HennepinHealthcare Research Institute

HUMAN RESEARCH PROTECTION

Post-Approval Audits

Number 20 Version Date 08 AUG 2022
Resource type OEQCR SOP-Compliance

OBJECTIVE

Describe the compliance activities conducted by the Office for Education and Quality in Clinical Research (OEQCR) to protect the safety of study subjects, promote consistent research quality, and ensure compliance with federal, state, local, and institutional regulations and guidelines that govern clinical research. These procedures apply to all non-exempt human research conducted through Hennepin Healthcare Research Institute (HHRI) that is subject to IRB approval by the Hennepin Healthcare IRB or approved for reliance on an external IRB.

RELATED HRP RESOURCES

HRPO 108 GUIDANCE Regulatory and external guidance references
HRPO 260 SOP Compliance activities
HRPO 262 SOP Institutional reporting of non-compliance, UPIRTSOs, suspensions, and terminations
HHRI Conflict of Interest Policy

ATTACHMENTS

Attachment A: Post-Approval Audit Notification Letter
Attachment B: Post-Approval Audit Preparation and Checklist
Attachment C: Post-Approval Audit Follow-up Letter

POST-APPROVAL AUDIT PROCEDURES

1) Audit Overview:
    a. Types of audits:
        - For Cause
        - Not for Cause (previously known as quality reviews)

    b. The need for a "for cause" audit will be based on specific information received or reviewed by the IRB/HRPO and/or the institutional official (See *HRPO 260 SOP Compliance activities*), which includes requests by an external IRB in accordance with the reliance agreement governing the research. HRPO or the institutional official will send a "for cause" audit request to OEQCR. OEQCR will follow the procedures in this SOP and the HRPO SOP 260 to complete the audit.

    c. A minimum of two "not for cause" audits will be completed yearly. The OEQCR reserves the right to audit a specific protocol or investigator more frequently as needed if circumstances suggest increasing problems with protocol conduct. The OEQCR also reserves the right to interview or survey research subjects and/or to observe the consent process as needed to ensure compliance with federal, state, and institutional regulations.

d. The selection of IRB approved protocols for the scheduled "not for cause" audits shall be a risk-based assessment. Assessment criteria shall include but not be limited to:
   - Investigator or research team new to clinical research
   - Investigator-initiated/sponsored protocols
   - the number of enrolled and/or consented subjects
   - Type and complexity of the trial
   - Level of risks to the trial subjects
   - Any identified problems

e. Audit activities will be managed by OEQCR, but will also include contracted auditors. OEQCR staff and contracted auditors will have training in auditing processes and compliance and will possess the professional experience and expertise to understand and apply the applicable federal, state, and institutional regulations and guidance.

f. The auditors will not be involved in any past or current aspect of the protocol under review. In addition, auditors will not be employed by the Principal Investigator (PI) in any research protocol.

g. Areas of the research process that can be audited include, but are not limited to, the following:
   - Informed consent process
   - Protocol adherence and/or violations
   - Serious/unanticipated adverse events
   - Documentation of research activities
   - Research team training
   - Confidentiality procedures

2) Audit Process:
   a. Identification of protocol for audit:
      - For Cause: A "for cause" audit will be identified as described in Section 1b of this SOP.
      - Not for Cause: Protocols will be identified from the HRPO Cayuse online database. Protocols will be chosen following a risk-based assessment as described in 1d.

   b. The PI and Primary Contact, as identified in the Cayuse database, will be notified in writing that their research protocol has been selected for audit by the OEQCR (Attachment A).

   c. The study team will be provided with an overview of what type of information the auditors will be reviewing and what type of questions to expect (Attachment B).

   d. The OEQCR audit team will contact the PI and Primary Contact to schedule a date and time for the audit. The date and time of the audit should be scheduled as soon as possible after the written notification.

   e. Audit activities can be on-site, remote, or a hybrid of both.

   f. HRPO will be notified of the audit and provided the final outcome report.

g. Any reporting of findings to the IRB will follow *HRPO 260 SOP Compliance Activities*.

3) Audit procedure:
   a. Review of Cayuse IRB information for the following:
      - Date of initial approval
      - Dates and description of modification(s) to the approved protocol with dates of approval
      - Serious and unanticipated adverse event reports
      - Any lapse of approval
      - Study personnel and updates
      - Enrollment

   In the case of a study relying on an external IRB, documentation needed to conduct the audit will be requested from the study team and/or reviewing IRB, as determined by the audit request and scope.

   b. The auditors may use many tools to track and document their review of the study documents. The audit questionnaire is one of the tools that may be used (Attachment B). Contracted auditors may use their own audit templates. OEQCR will retain a copy of the auditor's documents.

   c. At least 10% of study subject documents will be reviewed. Subjects will be selected at random. If deemed necessary, additional subject documents may be reviewed.

   d. If less than five (5) subjects have been enrolled, then all enrolled subject documents will be reviewed.

4) Post-audit procedures:
   a. A post-audit report will be completed and provided for review to the OEQCR Director.
      - The report will include the findings and outcome of the audit as well as any recommendations or requirements.
      - The report will outline follow-up procedures, if any are necessary. This may include a follow-up audit at the next six-month cycle or sooner to re-examine deficits identified for corrective action.

   b. A letter including the findings, a request for further information (if needed), required actions, and any suggested best practices will be sent to the PI and Primary Contact. (Attachment C)

   c. OEQCR staff and, if applicable, contracted auditors will then conduct a follow-up meeting with appropriate study personnel, including the PI, if available. The meeting will review the information provided in the letter and discuss any issues regarding: preliminary findings, any required actions, and next steps that are required or are best practice to improve the quality of the research process.

   d. The PI will have two weeks to complete the requirements and send a written response with the planned corrective action, if applicable.

   e. The written response will be sent to the OEQCR audit team email address listed in the follow-up letter. The audit team will review the response and if needed either, continue to follow-up with the PI until all issues have been resolved, or direct the PI to connect with HRPO about any issues that need to be reviewed by the IRB.

f. A copy of the written response will be sent to HRPO for inclusion in study records. Results of audits that include significant or multiple findings will be discussed with the IRB Chair and/or Vice Chair and any other relevant HHRI personnel. Any required next steps will follow the *HRPO 260 SOP Compliance activities* procedures.

g. Distribution of post-audit reports and letters will go to the following parties:
    a. Principal Investigator
    b. HRPO
        - For studies relying on an external IRB, the audit report will be shared with HRPO and HRPO will report to the external IRB, as applicable, in accordance with the reliance agreement governing the protocol.
    c. Others as determined appropriate by the OEQCR Director
    d. Reporting of determinations of UPIRTSO, serious and/continuing noncompliance, suspension or termination will follow *HRPO 262 SOP* for notifying the appropriate regulatory agencies and/or institutional official.

References

- OEQCR website: https://www.hhrinstitute.org/researcher-resources/office-for-education-quality-in-clinical-research/
- OEQCR network drive full path: N:\Resource Management\Active\ OEQCR 20-29 SOP Compliance

Revision history

Version date	Summary of substantive revisions
08 AUG 2022	Update to reflect updated process for naming/numbering conventions, creation/revisions to resource documents and alignment with HRPO process changes; other minor revisions for clarity and formatting.
08 JAN 2018	Origination

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ATTACHMENT A
POST-APPROVAL AUDIT NOTIFICATION LETTER

To:	Principal Investigator Cayuse Primary Contact
From:	Office for Education and Quality in Clinical Research (OEQCR)
Date:	DD Month YYYY
Subject:	Quality Assurance Program
Study to be reviewed:	**IRB # and Title:**

The Office for Education and Quality in Clinical Research (OEQCR) is committed to the quality and integrity of clinical research conducted on the Hennepin Healthcare System, Inc. campus. To support this commitment, the OEQCR oversees the quality assurance (QA) program which assesses clinical research activities conducted under the Hennepin Healthcare Research Institute Federalwide Assurance filed with the Human Research Protection Office (HRPO).

The purpose of the QA program is to ensure proper scientific, ethical, and regulatory behavior in the conduct of approved clinical research protocols. This program is designed to be educational as well as regulatory and to enhance research subject protection.

Your protocol, {add IRB #}, has been selected for an audit. Here's what to expect and have available:

- A member of the audit team will contact you and the Primary Contact listed in this letter to arrange for a mutually agreeable time to conduct the audit.
- A list (ID numbers only) of all consented subjects should be available when the auditor contacts you.

Items that will be needed the first day of the audit include:

- Study files (source documentation) for the chosen subjects
- Regulatory binder
- Investigator's brochure and protocol
- Any other study specific material

See Attachment B for more information on what to expect during the audit. All information will be held strictly confidential.

Please feel free to contact the EQ with any questions or concerns at EQ@hhrinstitute.org.

Sincerely,
Audit Team
Office for Education and Quality in Clinical Research

HennepinHealthcare Research Institute

ATTACHMENT B
POST-APPROVAL AUDIT PREPARATION AND CHECKLIST

Preparation:

- The study team will be asked to provide a list of study subjects (ID numbers only) of all consented subjects.
- The auditor will inform you of the subjects that are randomly chosen for review.
- The auditor may request time to speak with members of the study team.
- All regulatory and study documents are subject to review.
- Make sure the following study documents are available:
  - Study files (source documentation) for the chosen subjects
  - Regulatory binder
  - Investigator's brochure and protocol
  - Any other study specific material

Checklist

This list provides an overview of what topics may be reviewed. Other topics may be reviewed based on auditor's assessment.

Study Name:					
IRB#		PI Name:			
Select all that apply:	___Single Center ___ Multi Center __Drug study ___Device study				
Select all that apply:	___Industry ___Federal ___Investigator-Initiated				
Total # of subjects enrolled:		Total # of subjects to be reviewed:			
Auditor's Name:		Date:			
Area of Review	**Measure for Compliance**	**Yes**	**No**	**N/A**	**Comments**
External Monitoring	Sponsor monitored?				
	Monitoring log present?				
	Monitor Follow up letters reviewed?				
	Significant observations?				
	Is communication between the sponsor and research site on file?				
	Epic access obtained for external monitor?				
Regulatory	Is there a regulatory file/binder?				
	Hard copy, electronic, or hybrid?				
IRB	Is there an IRB approved protocol?				
	Original and all revisions?				
	Is there an IRB approved consent form?				
	Original and all revisions?				
	Did the protocol and informed consent receive initial approval				

	before the study was initiated?				
	Are there approval documents from other required committees, i.e., HHS Radiation or IBC Committee?				
	Original and all revisions?				
	Are there IRB approved recruiting materials (original and all revisions)?				
	Are all changes to the protocol, informed consent, and recruiting materials approved by the IRB prior to implementation?				
	Is there an Investigator Brochure or Device Manual?				
	Original and all revisions?				
	Are all IRB renewals submitted in a timely fashion so that there is no lapse of approval?				
	Were any subjects enrolled if there was a lapse of approval?				
	Serious Adverse Events reported per IRB policy?				
	UPIRTSO reported per IRB policy?				
	External New Information reported per IRB policy?				
	Non-Compliance reported per IRB policy?				
	Are all approvals from the IRB on file?				
	Are IRB member lists on file for the duration of the study?				
Personnel	Is there a signed FDA 1572 for IND studies?				
	Original and revisions as appropriate?				
	Is there a signed Investigator Statement for IDE studies?				
	Original and revisions as appropriate?				
	Is there a CV or relevant documents for all Investigators?				
	Updated within the past 2 years?				
	Signed and dated?				
	Valid licensure for each investigator/staff member on the 1572/Investigator Statement?				
	Is there a Delegation of				

	Authority/Signature Log identifying all persons obtaining Informed Consent?				
	Is there a Delegation of Authority/Signature Log identifying all persons with delegated study-related responsibilities?				
	Has the IRB been notified of all personnel changes?				
	Is there a current (and previous) Clinical Investigator Financial disclosure form on file for each investigator?				
	Is a Training Log maintained for study-specific training requirements?				
	Are all research support personnel compliant with HHRI's educational requirements?				
	Are research personnel able to locate clinical research guidance?				
Subjects	Is there a screening/enrollment log?				
	Are subject records maintained appropriately to protect subject confidentiality?				
	Is there an adverse/serious adverse event (AE/SAE) log?				
	Have AE/SAEs been recorded, assessed, and reported according to the protocol?				
Investigational Product	Is the test article properly stored?				
	Is there a dispensing log?				
	Are there decoding procedures for blinded trials?				
	For marketed products, is there a package insert/product information?				
Laboratory	Is there an up to date laboratory certification?				
	Is there a copy of normal laboratory values?				

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ATTACHMENT C
POST-APPROVAL AUDIT FOLLOW-UP LETTER

To:	Principal Investigator Cayuse Primary Contact
From:	Office for Education and Quality in Clinical Research (OEQCR)
Date:	DD Month YYYY
Subject:	Quality Assurance Program
Study to be reviewed:	**IRB # and Title:**

Thank you for your cooperation in the audit of the above named protocol. Please review the enclosed observations and, if applicable, provide a written response by (DATE). Your response should address all requests. If corrective action is warranted, please outline all actions to be implemented.

Please send a copy of your written response to:
EQ@hhrinstitute.org

The Director of the OEQCR will review your answers and corrective plan(s) as applicable and determine if further action is necessary.

Please feel free to contact me with any questions or concerns. I may be reached at (PHONE #) or (EMAIL).

Sincerely,

(Signature)

(NAME)
Post Approval Audit Team