If NO, did any Research occur during the lapse?	☐	☐	☐	

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.*[5]

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IRB SUBMISSIONS, APPROVALS, AND OTHER ACTIONS[6]					
PROTOCOL, AMENDMENTS, CONTINUING APPROVAL ETC.	IRB DATES[7] APPROVAL	IRB DATES[7] EXPIRATION	RESEARCH & DEVELOPMENT COMMITTEE APPROVAL DATE OR N/A[8]	SUBMISSION & APPROVAL LETTERS ON FILE?[9] Y/N/ N/A	*Comments*

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?

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IRB SUBMISSIONS, APPROVALS, & OTHER ACTIONS – INFORMED CONSENT[10]						
Informed Consent Date	*Informed Consent Version Number*	DATE OF IRB APPROVAL[11]	*Reason for Revision*	RE-CONSENT REQUIRED?[12] Y/N	IRB STAMP OR EQUIVALENT[13]	*Comments*

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?

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LOCAL UNANTICIPATED SERIOUS ADVERSE EVENTS (SAEs) UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS (UPRs) SIGNIFICANT SAFETY REPORTS / DATA MONITORING COMMITTEE (DMC) REPORTS[14]										
Date UPR/SAE Occurred [15]	Date Learned of Event[16]	Subject ID	Event	Date reported to IRB[17]	Reported to IRB within required time period Y/N/NA	Reviewed & categorized within required time period[18] Y/N/NA	Categorized by IRB*			Reported to ORO[18] Y/N/NA
							U Y/N	R Y/N	S Y/N	

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?

* U – Unanticipated R – Related to study participation S – Serious

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STUDY STAFF QUALIFICATIONS AND TRAINING[20]						
SITE PERSONNEL	ALL TRAINING CURRENT Y/N	NO EVIDENCE OF TRAINING EVER BEING COMPLETED Y/N	SCOPE OF PRACTICE OR EQUIVALENT DOCUMENTED[21] Y/N/NA	*Current WOC? Y/N*	*Role in Study PI/SC/SI*	*Comments*

- 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?

VHA Triennial Regulatory Compliance Audit

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SUBJECT RECORD REVIEW

INCLUSION/EXCLUSION CRITERIA SHOULD ONLY BE EVALUATED FOR HUMAN SUBJECTS RESEARCH THAT INVOLVES INTERVENTION OF MORE THAN MINIMAL RISK WITH SUBJECTS.

ASSESS TIMING OF CONSENT, COMPLIANCE WITH ELIGIBILITY CRITERIA, ETC.

TOTAL NUMBER OF SUBJECTS WHO PASSED SCREENING AND WERE INCLUDED FOR ANALYSIS IN STUDY IN THIS PERIOD =

IF 10 OR FEWER SUBJECTS IN THIS PERIOD, AUDIT ALL OF THEM

IF 11-100 SUBJECTS IN THIS PERIOD, AUDIT 10 OF THEM

IF 101-300 SUBJECTS IN THIS PERIOD, AUDIT 10% OF THEM

IF MORE THAN 300 IN THIS PERIOD, AUDIT 30 OF THEM

SUBJECT STUDY ID	DOCUMENTATION THAT CONSENT OBTAINED PRIOR TO INITIATION OF STUDY PROCEDURES[22] Y/N/NA	INCLUSION/EXCLUSION WERE CRITERIA CORRECTLY APPLIED[23] Y/N/NA	SUBJECT INCLUDED IN RESEARCH IN PRESENCE OF DOCUMENTATION THAT INC/EXCL CRITERIA WERE NOT MET Y/N/NA	*Other issues found, specify on line below*

- 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).

VHA Handbook 1058.01 - Research Compliance Reporting Requirements

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

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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.