HennepinHealthcare Research Institute

HUMAN RESEARCH PROTECTION

OEQCR Standard Operating Procedures (SOPs)

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Resource type SOP

Contents

10 OEQCR Resource Management

Purpose

This procedure establishes the process to review, create, revise, and retire standard operating procedures (SOPs) and other resources for the Office for Education and Quality in Clinical Research (OEQCR).

The OEQCR staff will use this procedure to conduct a review of the OEQCR resources to determine that a resource needs to be created, revised, or retired.

Responsibilities

The OEQCR Director or designee, in collaboration with other OEQCR staff, as applicable, manages the procedures described below to review, create, revise, or retire an OEQCR resource.

Procedures

Review the OEQCR resource:

Changes to regulations and guidelines, institutional policies, or Hennepin Healthcare current practices may require a new resource or a revision to a resource.

- The OEQCR Director and other OEQCR staff will review information, any applicable regulations, and institutional policies to decide if a resource needs to be created or revised.
- The OEQCR Director determines when to retire an OEQCR resource.

Create a new resource:

1. OEQCR Director confirms that a new resource should be created.
2. Assign a number, type, and title in the master list workbook; The master list is stored in the OEQCR network drive: **Resource Management\OEQCR Master List**
3. Draft the new resource (this is completed by the Director in collaboration with other designated staff)
4. OEQCR staff will collaborate and review the changes; tracked changes will be used for any edits
5. Director will make final approval
6. Once the resource is approved:
    a. Update the master list, as appropriate
    b. Save final version of the resource in the OEQCR network drive, in the applicable resource folder
    c. Update the OEQCR website, as appropriate
    d. Communicate the new resource, as appropriate
    e. Implement training related to the new resource, as appropriate

Revise an existing resource:

1. Confirm with OEQCR Director that a resource should be revised
2. Draft the revisions using tracked changes
3. Route the draft of the revised resource to the OEQCR Director for review
4. Manage the editing process with the OEQCR Director, as applicable
5. Document resource updates in the version history section
6. Once the revised resource is approved:
    a. Update the master list, as appropriate
    b. Archive the prior version in the OEQCR network drive: Resource Management\Archive
    c. Save final version of the resource in the OEQCR network drive: Resource Management\Active
    d. Update the OEQCR website, as appropriate
    e. Communicate the revised resource, as appropriate
    f. Implement training related to the revised resource, as appropriate

Resource update notification

The following communications will be used to notify researchers of updated resources:

- HHRI newsletter – managed by HHRI Communications office
- HRPO newsletter – managed by HRPO staff
- If necessary, email blasts to specific researchers
- OEQCR webpage notification announcement at beginning of webpage

Retire a resource as follows:

1. Confirm with OEQCR Director that a resource should be retired
2. Update the master list, as appropriate. The master list is stored in the OEQCR network drive: **Resource Management/OEQCR Master list**
3. Archive the retired resource in the OEQCR network drive: **Resource Management\Archive**
4. Update the OEQCR website, as appropriate
5. Communicate the retired resource, as appropriate
6. Implement training related to the retired resource, as appropriate

Resource Gallery organization

The OEQCR Resource list is organized as follows:

Numbering level	Resource type
10-19	SOPs Administrative
20-29	SOPs Compliance
501	Guidance in HRPO 501 Manual – Sections listed
600	Templates

References

- OEQCR website: Office-for-education-quality-in-clinical-research

11 HRPP Resources and Outreach

Purpose

Describe the processes for maintaining adequate resources for support of the Human Research Protection Program (HRPP) and provision of outreach to participants, prospective participants and the public.

Responsibilities

It is the responsibility of the HRPP to ensure that enough resources are available and allocated to ensure the protection of human participants. HRPP also takes on the responsibility to provide information to prospective participants about medical research in general and information about the specific research being conducted on the HHS/HHRI campus.

Procedures

The Hennepin Healthcare Research Institute (HHRI) will follow and refine procedures to assess and readjust resources for the support of the HRPP. This procedure for evaluation will occur no less than annually.

1. HHRI Administrative Management Committee meetings will be conducted monthly to discuss operational and budgetary issues, needs, or changes, and short- and long-term future goals. Attendees include senior representatives of the following offices:
   - Operations
   - Communications
   - Finance
   - Grants and Contracts Office
   - Human Resources
   - Information Systems
   - Office for Education & Quality in Clinical Research (OEQCR)
   - Purchasing
   - Veterinary Services
   - Human Research Protection Office (HRPO)

2. Short-term (one year duration) and long-term operational and budgetary planning will begin in the third quarter of each year. Planning will be based on needs, requests, and feedback identified by members of the Administrative Management Committee and HHRI staff. Items that will be addressed include, but are not limited to:
   - Space
   - Personnel
   - HRPP education programs
   - Legal counsel
   - Conflict of interest
   - Quality improvement planning

- Community outreach
- IRB/HRPO resource planning

Outreach

Outreach is key to connecting with potential participants, current participants, and the public. Outreach is accomplished in many ways at HHRI. One of those ways is the HHRI website which contains many options for participants to learn more about medical research and specific research taking place at HHRI. HHRI's outreach webpages include:

"Patients and Community" - contains several ways for potential participants and the community to get connected and learn more about research. Links include:

- General information about medical research
- Volunteering for a study
- Patient Advocacy
- HHRI Research Highlights

"Our Research" - provides information about the investigators and research groups conducting research on campus.

"Newsroom" - provides recent articles and information including press releases, recent grant awards, media coverage, communication resources, research community resources, and general research news

"About Us" – provides information about HHRI's Mission, Vision, and Values along with links to other key pieces of information about the institution.

Other Outreach Activities

HHRI's Podcast - The Y podcast focuses on showcasing research happening at HHRI and the staff who make research happen. They explore institutional process as well as ongoing projects. The webpage that houses past podcasts: HHRI's Podcast: Y - Hennepin Healthcare Research Institute (hhrinstitute.org) also provides an option for submitting answers to specific questions or connecting with general comments or questions.

Outreach Procedures

1. The HRPP will collaborate with the HHRI Corporate Communications Manager in evaluating and updating applicable information and pages on the HHRI website to ensure the latest information and links are available.

2. The HHRI Communications Manager will update the HHRI website with varying articles, posts, and videos to allow current and prospective participants and the community to observe various aspects about the research process. Researcher publications, based on sponsored research projects, are posted annually on the HHRI website.

3. Website analytics will be collected at the time of the annual assessment for the HRPP (OEQCR SOP 12). Data will be collected for the following web pages and/or links:
   - About Us
   - Our Research - with a focus on the main institutional focus areas
   - Newsroom
   - About Medical Research - link found on the Patients and Community webpage
   - Volunteer for a Study - link found on the Patients and Community webpage
   - Becoming a Research Volunteer Brochure - link found within the Volunteer for a Clinical Study link
   - How Are You Protected? AAHRPP Accreditation link found on the Patient Advocacy webpage

4. The OEQCR contact information will be publicly available on the HHRI website for current, prospective, or past research participants to discuss problems, concerns, or questions; obtain information; or offer input with an individual who was unaffiliated with the specific research protocol. Items that may be discussed include, but are not limited to:
   - Explanations concerning the research process
   - Providing information about clinical research conducted at HHRI
   - How and where to find studies based on the caller's needs
   - Discuss problems, concerns, or questions

   As appropriate to the content of the call, callers may be referred to the HRPO, Principal Investigator, applicable research personnel, or federal websites for more information.

5. Those who connect with OEQCR for information are logged into the OEQCR database. Information includes the nature of the question and answers/direction given to the caller. Uncharacteristic or worrisome findings will be shared immediately with the Institutional Official, the HRPO Director and/or IRB Chair, or the Principal Investigator as appropriate. Data collected will include, but not be limited to:
   - Number of individuals looking for research participation opportunities and type of opportunities requested (i.e., phase I, hypertension)
   - Number of individuals looking for information concerning clinical research
   - Individuals looking for volunteer opportunities within HHRI
   - Complaints received from research participants
   - Resolution to all inquiries

References

- HHRI website: Home - Hennepin Healthcare Research Institute (hhrinstitute.org)
- HHRI webpages: Patients & Community; Our Research; Newsroom; About Us

12 OEQCR Responsibilities

Purpose

It is the purpose of the Hennepin Healthcare Research Protection Program (HRPP) to have an office that provides education, guidance, and quality improvement opportunities for investigators, other research staff, and the HRPP. The Office for Education and Quality in Clinical Research (OEQCR) serves that purpose. This SOP describes the programs that OEQCR manages.

Programs

Education – online and in-person research training

OEQCR manages the initial and continued online and in-person training requirements for researchers to conduct human research. The 501 Manual – Conducting Human Research, Section 1.6 describes detailed education requirements based on type of research and study role.

Mentorship

During the initial training process and throughout a researcher's career, OEQCR identifies and connects to find ways to support researchers during their career at HHRI. This mentorship may include hands on training for a specific study task, help acclimating to HHS/HHRI organizational systems, and/or help learning a new role within a research team.

Study start-up program

This program is designed to provide support for investigator-initiated interventional studies that will be reviewed by the convened IRB. Since the IRB requires study pre-review for these types of studies, the OEQCR continues to work to identify these studies as early as proposal time to help provide feedback and support during the planning phase for study feasibility and implementation, as well as working towards a quicker IRB review. See OEQCR SOP 21 Study Start-up Review and 501 Manual Conducting Human Research Section 18.2 for more details about the program.

Quality Assurance Program

OEQCR is responsible for managing the quality assurance program. OEQCR collaborates with many departments such as Human Research Protection Office (HRPO) and Office for Grants and Contracts to actively look for ways to improve process, connect with researchers, and find solutions to issues as they develop. OEQCR is also responsible for managing the "not for cause" annual audits and any "for cause" audits requested by the IRB or Institutional Official. For more detailed information see OEQCR SOP 20 Compliance Activities, OEQCR SOP 22 HRPP Monitoring, and OEQCR SOP 23 IRB Minutes Quality Review.

20 Compliance Activities

Purpose

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.

Post-approval Audit

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
   - Compliance with federal regulations and guidance, as applicable
   - 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 will 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 report 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 final report.

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

4. After-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. Once the audit process has been completed, OEQCR will complete the Post-approval Audit Completion Checklist (Attachment D) and direct the PI to submit the checklist and any other relevant documents as an incident report in the IRB online system Cayuse.

   g. Results of audits that include significant or multiple findings will be discussed with the IRB Chair and/or any other relevant HHRI personnel. Any required next steps will follow the *HRPO 260 SOP Compliance activities* procedures.

   h. Distribution of post-audit reports and letters will go to the following parties:
      i. Principal Investigator
      ii. 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.

iii. Others as determined appropriate by the OEQCR Director
iv. 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.

IRB Noncompliance

1. Any report of IRB noncompliance will be sent to the Institutional Official (IO) and a review initiated.
2. Reviewers may include OEQCR, IO, other institutional leadership, and/or outside auditors.
3. HRPO and the IRB will respond to any requests for information and provide any necessary documentation.
4. After review, reports without finding of IRB noncompliance will be provided to the IO, IRB Chair, and OEQCR Director. OEQCR will file a copy for record keeping purposes.
5. After review, reports that necessitate corrective action will require that the IRB Chair (or designee) and HRPO leadership provide a written corrective action and preventative action (CAPA) plan within a specified timeframe to the IO, OEQCR Director and any other designated leaders. The CAPA will include actions to be implemented and date of implementation.
6. IO will provide written approval if the corrective actions are appropriate.
7. IO and OEQCR Director may require or choose to follow up with the IRB Chair (or designee) and HRPO leadership to ensure corrective actions continue to be appropriate; any such follow-up will be communicated in writing to the IRB Chair (or designee) and HRPO leadership.
8. If necessary, the IO will direct appropriate personnel to report findings to outside agencies.

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
- 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

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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 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 the attached Post-Approval Audit Preparation and Checklist 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

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Attachment B (645 TEMPLATE)

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 approval 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?				
	Is the informed consent form (ICF) the appropriate version?				
	Has the ICF been signed and dated by both the subject and the person obtaining consent?				
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

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Attachment D

POST-APPROVAL AUDIT COMPLETION CHECKLIST

IRB #		Study Title:	
Principal Investigator:			
Study Coordinator(s):			

Type of Audit:

☐ Not for Cause

☐ For Cause

Requested by and reason:	

☐Auditor report is included

☐If necessary, study team has provided a corrective and preventative action plan (CAPA)

☐No additional actions are required

☐Additional actions will be reported to the IRB. Those actions include:

{add name}
Director, Office for Education and Quality in Clinical Research

Date

Note: Study team must submit this form and any attachments to the IRB as an Incident Report through the Cayuse system.

21 Study Start-up Review

Purpose

Describe the process by which the Office for Education and Quality in Clinical Research (OEQCR) conducts a study start-up review. These procedures apply to all human research activities approved by the Human Research Protection Office (HRPO) conducted within the Hennepin Healthcare System.

Responsibilities

OEQCR in collaboration with HRPO manages the procedures described below.

Study start-up review requirement

- All investigator-initiated research reviewed by the Hennepin Healthcare convened IRB must complete the study start-up review.
- Applies to ceded research for which the Hennepin Healthcare PI is the overall PI of an investigator-initiated study and/or the holder of a test article IND and/or IDE
- IRB has discretion to establish the requirement for other research based on review of an IRB submission and identification of need for additional support from OEQCR.
- See also 501 Manual – Conducting Human Research Section 18.2

Procedures

1. HRPO, OEQCR, or PI identifies a study that meets criteria for review or requests a review.

2. OEQCR connects with the Principal Investigator and other study staff.
   - Communication is sent to ensure the study team is aware of the review and to ensure all study documents are received/available for review.

3. OEQCR decides whether the review qualifies for an expedited review or a full review and initiates the study start-up checklist. The review process begins. See section “Types of Study Start-up Reviews” for more detail.

4. OEQCR, PI, and/or study staff continue to connect until all issues are addressed and review is complete to the satisfaction of the EQ reviewer(s).

5. OEQCR provides a completed checklist to PI/study staff.

6. PI or study staff submit completed checklist in the Cayuse HE initial submission.

Types of Study Start-up Reviews

1. Full study start-up review

a. This type of review is the most common. The goal of this review is to work through common regulatory and logistical issues that are often overlooked or underrepresented during study design. Those issues include but aren't limited to:
    - Assessing criteria for FDA oversight of a study
    - Assessing other federal regulatory requirements
    - Understanding adverse/serious adverse events and requirements for recording, assessing, and reporting those events
    - Ensuring congruency between informed consent form and protocol
    - Identifying areas in the protocol or consent form that need to include further information
    - Providing appropriate information in the protocol for study staff to conduct the study
    - Identifying appropriate staff for study activities
    - Identifying external collaborations and agreements
    - Ensuring data management and sharing plan has been established
    - Discussing appropriate funding for conducting the study
b. Study documents for review will include but are not limited to:
    - Protocol
    - Informed consent form(s)
    - Recruitment materials
    - Informational sheets
    - Investigator brochures
    - Any other relevant materials
c. Can involve several rounds of reviews before all issues/concerns are addressed.
d. OEQCR reviewers will encourage Cayuse submissions to be started during this process.
e. Study staff are requested to fill out a review checklist and EQ updates the checklist including what was reviewed, resolved, and any outstanding issues that will need to be addressed at the HRPO/IRB level.
f. PI/study staff submit the completed checklist in the Cayuse HE Initial submission in the "Sponsor info" section.

2. Expedited study start-up review
    - This type of review is reserved for well-established Principal Investigators who have previously conducted investigator-initiated studies with an established research team.
    - A shortened review of study materials is conducted.
    - EQ completes an expedited review checklist that provides an explanation for expedited review.
    - PI/study staff submit the completed checklist in the Cayuse HE Initial submission in the "Sponsor info" section.

22 HRPP Monitoring

Purpose

Describe the process by which information is collected and monitored to assess the quality, efficiency, and effectiveness of the Human Research Protection Program (HRPP). These procedures apply to all human research activities approved by the Human Research Protection Office (HRPO) conducted within the Hennepin Healthcare System.

Responsibilities

The Office for Education and Quality in Clinical Research (OEQCR) in collaboration with HRPO manages the procedures described below.

Procedures

1. Annually assess the quality, efficiency, and effectiveness in three areas of the HRPP.
    a. IRB metrics
    b. Audits concerning the research process
    c. Investigator and other study staff feedback

2. IRB metrics to be collected annually will include but not be limited to:
    - Number of researchers
    - Mean number of days from submission to review at meeting and final determination for new protocols reviewed in the last year by the convened IRB
    - Mean number of days from submission to review and final determination for new protocols reviewed in the last year by the expedited procedure
    - Mean number of days from protocol submission to exempt determination in the last year
    - Number of protocols disapproved by the IRB in the last year
    - Number of reported protocol deviations in the last year
    - Number of cases of alleged non-compliance investigated in the last year
    - Number of determinations of serious non-compliance in the last year
    - Number of determinations of continuing non-compliance in the last year
    - Number of unanticipated problems in the last year
    - Number of unanticipated problems involving risks to participants or others in the last year

3. Audit findings concerning the research process will include, but not be limited to:
    - The informed consent process
    - Documentation of research activities
    - Confidentiality procedures
    - Protocol adherence and/or violations
    - Completion of research team required training

4. Annual Investigator and study staff feedback via survey will be reviewed to understand investigator perspective about:

- Interactions/communication between the study team and HRPO staff
- Quality of information provided for researchers
- Usability of online IRB system
- Turnaround time for exempt/expedited review
- Turnaround time for full committee review
- Interaction/communication with OEQCR staff
- Usability of required training
- Any other feedback the researcher would like to provide

5. The OEQCR will annually compile results. Results will be compared to published metrics from AAHRPP. In addition changes noted over the past year will be highlighted.

6. Findings will be shared with the Institutional Official, the IRB Chair, and the HRPO Director.

7. Noted outliers or changes will be highlighted and plans to correct or make improvements will be discussed and instituted as needed.

8. Results of improvement plans will be discussed during the next annual assessment or earlier if deemed necessary.

23 IRB Minutes Quality Review

Purpose

Describe the compliance activities conducted by the Office for Education & Quality in Clinical Research (OEQCR) to assure that the Institutional Review Board (IRB) documents discussions and decisions relevant to a research protocol in accordance with legal, regulatory, sponsor, and organizational requirements. These procedures apply to all human research reviewed by the Hennepin Healthcare convened IRB.

Procedures

1. IRB Minutes Quality Improvement:
    a. A minimum of two reviews will be done yearly. The OEQCR reserves the right to review minutes' content more frequently.

    b. The selection of minutes for scheduled reviews shall be a risk-based assessment. Selection criteria shall include but not be limited to: Investigator or research team new to clinical research; Investigator-initiated/sponsored protocols; type and complexity of the trial and decision making by the IRB members; level of risks to the trial subjects; and problems identified during "not for cause" or "for cause" audits.

    c. The reviewer(s) will have training in auditing processes and compliance as needed and possess the professional experience and expertise to understand and apply the applicable federal, state, and institutional regulations.

    d. Areas of the minutes that will be reviewed include, but are not limited to, the following:
        - Meeting attendance
        - Actions taken by the IRB
        - Vote on Actions
        - Required determinations and protocol-specific findings to justify a determination
        - Decisions about informed consent
        - Expedited Activities and Continuing Review
        - Unanticipated problems, serious or continuing noncompliance, suspension or termination of IRB approval

2. Review process:
    a. IRB minutes to be reviewed will be identified from the IRB Cayuse database. Selected minutes will be chosen following a risk-based assessment.

    b. The reviewer will discuss minute review with the HRPO staff.

    c. The review will be conducted using the IRB Cayuse online system database. The reviewer will address any questions with HRPO staff.

    e. A review questionnaire will be used as a tool to conduct the review (Attachment A). If needed, all minutes about a specific ongoing action are subject to review.

3. Post-review process:
   a. A post-review summary will be completed or reviewed by the OEQCR Director.

   b. The summary will include the findings and outcomes of the review as well as any recommendations or requirements.

   c. The report will outline follow-up procedures, if necessary.

   d. After completion of the review, a follow-up letter (Attachment B) will be sent to HRPO@hhrinstitute.org. The letter will include the summary of the review.

   e. IRB minutes quality improvement reports and letters will not be shared with outside agencies.

   f. The HRPO will have two weeks to provide a written response to the post-review follow-up letter and planned corrective action as needed.

   g. If needed, the written response will be sent to OEQCR via EQ@hhrinstitute.org. The Director will review the response and decide if further review is required. If further review is required, the OEQCR Director will connect with the HRPO Director, and if deemed necessary the IRB Chair and/or Institutional Official.

Attachment A

IRB Minutes Quality Improvement Assessment Tool

Date of IRB meeting:	Person completing: Date of Assessment:

AREA OF REVIEW	MEASURE FOR COMPLIANCE	YES	NO	N/A	COMMENT
Attendance at the meeting	Is the date, time, and location of the meeting documented				
	Are the full name and representative capacity (scientist, nonscientist, unaffiliated) of each member present				
	Is at least one nonscientist member present				
	Are members participating by electronic means documented				
	Is the replacement of a primary member by an alternate member documented				
	Is the name of any consultants present at the meeting and their expertise documented				
	Are the names of non-members and guests that attended a meeting documented				
	Is a quorum present *(Divide the number of members by two and select the next whole number. For example, if there are 10 IRB members on the roster, then 10/2 = 5 and the next whole number is 6. If there are 11 IRB members on the roster, then 11/2=5.5 and the next whole number is 6.)*				
	Are the name(s) of members who leave the meeting due to COI documented along with the fact that COI is the reason for the absence				
	Has a quorum been maintained for each vote				
Actions taken by the IRB	Are the actions taken by the IRB (approval, require modifications, defer, disapprove) documented				
	Are there separate deliberations for each action				
	Is there sufficient detail to justify IRB actions				
	Is there a summary of discussion of controverted issues and their resolution				
	Is there sufficient detail to show the basis for requiring changes in the study or disapproving research				
Vote on actions	Are votes for each protocol listed as numbers for, against, or abstaining documented				
	Is the approval period documented for initial and continuing review				

	Has there been a vote to suspend or terminate approval of previously approved research				
	Is there documentation of the reasons to suspend or terminate approval of previously approved research				
	Has there been a vote to lift suspension of a study or to terminate a previously suspended study				
	Is there documentation of the reasons to lift suspension of a study or to terminate a previously suspended study				
	Are votes for presence of conflict of interest and recusals documented				
Are required determinations and protocol-specific findings to justify a determination documented	Waiver or alteration of the consent process				
	Research involving pregnant women, fetuses, and neonates (Subpart B)				
	Research involving prisoners (Subpart C)				
	Research involving children (Subpart D)				
	Research involving subjects with diminished capacity				
	Research involving children who are wards of the state or any other agency				
	Rationale for determining risk associated with using a medical device in a study deemed significant or non-significant				
	Research involving an exception from informed consent for emergency research				
Consent	Has the informed consent been reviewed and determined that it meets applicable regulatory requirements				
	Are required changes documented				
Expedited Activities and Continuing Review	Have expedited review activities been presented				
	Are continuing review assignments and requirements documented				
Compliance	Unanticipated problems, serious or continuing noncompliance, suspension or termination of IRB approval: If existing, have these been presented and reviewed				

Attachment B

IRB MINUTES QUALITY IMPROVEMENT FOLLOW-UP LETTER

To:	IRB Vice Chair IRB Analyst
From:	Reviewer Name/Title
Date:	xx/xx/xxxx
Subject:	IRB Minutes {add date of minutes}

Thank you for your cooperation in the review of the above named IRB minutes. 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. {Sample wording can be adjusted as needed}

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

The OEQCR Director 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, {Email}.

Sincerely,

{PDF electronic Signature}

{Name and Title}

24 Post-approval Monitoring

Purpose

Describe the procedures and processes for internal post-approval monitoring activities conducted by Hennepin Healthcare Research Institute (HHRI) employees, designees, or OEQCR monitors for clinical research studies conducted under the auspices of the Hennepin Healthcare System (HHS). In addition, describe oversight responsibilities of the Office for Education & Quality in Clinical Research (OEQCR). These procedures and processes apply to all clinical research reviewed by the Hennepin Healthcare convened IRB, or another IRB of record and designated with a post-approval monitoring requirement either through federal regulation or as specified by the IRB.

These procedures and processes do not apply to post-approval monitoring activities that are conducted by an external organization or consultant. The sponsor or sponsor-investigator is responsible to ensure that external organizations or consultants are conducting monitoring activities in accordance with all applicable federal and state regulations and institutional policies and guidance.

Definitions:
Post-approval monitoring - For the purpose of this SOP, post-approval monitoring is defined as internal data and safety monitoring activities required to be completed for the purpose of ensuring safety for research participants, integrity of study data, and compliance of study activities with all applicable federal, state, and institutional regulations and guidance.

Sponsor-investigator (FDA) – An individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term applies only to an individual, i.e., it does not apply to a corporation or agency. The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator. See also Glossary 501-MANUAL-Conducting-Human-Research.pdf (hhrinstitute.org).

Procedures

HRPO 150 GUIDANCE Data and safety monitoring in clinical research provides an overview of data and safety monitoring requirements and responsibilities. 150-GUIDANCE-Data-and-safety-monitoring-in-research.pdf (hhrinstitute.org)

This SOP describes what is required for internal post-approval monitoring.

1. Internal post-approval monitoring conducted by HHRI/HHS employee or designee: A sponsor-investigator may choose to conduct internal post-approval monitoring by designating an HHRI employee or designee as a monitor. The following requirements apply:

    a. The HHRI employee or designee may not be involved in the study for which they will serve as a monitor. For example: an HHRI employee who is approved by the IRB to conduct human research activities may not be the monitor for that study.

b. All HHRI/HHS employees or designees who will be conducting post-approval monitoring activities must complete monitor training. Mentorship while learning to conduct post-approval monitoring activities is pivotal for success. Opportunities for mentorship are available through the OEQCR office. **See 501 Manual – Conducting Human Research – Section 1.6 for more details about training and mentorship.**

c. Before post-approval monitoring activities begin, two (2) key activities must be completed by the Principal Investigator (PI) and it is recommended to include other designated study team members, and when possible, the designated monitor:

- A risk assessment must be completed to identify key areas for monitoring. The details of the risk assessment are based on the complexity of the clinical trial. The risk assessment must be documented.
- A risk-based monitoring plan must be created and completed. The monitoring plan must provide the study type, what will be monitored, who will be the monitor, how often the study will be monitored, and a description of the monitoring activities. OEQCR has created a Monitoring Plan Template (Attachment A). Although this template is available and recommended, other monitoring plans may also be acceptable but must address the key areas listed in the template and follow applicable federal, state, and institutional guidance.
- OEQCR staff are available to provide guidance and mentorship during this process. Contact OEQCR: EQ@hhrinstitute.org

d. Monitors must follow the monitoring plan, document monitoring visits, and follow-up on any outstanding issues until those issues have been resolved.

e. Contact OEQCR, EQ@hhrinstitute.org, to work through any compliance issues or questions that require additional guidance or assistance.

f. All internal monitoring activities are subject to OEQCR oversight. See Procedures Section 3 and Process Section 3 Quality Reviews for more information about OEQCR oversight activities.

2. Internal post-approval monitoring conducted by OEQCR – A sponsor-investigator may choose to request OEQCR monitor services. The following requirements apply:

a. OEQCR monitors will follow the same requirements as listed above in Section 1.

b. The OEQCR monitor will charge effort to the study's HHHRI project account during specific planned monitoring visits and follow-up activities. If the OEQCR monitor is helping train and mentor another monitor for a study or providing guidance and mentorship on the study risk assessment or monitoring plan documentation, those activities fall under the OEQCR infrastructure services and will not be charged to the study.

c. An OEQCR monitor may not conduct OEQCR audit activities for a study when they are providing monitoring services for that study.

d. Please note: OEQCR monitoring services is dependent on availability.

3. OEQCR will retain institutional oversight responsibilities for internal post-approval monitoring activities. The responsibilities include, but are not limited to:

   a. Training – See Section 1.6 501-MANUAL-Conducting-Human-Research.pdf (hhrinstitute.org)

   b. Mentorship – mentorship may be defined in many ways. Possible options may include, but are not limited to:
      - connecting with monitors about specific questions
      - ongoing interactions to provide support and guidance during monitoring activities
      - specific guided shadow experiences and case scenario reviews

   c. OEQCR Quality reviews – See Process, number 3 below for details.

Process

1. HHRI employee or designee monitor – The PI, or the person designated by the PI, is responsible for connecting with OEQCR, EQ@hhrinstitute.org, to provide information about a new monitor and start the post-approval monitoring procedure as described above in Procedures, number 1.

2. Monitoring by OEQCR – The PI, or the person designated by the PI, is responsible for connecting with OEQCR, EQ@hhrinstitute.org, to set up use of monitoring services as described above in Procedures, number 2.

3. Quality reviews –

   a. OEQCR will conduct two quality reviews annually. Exception: If only one internal monitoring visit has been conducted for the review year, then only one quality review will be conducted.

   b. To assess compliance with federal, state, and institutional regulations and guidance, the review will include, but may not be limited to, the following:
      - Reviewing documentation of the risk assessment and monitoring plan (only needs one-time review if documentation meets requirements at initial review)
      - Monitor visit documentation
      - Any follow-up documentation related to the monitor visit
      - Any unresolved issues relating to the monitor visit

   c. OEQCR staff will use the study monitoring plan as guidance during the quality review. OEQCR Staff will document the review and any questions involving the monitoring visit.

   d. A post-review summary will be completed or reviewed by the OEQCR Director.

      - The summary will include the findings and outcomes of the review as well as any recommendations or requirements.

      - The report will outline follow-up procedures, if necessary.

e. After completion of the review, a follow-up letter (Attachment B) will be sent to the monitor, monitor's supervisor, and Principal Investigator of the study. The letter will include the summary of the review and either finalize the review process or request a response to any findings.

f. If a response is requested in the follow-up letter, the study team will have two weeks to provide a written response to the post-review follow-up letter and provide a planned corrective action, as needed. OEQCR mentorship may be requested as part of the corrective action plan.

g. When a response has been provided, the OEQCR Director will review the response and decide if further review is required. If not already requested and deemed necessary, specific OEQCR mentorship may be assigned as a corrective action. If all issues have been resolved, the OEQCR Director will provide a written response with final outcomes.

h. If issues are not resolved through the quality review process, HRPO and/or the Institutional Official may be included in the review process. If necessary, HRPO and the IRB will then decide further action that needs to be taken.

Attachment A
Monitoring Plan (646 TEMPLATE)

Monitoring Plan: Investigator-Initiated Clinical Trials

Principal Investigator (PI):	
Mentor (when applicable):	
Monitor:	
IRB Number:	
Protocol Title:	
Sponsor:	*(Add Sponsor-Investigator (PI) name)*
Institutional Delegate:	*(will typically be the Director, Office for Education and Quality in Clinical Research unless otherwise specifically delegated in this document)*

Prepared By (print name)	Signature	Date (dd-mm-yyyy)

Sponsor-Investigator/PI Approval (print name)	Signature (PI)	Date (dd-mm-yyyy)

Mentor Approval (print name)	Signature (Mentor)	Date (dd-mm-yyyy)

Glossary

AE	Adverse Event
CRF	Case Report Form
DCF	Data Correction Form
e-CRF	Electronic Case Report Form
EDC	Electronic Data Capture
ICF	Informed Consent Form
ICH-GCP	International Conference on Harmonization Good Clinical Practice
IP	Investigational Product
IRB	Institutional Review Board
PI	Principal Investigator
SOP	Standard Operating Procedure
SAE	Serious Adverse Event

1.0 Purpose

The purpose of post-approval monitoring is to verify the following:

1. The rights and well-being of human participants are protected.
2. The reported clinical trial data are accurate, complete, and verifiable from source documents and accessible for review.
3. The conduct of the clinical trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirements.

This document identifies key monitoring activities and specifies the data to be reviewed. Study monitoring is a Sponsor responsibility as outlined in FDA and NIH regulations and guidance and is the responsibility of the Sponsor-Investigator/Principal Investigator who has delegated this responsibility to the assigned Monitor of the study.

2.0 Monitor

Monitors are responsible for ensuring the appropriate conduct and documentation of a study. As delegated by the sponsor or sponsor-investigator, monitoring is the responsibility of the PI, but may be delegated to an appropriately trained monitor.

Delegation of this task has been indicated on the study Delegation Log and training and qualification documents kept on file. The monitor is familiar with the investigational product(s) (IPs), as applicable, protocol, written informed consent form(s) (ICFs), internal SOPs, ICH-GCP and any other applicable regulations and/or guidance.

3.0 Responsibilities

The monitor is responsible for verifying that:

1. The study team has adequate documentation of the study team's qualifications, delegation of authority, training records including required institutional training and protocol specific training
2. All study communications are kept and updated in the regulatory binder, including IRB communications and study communications, including but not limited to:
    a. All IRB approvals
    b. Reporting to IRB, as required, of protocol deviations, protocol changes, and noncompliance
    c. Study pauses or closures
    d. Discussions about process improvement or quality improvement
    e. Any study related email communications
3. Storage of all paper and electronic study data files are appropriately maintained according to HIPAA requirements, HHS/HHRI policies, and secure on the HHS/HHRI campus.
4. The study team is following the approved protocol and all approved amendments.
5. Written informed consent was obtained before each participant is enrolled in the clinical trial or IRB approved waiver of consent is following any other requirements such as providing an Information Sheet to each subject enrolled.
6. Only eligible participants are enrolled.
7. Source documents and other clinical trial records are accurate, complete, kept up-to-date and maintained.
8. Investigator completes/submits all notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated and that they identify the clinical trial.
9. Paper and/or electronic CRF entries, source documents and other clinical trial-related records are verified against each other for accuracy and completeness. Specifically, the monitor will verify that:
    a. The data required by the protocol are recorded accurately on the CRFs and are consistent with the source documents.
    b. All CRFs have date and signature of study staff who collected the data.
    c. Any dose modifications are documented for each participant.
    d. Adverse events (AEs), concomitant medications and inter-current illnesses are recorded in accordance with the protocol on the CRFs.
    e. Any protocol deviations (e.g., missed or outside of window visits/tests/examinations etc.) are clearly recorded as such on the CRFs and reported as required.
    f. All participant withdrawals are reported and explained on the CRFs.
    g. Ensure that any corrections, additions, or deletions that are made to the CRFs are dated, explained (if necessary) and initialed by the investigator or a delegate.
    h. Determine whether all AEs are appropriately reported within time periods required by ICH-GCP, the protocol, internal SOPs, and the IRB
    i. Ensure that the essential documents are maintained for the trial.
    j. Communicate deviations from the protocol to the IRB and take appropriate action to prevent recurrence.

10. Investigational Product
    a. Storage times and conditions (includes temperature monitoring) are acceptable, and that supplies are sufficient throughout the trial.
    b. IPs are supplied and administered at the protocol specified dose(s) only to participants who are eligible to receive it.
    c. There is a plan to explain to participants how to correctly use and return (if applicable) the IP.
    d. The receipt, use, and return of the IPs at the site are controlled and documented.
    e. The disposition of unused IPs at the site complies with applicable regulatory requirements.

4.0 Procedures

The "risk-based" approach to monitoring should be used to assess the need for additional monitoring visits past the listed requirement in 4.2. This approach is based on the research category (clinical phase/type of research) and risk exposure to participants and the institution.

4.1 Monitoring Process

1. Frequency of future monitoring visits will be based on enrollment status, safety concerns, data quality, and protocol compliance.

2. Monitoring visits will review all of the responsibilities listed above.

3. In addition, the following key areas are required to be reviewed:

Topic	Review Frequency
• *ADD study specific review topics here – this information is based on the topics identified during the risk assessment*	• *Examples of frequency "at each visit", "at least annually", "after this # of participants have been enrolled" etc.)*
•	•
•	•

4. Following each monitoring visit, a monitoring report will be submitted to the PI, designated study staff and if applicable, to the Institutional Delegate (See section 6.0 for monitoring report details.)

4.2 Monitoring Visit Activities

The following activities may take place during each monitoring visit:

Data for all participants will be monitored over the course of the clinical trial, but not necessarily at each monitoring visit.

Number of anticipated monitor visits/ year:

At least 3x/year	☐
At least 2x/year	☐
At least 1x/year	☐

The participants selected for monitoring and the extent of record review at each visit will be based on the progress of enrollment, as well as any concerns that may emerge about the safety of human participants, the integrity of study data or protocol compliance.

The following participant data will be source data verified for the indicated percentage of participants enrolled in the trial and all incidences reported since the last monitoring visit:

100% of consent or re-consent documents (as applicable)
100% of information sheets (as applicable)
100% of eligibility criteria
100% of SAEs (as applicable)
100% of drug accountability records for participants dosed (as applicable)
20% of participant CRFs (with the goal of 100% CRF review by end of study)

Any updates and/or revisions to the following study documents since the last monitoring visit will also be reviewed:

- Training documentation/records and Delegation Log updates
- Regulatory documentation including approval/amendments

Requirement: It is key that the monitor connect with the PI during each monitoring visit. During the connection the monitor will provide an overview of the visit and address any findings. Documentation of the monitor/PI connection is required.

HHRI Monitoring Visit Worksheets will provide specific required activities based on the study type. Depending on the type of study, the following activities may be conducted at each monitoring visit:

a) Trial Master File

- Ensure that essential document files are complete and current.

b) Investigator and Site Personnel Responsibilities

- Ensure that the Delegation Log is complete and signed.
- Verify that the PI and site personnel are adhering to the protocol and conducting the study according to regulatory requirements, SOPs and ICH-GCP.
- Verify that study activities are being performed by the PI or have been delegated to personnel qualified by appropriate education, training, and experience.

- Provide and document any necessary training for the PI and site personnel, such as training on GCP, SOPs, protocol, FDA regulations.

c) Informed consent form review - All participants. Verify the following:

- Original signed consent (not copy) present on site; all pages present
- The correct IRB approved version of the consent document was signed and dated
- Consent was obtained prior to initiating any study procedures
- All appropriate signatures and dates were obtained prior to initiating any study procedures
- Re-consenting with updated consent forms (if applicable and as directed by IRB) completed in a timely manner (i.e. next visit at the latest)
- Copy of signed consent form provided to participant(s)
- Local privacy requirements followed
- Source documentation includes a description of the consent process
- Patient information sheet, if applicable

d) CRF Review / Source Documentation Verification. Verify the following (as applicable):

- Accurate, complete, and current source documentation is maintained.
- Participants' eligibility reviewed and signed off by PI/Sub-I.
- All procedures outlined in the protocol were completed.
- Missed visits, clinical procedures, and/or tests are recorded appropriately and reported to the IRB (if applicable) as protocol deviations, as defined by IRB policy
- PI/Sub-I assessed all abnormal lab values for clinical significance or as outlined in protocol, and reported as AEs/SAEs when appropriate.
- All participant discontinuations and/or withdrawals recorded appropriately in source documentation.
- AEs, SAEs, concomitant medications and protocol deviations documented and reported according to the protocol.
- All withdrawals and dropouts of enrolled subjects are recorded in the source documentation and on the CRF.

- The PI has reviewed, signed, and dated all required CRF pages in a timely manner
- Data entries in the CRF and/or eCRFs coincide with the source documentation, and note any errors, omissions, or discrepancies by issuing queries
- Provide the site staff with copies of DCFs.
- Verify that previously outstanding data queries have been resolved, signed, and dated by the PI or designee.

e) Adverse Events, and Serious Adverse Events

- Verify all newly reported AEs and SAEs against source documentation.
- Follow up on previously reported AEs and SAEs.
- Confirm that all AEs and SAEs have been reported to the IRB as required.
- Identify any unreported AEs and SAEs in source documentation.
- Review AE and SAE reporting procedures, as necessary.

f) Laboratory and Specimen Management

- Assess maintenance of research specimen logs and associated documentation.
- Review handling of laboratory specimens.
- Review specimen storage conditions and maintenance of temperature logs.
- Ensure organization and storage of specimens in a secure location.
- Ensure appropriate specimen labeling.

g) Protocol Specific Procedures / Investigations

- Ensure protocol mandated lab test results are recorded and reviewed* by PI or qualified medical delegate.
- Ensure protocol mandated radiology test results are recorded and reviewed* by PI or qualified medical delegate.
- Ensure all other protocol mandated test results are recorded and reviewed* by PI or qualified medical delegate (if applicable).
  * as evidenced by documented medical oversight (signature and date)

h) Investigational Product Treatment / Administration

- Ensure the correct dose as outlined in the protocol was administered.
- Ensure any dose modifications as outlined in the protocol were administered.
- Ensure compliance is recorded in source documentation.

i) Investigational Product Accountability / Pharmacy Documentation

- Confirm that investigational product is stored at the correct temperature in a secure storage area.
- Review temperature logs to confirm stability of storage/shipping conditions.
- Confirm that investigational product is being dispensed according to protocol.
- Confirm that product accountability records are accurate, current, and reconciled.
- Ensure no discrepancies exist between drug accountability log and participant data on CRF.
- Ensure drug accountability log documentation is completed in chronological order in a timely fashion.
- Ensure all transactions are documented on drug accountability log.
- Ensure the balance on the drug accountability log matches the inventory balance.
- Ensure all shipment receipts are retained.
- Ensure Certificate of Analysis (or other acceptable documentation) is on file for each batch/lot received (Sponsor only).
- Ensure all product orders are retained.
- Ensure product is returned/destroyed as mandated by protocol.
- Ensure no products is returned/destroyed prior to authorization to proceed.
- Ensure product return/destruction documents are retained.

j) Protocol Deviations

- Verify that all protocol deviations are documented appropriately in each participant's research record and on the appropriate protocol deviation form.

- Ensure that the site has reported all protocol deviations to the IRB, as required by IRB policy and/or SOPs.
- Address any protocol deviations with site personnel during the monitoring visit and identify ways to prevent a recurrence of similar issues.

k) General

- Confirm all data is verifiable against source documentation.
- Confirm no transcription errors have been made.
- Ensure corrections are made according to GCP standards.

l) Visit Conclusion

At the conclusion of the visit, the monitor will meet with the PI and site research staff to review visit findings and answer questions. The following is a list of possible topics the monitor may discuss (discussions may vary and are not limited to these topics):

- Consent process and documentation.
- Study conduct and documentation of study activities.
- AEs and SAEs experienced by study participants.
- Deviations.
- Scheduling of the next Monitoring Visit.

m) Reporting for Identified Issues

During the monitoring process, the monitor will assess study files and documentation against ICH-GCP, regulatory requirements, institutional requirements and guidance, protocol, SOPs and any study-specific SOPs.

- All observations noted during the monitoring visit will appear in the monitoring report and associated follow-up letter.
- The monitor will address deficiencies to the appropriate study team member in order to implement corrective actions or to recommend follow-up procedures.
- Opportunities for the monitor to meet with the PI or study coordinator will be made periodically during the visit. These meetings will allow study staff to provide clarification of findings, ask questions, and work with the monitor to address certain issues at the time of the monitoring visit.

4.3 Close-Out Procedures

The monitor will conduct close-out procedures when appropriate. During close-out visit, the monitor will perform the following:

- Ensure the completion of outstanding case report forms and queries.
- Ensure all previous monitoring corrections have been addressed.
- Ensure the return or destruction of the IP (if applicable).
- Collect outstanding participant data forms and study forms (ex. screening and monitoring logs).
- Perform a final review of the study file documents.
- Review the plans and location for record retention.
- Ensure all SAEs have been reported appropriately.
- Ensure the PI has notified the local IRB of the site closure.

The monitor will prepare the final monitoring report and provide a copy to the PI/ designated study staff for their records, and when applicable, the Mentor and the Institutional delegate. The site will address all monitoring observations (including observations from previous monitoring reports) prior to final study closeout.

5.0 Non-compliance

Non-compliant conduct of the study will be documented in a monitoring report and forwarded to the Principal Investigator, and when applicable, the Mentor. It is the responsibility of each Principal Investigator to address all observations outlined in the monitoring report and ensure appropriate and compliant procedures are implemented in a timely manner.

It is the responsibility of the Principal Investigator to review Sponsor and/or IRB reporting requirements and, when applicable, report noncompliance activities to the Sponsor and/or the IRB.

For more information: Review HRPO 133 GUIDANCE New information/incident reporting or 113 GUIDANCE Notifications to HRPO for ceded studies.

6.0 Monitoring Report

The report will include the following:

- Date
- Monitor name
- Mentor name
- Principal Investigator name
- Study status overview
- Summary of reviewed documents
- Observations detailing:
    - Findings

- Recommended corrective and/or preventative actions (CAPAs)
- Action Items/Follow up plan
- Comments

The study monitor will generate monitoring reports after the completion of every monitoring event. The report will be sent to the Principal Investigator, any designated study staff, and the Mentor (if applicable). If required, the Institutional Delegate may also receive a copy. Note the following:

- The study monitor will communicate findings to the site in a timely manner.
- The site will respond to any queries, observations and/or comments listed in the monitoring report.
- The PI will sign, date, and return a signed copy of the monitoring report to the monitor.
- The monitored site will keep a signed monitoring report in the site files for their records and will use the report as a reference in any subsequent monitoring visits.

HennepinHealthcare
Research Institute

Attachment B

Post-approval Monitoring Quality Review Follow-up Letter

To:	Monitor Supervisor PI
From:	Reviewer Name/Title
Date:	xx/xx/xxxx
Subject:	Quality Review – {IRB#, study title, monitor visit date}

Thank you for your cooperation in the review of the above-named monitoring visit. The purpose of these quality reviews is to ensure monitoring activities are providing the level of safety and data monitoring as described in the monitoring plan. Quality reviews allow HHRI to document that these activities are being conducted appropriately or find opportunities for improvement and professional development. 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. {Sample wording can be adjusted as needed}

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

The OEQCR Director 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, {Email}.

Sincerely,

{PDF electronic Signature}

{Name and Title}

References

Monitoring Guidance

FDA: Guidance for Industry Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring - Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring | FDA

NIH: Data and Safety Monitoring | grants.nih.gov

HRPO 150 GUIDANCE Data and safety monitoring in research

501 Manual – Conducting Human Research – Section 2.7 Does my research need a data and safety monitoring plan?

Monitoring Regulation

FDA Regulations:

Overarching responsibilities set in 21 CFR 312 and 812

IND 21 CFR 312.50 (responsibility of sponsor to ensure proper monitoring) - eCFR: 21 CFR 312.50 -- General responsibilities of sponsors.

IND 21 CFR 312.53(d) (selection of monitors) - eCFR: 21 CFR 312.53 -- Selecting investigators and monitors.

IND 21 CFR 312.56(a) (shall monitor progress) - eCFR: 21 CFR 312.56 -- Review of ongoing investigations.

IDE 21 CFR 812.40 (ensuring proper monitoring) - eCFR: 21 CFR 812.40 -- General responsibilities of sponsors.

IDE 21 CFR 812.43(d) (selecting a monitor) - CFR - Code of Federal Regulations Title 21 (fda.gov)

IDE 21 CFR 812.46 (securing compliance) - CFR - Code of Federal Regulations Title 21 (fda.gov)

IDE 21 CFR 812.140(b) (sponsor records – includes monitoring) - CFR - Code of Federal Regulations Title 21 (fda.gov)

IDE exemption (exempt from 812 requirements)

21 CFR 812.2 (c) Must meet ONE (1) of these criteria to be exempted

IND exemption (marketed drug)

21 CFR 312.2(b) exempt if specific criteria are met – note that EFIC studies are not exempt from an IND

NIH Regulations:

NIH Policy for Data and Safety Monitoring - June 10th, 1998

NIH 3014-503-Data and Safety Monitoring

OEQCR SOP Version history

Version date	Summary of substantive revisions
07 FEB 2024	**24 Post-approval Monitoring - NEW**
06 FEB 2023	Origination of SOP compilation format Rearranged order of SOPs and numbering **20 Compliance Activities** Renamed from Post-approval Review Added Attachment D Updated process to include Attachment D Added procedures for report of IRB noncompliance **21 Study Start-up Review - NEW** **22 HRPP monitoring** Updated process to include study staff in annual survey **23 IRB Minutes Quality Review** Updated name of SOP to more accurately reflect procedures