OFFICE FOR EDUCATION & QUALITY IN CLINICAL RESEARCH	CATEGORY	Clinical Research: Study Management
	SUBJECT	Study Conduct
	SOP #	2.11
	EFFECTIVE DATE	August 6, 2008
	REVISION DATE	September 13, 2019

OBJECTIVE
Describe the activities in the conduct of a clinical research trial. These procedures apply to all clinical research activities approved by the Office for Human Subjects Research conducted within the Hennepin Healthcare System campus.

APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46	Protection of Human Subjects
21 CFR 50	Protection of Human Subjects
21 CFR 56	Institutional Review Boards
21 CFR 312	Investigational New Drug Application
21 CFR 812	Investigational Device Exemptions

https://clinicaltrials.gov/ct2/manage-recs

REFERENCES TO RELATED SOPs
All SOPs are related to this SOP

ATTACHMENTS
Review: Unanticipated Problems Involving Risks to Subjects or Others
Access for Research Monitors

1) Study conduct is ultimately the responsibility of the Principal Investigator (PI). Review with the PI if study needs to be registered on clinicaltrials.gov

2) All members of the study team should have a clear understanding of their individual and team member responsibilities regarding safe and ethical study conduct.
   a) Each team member must be kept aware of the study's progress, protocol changes, HSRC standing, and other new or recently received information that is required to conduct the study
   b) Ensure that pertinent HCMC staff remains informed about the research study.

3) Place EPIC RESEARCH BANNER in electronic medical record when a subject is enrolled into a study.
   a) Go to the FYI.
   b) Choose the RESEARCH/PROTOCOL FYI; insert critical information about the study that may affect subject care. Add accessible study contact information.
   c) A green banner will appear on the major EPIC reports.
   d) The banner will remain on the chart across all encounters. Study personnel must deactivate the banner when the subject has completed the study.

4) A copy of the consent must be placed in EPIC.
   a) Consents should be sent to Medical Records as soon as possible.

b) Use blue Interoffice to HIM envelopes marked "Confidential" (contact Medical Records for envelopes as needed)

5) Conduct study as outlined in study protocol.
   a) Perform study related visits/procedures.
      i) Ensure that informed consent has been obtained.
      ii) Confirm that the subject remains eligible be reviewing inclusion/exclusion criteria.
      iii) Perform study examinations, laboratory testing, and study visits.
      iv) Review use of study aids such as electronic diaries with the subject.
      v) Review all study requirements with the subject.
      vi) Provide the primary care provider acknowledgement of the subject's enrollment into the study if the subject is agreeable.
      vii) Update subjects on changes or information that may affect a subject's decision to continue the trial. Re-consent subjects if applicable.
      viii) Document unscheduled subject encounters, including telephone conversations.
   b) Administer the investigational product as applicable.
      i) Confirm that the investigational product is dispensed according to protocol outline.
      ii) Document who dispensed the investigational product.
      iii) Document the time, route, dose, and administrator of the investigational product as applicable.
      iv) Document any untoward effects. Institute appropriate therapy if required as directed by the PI or sub-investigator.
   c) Monitor subject safety.
      i) Observe, query for, and document unanticipated problems involving risks to subjects or others, protocol violations, and incidents of unexpected serious harm.
      ii) Report unanticipated problems involving risks to subjects or others, protocol violations, and incidents of unexpected serious harm to the HSRC and sponsor as applicable.
      iii) Notify the PI and appropriate non-study healthcare providers of urgent abnormalities disclosed by protocol testing. This may include, but not be limited to, abnormal blood or imaging results, abnormal electrophysiologic test results, or written questionnaires (e.g., endorsement of suicidality).
   d) Implement PI's plan for treatment of unanticipated problems involving risks to subjects or others and unexpected serious harm which may include, but are not limited to:
      i) Notify the subject.
      ii) Notify relevant healthcare providers.
      iii) Stop the investigational product.
      iv) Follow up with additional testing.
      v) Initiate specific treatment interventions.
      vi) Notify sponsor, HSRC, and regulatory authorities.
      vii) Follow-up to ascertain resolution of adverse events.
   e) Continue the informed consent process.
      i) Keep the subject updated on the study process and progress.
      ii) Assess the subject's level of comfort with the study, may need to remind him/her that they have the right to withdraw from the study.
      iii) Inquire if the subject has any questions, answer subject questions.
      iv) May need to re-consent subjects if information becomes known that may alter subjects' desire to participate in the study.
   f) Maintain primary source documents. Primary source documents must include:
      i) That a subject was enrolled into the study.
      ii) Notification of sponsor approved protocol waivers.
      iii) When study treatment(s) were administered.

iv) All incidents of unanticipated problems involving risks to subjects or others and unexpected serious harm along with treatment if applicable.
v) Protocol deviations
vi) If the subject completed, withdrew, or was discontinued from the study.

g) Complete primary source documents.
   i) Paper
      (1) Use black ink unless instructed otherwise. Never use pencil.
      (2) Include name and date of person completing the source document.
      (3) Correct errors by striking through errors with a single line. Write correct entry next to the incorrect one, date, and initial change(s).
      (4) Do not write over an entry to attempt to correct it.
      (5) Do not erase, do not use white-out.
      (6) Obtain PI signatures as required.
      (7) Report loss of data immediately.
   ii) Electronic case report forms
      (1) Complete forms as instructed by sponsor.
      (2) Include name and date of person completing the source document.
      (3) Do not leave computer unattended.
      (4) Do not allow anyone to use computer access code.
      (5) Report any loss of electronic hardware immediately.

h) Primary source documents are made at the time any assessment is performed and include, but are not limited to:
   i) Interviews
   ii) Baseline physical
   iii) Diaries or other records maintained by the subject
   iv) Physician and nursing notes
   v) Clinical assessments
   vi) Vital signs
   vii) Laboratory, radiology, or results of other testing
   viii) Phone logs

i) Maintain regulatory notebook.
   i) Add new sponsor information
   ii) Add correspondence from/to sponsor and HSCR
   iii) Maintain monitoring logs and delegation of authority logs.
   iv) Ensure that all certifications and accreditations are up-to-date

j) Maintain case report forms
   i) Maintain complete and accurate source documentation
   ii) Collect data from source document(s).
   iii) Source documents may include, but are not limited to:
      (1) Site created worksheets
      (2) Sponsor created worksheets
      (3) Electronic Health Record reports
   iv) Follow case report form completion procedures supplied by the sponsor if applicable
   v) Protect all study materials and any protected health information.
      (1) Do not leave materials unattended.
      (2) Keep all study materials in a locked file drawer or locked office when unattended.
      (3) Ensure that only appropriate study personnel have access to study material.
      (4) Do not allow anyone to use a personal EPIC or other computer access code.

k) Complete case report forms.
   i) Paper
      (1) Use black ink unless instructed otherwise. Never use pencil.

(2) Include name and date of person completing the case report forms.
(3) Correct errors by striking through errors with a single line. Write correct entry next to the incorrect one, date, and initial change(s).
(4) Do not write over an entry to attempt to correct it.
(5) Do not erase, do not use white-out.
(6) Obtain PI signatures as required.
(7) Report loss of data immediately.

ii) Electronic case report forms
(1) Complete forms as instructed by sponsor.
(2) Include name and date of person completing the case report forms.
(3) Do not leave computer unattended.
(4) Do not allow anyone to use computer access code.
(5) Report any loss of electronic hardware immediately.

l) Interact with the sponsor.
i) Clarify questions and respond to queries.
ii) Schedule and prepare for monitoring visits.
iii) Arrange for source document review.
iv) Arrange for ancillary visits as needed (i.e., study pharmacist).

m) Respond to data queries.
i) Receive data clarifications/queries from the sponsor.
ii) Review/resolve queries by comparing it to the applicable primary source document(s). Change data on the query form as needed if a discrepancy is noted. If the previously submitted data is accurate, provide an explanation on the query form.
iii) Make data changes per the sponsor's instructions.
iv) Sign, date, and return to the sponsor per sponsor instructions.
v) File resolved queries in the appropriate case report forms.

n) Interact with Clinical Research Associate (monitor) as applicable.
i) Schedule a mutually convenient time for monitor to visit.
ii) Confirm which case report forms (CRFs) the monitor wishes to review.
iii) Contact the Office for Education & Quality in Clinical Research (OEQCR) to obtain monitor EPIC access.
iv) Ensure that all original source documents are available for the monitor- provide only those records and files applicable to the study under review.
v) Ensure that the regulatory binder is current and available for review.
vi) If applicable, notify research pharmacy or other ancillary departments of the monitor's visit.
vii) Provide a suitable work area for monitor.
viii) Schedule adequate time to spend with the monitor to discuss protocol related issues, review of the regulatory binder, verification of data in the case report forms, and study drug dispensing and accountability requirements.

o) De-identify subject treatment or diagnostic records before sending to sponsor leaving study specific identifiers.
i) Remove all identifiers based on the HIPAA identifier list.
ii) Remove identifiers within a document body as well as the name and medical record number.
iii) Ensure that personal identifiers cannot be discerned when covered.
iv) Ensure that personal identifiers cannot be seen if source record is copied (wax pencils ("china markers") are highly recommended for paper copies.

p) Maintain financial study records.
i) Reimburse subject stipends per payment schedule.
ii) Reconcile monthly HHRI statements with outstanding study income and outgoing vendor payments.
iii) Reconcile HCMC and external billings for research related tests.

iv) Compare costs to previously agreed upon costs, mark conventional care costs as not-research.

q) Maintain documentation of subjects who drop out or withdraw from the study.
   i) Document the reason(s) the subject dropped out or withdrew from the study.
   ii) Maintain a record of attempted and actual subject contacts, i.e., phone calls or certified letters sent to subject.
   iii) If the subject agrees, follow all protocol procedures identified to be performed for subjects who withdraw from the study.
   iv) Obtain all unused investigational product if applicable.
   Document a subject as lost to follow up if subject refuses further contact or participation in the study.

REVIEW: UNANTICIPATEDROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS

Unanticipated problem involving risks to subjects or others
is a problem that:

1. is unanticipated or unexpected;
2. involves risks to subjects or others; and
3. is reasonably believed to be related to research participation

Is this an **unanticipated problem involving risks to subjects or others**?

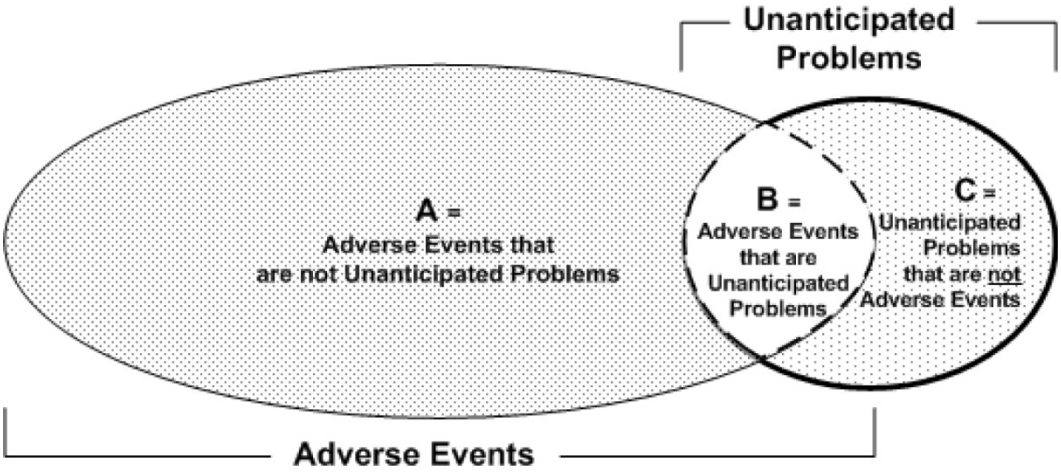
_____ NO _____ YES

If yes, is additional information needed and if so, what information?

If yes, does it reasonably appear that study subjects are at increased risk if the protocol were to continue? _____ NO _____ YES

If yes, possible actions include:

- suspend approval of the research pending further investigation;
- refer the matter to the Chair; and/or
- refer the matter to the HSRC for discussion and further action



Under applicable regulations: Do not report A, Do report (B+C)

Note: Adverse events that are not unanticipated problems involving risks to participants or others (A) are either not caused by the research procedures or were expected.

ACCESS FOR RESEARCH MONITORS/AUDITORS

The following steps need to be taken for setting up a research monitoring/auditor visit with EPIC Reviewer Access at Hennepin County Medical Center (HCMC). This will be the responsibility of HHRI applicable personnel.

1. Notify the Director of the Office for Education & Quality in Clinical Research (EQ) as soon as possible that a monitor/auditor needs access to EPIC or if there is a monitor or auditor change in an ongoing study. Contact info: bcrissman@hhrinstitute.org

2. Information that the Director will need is:
    a. The name of the monitor/auditor (first name, (middle initial if available), and last name)
    b. Name of the company employing the monitor/auditor
    c. PI name on the study
    d. Coordinator name
    e. Study title the monitor/auditor is auditing-the title must be exactly as written on the informed consent
    f. HSRC number of the pertinent study

3. The Director of EQ will inform the appropriate personnel in HCMC Health Information Management (HIM) of any monitors not yet registered with HIM. This will be done via email on HHRI letterhead stationery; the information outlined in #2 will provide formal notification to HCMC. One memo will be sent per research monitor/auditor for each study s/he will inspect.

4. The OEQCR will contact the HCMC IT Self Service to request an Epic account be created for the monitor. Seven days contiguous access will be requested.

5. The research coordinator will send a subject list of individuals to be monitored/audited to HIM personnel, names and email information will be provided to the coordinator by the Director of OEQCR. Health Information Management personnel will need 24 hours minimum warning to prepare for the monitor/auditor.

6. Health Information Management will set up an “in-basket” in EPIC for the monitor/auditor consisting of the subjects the research coordinator has identified. These charts will be the only ones the monitor/auditor will see.

7. On the day(s) of monitoring/auditing, escort the monitor/auditor to HIM. S/he will need to show a picture ID (i.e. HCMC ID badge, driver’s license, employee ID badge-no numbers will be recorded) to HIM personnel to verify identification.

8. The monitor/auditor will view the records in HIM.

***PLEASE NOTE: Due to HCMC policy EPIC has to be requested EACH time a monitor comes. Step #2 only needs to be completed the first time a monitor visits or if a different study is assigned to a returning monitor.**