HUMAN RESEARCH PROTECTION

HRPO standard operating procedures (SOPs)

Number 200 series | Version date 25 AUG 2023

Resource type SOP

201 Resource gallery management

PURPOSE

This procedure establishes the process to review, create, revise, and retire standard operating procedures (SOPs) and other resources for the Human Research Protections Office (HRPO) (*Resource Gallery*).

HRPO leadership will use this procedure to conduct a review of the HRPO Resource Gallery and when they determine that a resource needs to be created, revised, or retired.

Responsibilities

The HRPO Director and Assistant Director, in collaboration with HRPO/IRB leadership and staff, as applicable, manage the procedures described below to review, create, revise, or retire HRPO resources. The HRPO Director has final authority for oversight of HRPO Resource Gallery documents.

PROCEDURE

Changes to regulations and guidelines, institutional policies, or Hennepin Healthcare current practices may require a new resource gallery document or revision to one or more existing documents.

- HRPO leadership will conduct a comprehensive review of the 200 series SOP compilation no less than every two years. Comprehensive review will be documented in the version history.
- Other Resource Gallery documents (e.g., manuals, worksheets, forms, FAQs) are reviewed periodically and updated as necessary, in response to regulatory changes, user feedback, or other factors.

Creating a new resource

1. Confirm with HRPO leadership that a new resource should be created
2. Assign a number, type, title, and author in the master list workbook; the master list is stored in the HRPO network drive: **Resource gallery management/00_master list**
3. Draft the new resource
4. Manage the editing and approval process, as applicable, using tracked changes
5. Once the new resource is approved:
    - Update the master list, as appropriate
    - Save final version of the resource in the HRPO network drive, in the applicable resource gallery folder
    - Update the HRPO website, as appropriate
    - Communicate the new resource, as appropriate
    - Implement training related to the new resource, as appropriate

Revising an existing resource

1. Confirm with HRPO leadership that a resource should be revised
2. Track the number, type, title, and author in the master list workbook; the master list is stored in the HRPO network drive: **Resource gallery management/00_master list**
3. Draft the revisions using tracked changes
4. Manage the editing and approval process, as applicable, using tracked changes
5. Once the revised resource is approved:
    - Update the master list, as appropriate

- Archive the prior version in the HRPO network drive: **Resource gallery management/zzz_archive/**
- Save final version of the resource in the HRPO network drive: **Resource gallery management/01_active**
- Update the HRPO website, as appropriate
- Communicate the revised resource, as appropriate
- Implement training related to the revised resource, as appropriate

Retiring a resource

1. Confirm with HRPO leadership that a resource should be retired
2. Update the master list, as appropriate. The master list is stored in the HRPO network drive: **Resource gallery management/00_master list**
3. Archive the retired resource in the HRPO network drive: **Resource gallery management/zzz_archive/**
4. Update the HRPO website, as appropriate
5. Communicate the retired resource, as appropriate
6. Implement training related to the retired resource, as appropriate

Resource Gallery organization

The HRPO Resource Gallery is organized as follows:

Numbering level	Resource type
100	Guidance
200	SOPs
300	Forms
400	Checklists
500	Manuals
600	Templates
700	Worksheets
800	Letters
900	FAQs

References

- HRPO website: https://www.hhrinstitute.org/researcher-resources/ohsr/
- HRPO network drive full path: **..\\Dropbox (MMRF)\HRPP Admin\HRPO admin\Resource gallery management**

203 Using worksheets with Cayuse HE

PURPOSE

This SOP outlines how IRB analysts and primary/designated reviewers are expected to use the 7xx-series Worksheets to support review of IRB submissions.

Requirement matrix

Worksheet	Review type			
	Exempt	Expedited	Convened IRB	Ceded
706 Limited IRB review	when applicable	N/A	N/A	N/A
708 Reviewer worksheet list	☑ Initial (follow-on as applicable)	☑ Initial (follow-on as applicable)	☑ Initial ☑ Follow-on	N/A
708-A-Regulatory oversight	N/A*	N/A*	N/A*	N/A*
709 Initial review	☑	☑	☑	N/A
710 Convened meeting requirements	N/A	N/A	☑	N/A
711 Reliance pre-review	N/A	N/A	N/A	☑ as applicable to submission type
711-A Local context considerations	N/A	N/A	N/A	N/A*
712 Reliance review	N/A	N/A	N/A	☑
713 Incident/new information review	☑ N/A for non-reportable events/information	☑ N/A for non-reportable events/information	☑	N/A
714 Expert consultant review	when applicable	when applicable	when applicable	when applicable
717 Drugs and IND requirement	N/A	when applicable	when applicable	N/A
718 Devices and IDE requirement	N/A	when applicable	when applicable	N/A
719 HUD criteria for approval	N/A	N/A	when applicable	N/A
720 Informed consent	N/A	when applicable	when applicable	N/A
720-A HIPAA authorization elements	N/A*	N/A*	N/A*	N/A*
724 Modification review	☑ N/A for-personnel, minor doc revisions	☑ N/A for-personnel, minor doc revisions	☑ N/A for-personnel, minor doc revisions	N/A
724-A Modifications-minor changes	N/A*	N/A*	N/A*	N/A*
727 Renewal review	N/A	when applicable (CR required)	☑	N/A
731 Research involving pregnant women, fetuses, and neonates	N/A	when applicable	when applicable	N/A
732 Research involving prisoners	N/A	when applicable	when applicable	N/A
733 Research involving children	N/A	when applicable	when applicable	N/A
740 Waiver or alteration of consent	N/A	when applicable	when applicable	N/A
741 HIPAA waiver or alteration of authorization for research	when applicable	when applicable	when applicable	when applicable
750 Data and safety monitoring	N/A	when applicable	when applicable	N/A
752 ICH-GCP requirements	when applicable	when applicable	when applicable	N/A

757 International research	when applicable	when applicable	when applicable	N/A
763 IRB authorization agreement	N/A	when applicable	when applicable	☑ Initial
781 DoD criteria for approval	when applicable	when applicable	when applicable	N/A
782 DoJ criteria for approval	when applicable	when applicable	when applicable	N/A
787 EFIC	N/A	N/A	when applicable	when applicable
788 Emergency use of a test article	N/A	when applicable	N/A	N/A

*for reference when applicable

PROCEDURE

The 708 *Reviewer worksheet list* should be completed first to determine additional worksheets that are applicable to a review. Worksheets that are designated as required (see matrix) or determined to be applicable per the 708 Worksheet must be completed and saved in the Cayuse HE submission.

For reviews using the expedited procedure, the designated reviewer completes worksheets to document determinations required by the regulations along with protocol specific findings justifying those determinations.

For reviews using the convened IRB, the IRB analyst on behalf of the convened IRB compiles the necessary worksheets required for a submission. The primary reviewer assigned to the submission will complete all required worksheets and the completed worksheets will be made available to all IRB members during their own reviews. Any discrepancies or corrections noted during the convened IRB meeting will be discussed by the convened IRB at the meeting. The primary reviewer completes the reviewer worksheets to document their own review and make their comments or concerns available to all IRB members prior to the IRB meeting. Final determinations are made by the full committee during the convened IRB meeting and documented in the final decision in Cayuse HE.

For reviews using the convened IRB, the primary reviewer often completes reviewer worksheets several days prior to the IRB meeting and may not represent all information finalized prior to or during the IRB meeting. When the primary reviewer indicates clarifications needed to confirm criteria for approval, the IRB analyst will request clarification from the PI. Clarification will either be provided as attachments in the submission in Cayuse HE or discussed by members during the IRB meeting. For submissions where the PI is in attendance, such as a new initial, the clarification may also be provided during the discussion with the PI. Any indication in the reviewer worksheets that criteria for approval is not yet met will be addressed during the IRB meeting and resolution or final determinations would be documented in the IRB minutes.

Saving worksheets in Cayuse HE

1) Once a submission is ready to be assigned to a designated reviewer, the IRB analyst will save all required worksheets as a restricted comment in the submission with instructions (when applicable) for the designated reviewer. The IRB analyst may add notes to worksheets to capture relevant information obtained during pre-review; however, the designated reviewer will review and ensure completeness of all required worksheets before completing their review. NOTE: for exempt and expedited reviews, the IRB analyst may serve as the designated reviewer.
    a. For *Initial* and *Modification* submissions, the worksheets are attached on the Submission Intro page, under the PI name.
    b. For *Renewal* submissions, the worksheets are attached on the Criteria Check page, under the study status question.
    c. For *Incident* submissions, the worksheets are attached on the Incident/New Information Report page, under the incident type question.
2) For submissions reviewed under expedited review, the designated reviewer must reply to the IRB analyst's comment and attach all final reviewer worksheets before completing the Make Decision function in Cayuse HE. When any reviewer worksheets are completed, the analyst will include a link to the 708 Worksheet in the Make Decision function.

    When the IRB analyst also serves as the designated reviewer (for example, when reviewing certain submissions eligible for expedited review), the IRB analyst will only attach final versions of the required worksheets.

3) For submissions reviewed by the convened IRB, the primary reviewer must reply to the IRB analyst's comment and attach all reviewer worksheets required. If any changes are made during the convened IRB discussion, the IRB analyst will reply to the comment and attach any revised worksheets. The analyst will include links to all final reviewer worksheets in the Make Decision function and meeting minutes.

Special considerations for specific worksheets

708 Reviewer worksheet list

The 708 is completed by the IRB analyst as a reference document for preparing the submission for the designated reviewer; it serves as a tool to confirm all worksheets that may be required. This worksheet is shared with the designated reviewer as a reference document and is not to be completed by the designated reviewer. For this reason, the 708 is NOT completed for modification submissions where the only changes requested are personnel changes and/or minor corrections or updates to study documents (such as validation modifications without changes to previously approved study information/materials, updating contact information, fixing grammatical errors in the consent, or the submission of translated materials previously approved).

When completing the 708, the IRB analyst will check the boxes under **Regulatory oversight** (first column) for oversight that applies to the study overall and will check the boxes under **Required reviewer WORKSHEET** (second column) for worksheets that must be completed for the submission being reviewed. For follow-on submissions (such as modifications and renewals), worksheets will be required when the determinations previously made are being changed. For example, if a Modification submission requests permission to include children on a study not previously approved to include children, the 733 Worksheet (*Research Involving children (Subpart D)*) must be completed as a part of the Modification review.

708-A Regulatory Oversight

This is an optional reference for the 708 Worksheet to support HRPO to identify applicable regulations for a specific submission under review. This worksheet is not completed or saved by a reviewer but can be used for additional guidance.

710 Convened meeting requirements

The 710 is completed by the IRB analyst to ensure a quorum for any convened IRB meetings. The 710 is saved in the **Meeting Details** section of Cayuse HE, under the *Attachments* tab. The IRB analyst completes the 710 prior to the convened IRB meeting and consults the document if members do not attend as previously indicated. If revisions are necessary, the IRB analyst will save a revised version. If the IRB analyst confirms that a quorum is no longer met during the meeting, the IRB analyst will inform the IRB chair immediately.

720 Informed Consent

The 720 is required for any non-exempt study that does not involve a waiver of consent (or does not meet criteria per 2006 FDA guidance, i.e., informed consent is not applicable). The IRB analyst will complete a 720 for each distinct consent form. These will be included in the reviewer worksheets assigned to the designated or primary reviewer for their review; however, the designated or primary reviewer does not need to make any changes to the 720 if no changes are needed.

If a waiver of documentation is approved, a 720 must be completed to confirm all required elements are included in the information sheet/script for consent.

If an alteration of consent is approved, a 720 must be completed and specific approved alterations can be disclosed in the notes sections of the 720.

When minor revisions are made to a consent form (via a Modification submission), the 720 may be consulted for guidance but does not need to be completed.

720-A HIPAA authorization elements

The 720-A is an optional reference for the 720 Worksheet to identify required elements of the HIPAA authorization. This worksheet is not completed or saved by a reviewer but can be used for additional guidance.

724-A Modifications- minor changes

The 724-A is an optional reference for the 724 Worksheet to identify criteria for a minor change. This worksheet is not completed or saved by a reviewer but can be used for additional guidance.

750 Data and safety monitoring

The 750 is required for all FDA-regulated and/or DoD-funded protocols and all new *Initial* submissions reviewed by the convened IRB. For all other submissions, it may be used as a reference (along with 150 GUIDANCE Data and safety monitoring in research) but does not need to be completed/saved.

209 OHRP registrations

PURPOSE

This SOP describes HRPO oversight of the institutional FWA and IRB registrations filed with federal Office for Human Research Protections (OHRP).

Related: **200-A1 APPENDIX *Compliance statement***

PROCEDURE

HRPO staff is responsible for maintaining FWA and IRB registrations filed with OHRP as required, including:

- Maintaining an active FWA registration and submitting updates when changes are required or updating status to prevent expiration (i.e., every 3 years)
- Maintaining active IRB registration(s) and submitting IRB membership changes
- Maintaining internal records to track FWA and IRB registration information

210 IRB jurisdiction

PURPOSE

This SOP describes the scope of Hennepin Healthcare IRB jurisdiction for research and non-research activities.

PROCEDURE

Activities that are subject to IRB jurisdiction must be submitted via the electronic IRB system to receive IRB pre-review and assignment to the applicable level of IRB review. Activities that are NOT subject to IRB jurisdiction that are submitted via the electronic IRB system will be processed accordingly within the Cayuse workflow and do not require IRB pre-review/review.

For all electronic submissions, principal investigators will receive notifications of submission status throughout the submission cycle via Cayuse HE.

Human research activities

The Hennepin Healthcare Human Research Protection Program (HRPP) has jurisdiction over human research, as defined by federal regulation (DHHS, FDA) and Minnesota law. Refer to the **200-A2 APPENDIX *HRPP components*** for an overview of the Hennepin Healthcare HRPP.

HRPO will confirm that activities described in a Cayuse HE submission are considered research involving human subjects. Jurisdiction of the Hennepin Healthcare IRB is based on the following:

- Activities meet the definition of human research as defined under the federal regulations.

  (1) For DHHS regulated activity, research involving human subjects is determined by first deciding whether the activity is research as defined by DHHS regulations, and if so, confirming that it involves human subjects as defined by DHHS regulations (45 CFR 46).

(2) For FDA regulated activity, research involving human subjects is determined by first deciding whether the activity is a clinical investigation as defined by FDA regulations, and if so, confirming that it involves human subjects as defined by FDA regulations (21 CFR 50).

- The human research activities are performed by an employee of the Hennepin Healthcare System (HHS) including the Hennepin Healthcare Research Institute (HHRI) under the auspices of their Hennepin Healthcare employment, and for which the institution is engaged in the research; if there is a question regarding engagement of the institution in a particular research project, guidance from HRPO, HHRI Grants and Contracts Office, or other individual(s), and/or legal consultation shall be sought, as appropriate.
- Whether another IRB is providing oversight of human research activities

Human research conducted under the auspices of Hennepin Healthcare must be reviewed and approved by the Hennepin Healthcare IRB or another designated IRB prior to the initiation of research unless it has been determined that Hennepin Healthcare is not engaged in the research. Research not approved by the IRB cannot be otherwise approved by Hennepin Healthcare, including research subject to an RB reliance agreement.

Non-human research activities

Proposed research not subject to FDA oversight that involves only deidentified data and/or human biological specimens may be considered research that does not involve human subjects; such research is not subject to IRB jurisdiction.

Research activities involving only secondary deidentified data and/or human biological specimens where all direct personal identifiers are permanently removed from the data or specimens, no code or key exists to link the materials to the original source(s), and the remaining information cannot reasonably be used by anyone to identify the source(s) may be considered research that does not involve human subjects; such research is not subject to IRB jurisdiction.

Proposed research not subject to FDA oversight that involves non-living individuals (i.e., deceased subjects) does not fall under IRB jurisdiction.

For research that is not subject to IRB jurisdiction, researchers may be referred to HHS Information Security & Privacy, if applicable.

Non-research activities

Quality improvement, program evaluation, surveillance activities, and case reports that are not research involving human subjects do not require IRB oversight; Hennepin Healthcare departments may contact HRPO with questions and guidance regarding IRB jurisdiction on specific activities in which it is unclear whether they meet the criteria for research involving human subjects. The IRB Chair (or designee) will evaluate such activities on a case-by-case basis to make a determination regarding jurisdiction.

Quality improvement, program evaluation, and/or surveillance activities are not considered research if the intention of the activity is to improve or inform within the institution. If the results will be generalized outside of the institution, the activity will be evaluated on a case-by-case basis. Quality improvement activities are projects that are completed to improve quality of programs, improve services, or improve the provision of medical care, customer service, etc. and are usually done for internal purposes only. Program evaluation activities are projects with a systematic collection of information about the activities, characteristics and outcomes of programs to make judgments about the program, improve program effectiveness, and/or inform decisions about future program development. Surveillance activities are projects that collect, analyze, and interpret health-related data essential to planning, implementing, and evaluating health care practice. Case reports are a retrospective analysis of a clinical case that are prepared and disseminated for educational purposes are not considered systematic investigations and, therefore, not research.

211 Single IRB review: Hennepin Healthcare as sIRB and reliance on external IRBs

PURPOSE

This Standard Operating Procedure provides the process for Hennepin Healthcare serving as single IRB (sIRB) and relying on an external IRB or sIRB to conduct the IRB review and oversight of multisite or collaborative human research in which Hennepin Healthcare Research Institute or Hennepin Healthcare, Inc. (Hennepin Healthcare) is "engaged."

Serving as sIRB: Hennepin Healthcare agrees to serve as the IRB of Record for multi-site or collaborative human research only under limited circumstances, which will be evaluated on a case-by-case basis, as described in 115 GUIDANCE *Criteria for serving as sIRB for multi-site or collaborative research*.

Relying on external IRBs: It is the policy of the Human Research Protection Office (HRPO) to evaluate requests to rely on a sIRB or external IRB on a case-by-case basis, as described in 110 GUIDANCE *Criteria for external IRB reliance*. This procedure does not apply to exempt research.

This Standard Operating Procedure has been developed to comply with the *cooperative research* provision of the revised Common Rule (2018 Common Rule) and the *NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research*.

PROCEDURE

Hennepin Healthcare as sIRB

Initial HRPO determination

HRPO will review a request to serve as sIRB submitted by the Principal Investigator as described in 115 GUIDANCE *Criteria for serving as sIRB for multi-site or collaborative research* to confirm the following:

a. Hennepin Healthcare and the proposed relying site(s) is/are engaged in research
b. The research involves human subjects
c. The research is non-exempt
d. The research meets the criteria for Hennepin Healthcare IRB to serve as sIRB Reliance as described in in 115 GUIDANCE *Criteria for serving as sIRB for multi-site or collaborative research*

If HRPO determines that the research does not meet all of the conditions 1a-d, HRPO will communicate its determination to the Principal Investigator.

If HRPO determines that research meets all of the conditions 1a-d, HRPO will provide either (1) the letter of support for the grant submission permitting Hennepin Healthcare to be named as the sIRB OR (2) provide next steps for the review to proceed in Cayuse HE.

Hennepin Healthcare IRB review of an sIRB study

Overall protocol approval. Review of an sIRB study will be reviewed and approved in accordance with the Hennepin Healthcare SOPs and applicable reviewer worksheets. The Hennepin Healthcare Principal Investigator will submit a new *Initial* submission in Cayuse HE for overall protocol review and approval, including approval of the Hennepin Healthcare site. The Hennepin Healthcare Principal Investigator is responsible for communicating the overall protocol approval and IRB approved documents to the relying site(s).

Initial relying site approval. IRB review of a relying site will occur when the Hennepin Healthcare Principal Investigator submits a *Modification* in Cayuse HE for each relying site with all required documents described below:

1. Executed IRB authorization agreement per 763 WORKSHEET *IRB authorization agreement* between Hennepin Healthcare Research Institute and the Relying Institution [694 TEMPLATE SMART IRB LoA and 695 TEMPLATE Study-specific reliance plan or another IRB authorization agreement meeting the requirements of 763 WORKSHEET.]

2. Local context considerations (395 FORM *Local context consideration*)
3. COI management plan (if applicable)
4. Site specific content(s) or recruitment materials

The HRPO Assistant Director or other HRPO staff complete pre-review of the *Modification* submission to add a relying site.

IRB review of a *Modification* to add a relying site will follow applicable Hennepin Healthcare SOPs and worksheets.

The study Principal Investigator and Primary Contact will receive automated communications in Cayuse and will be responsible for sharing the relying site(s) approval and associated IRB approved documents with the relying site(s).

Continuing Review and Modifications. The Hennepin Healthcare Principal Investigator is responsible for facilitating the submission of any relying site modifications and continuing reviews via Cayuse HE and providing the IRB approval and any related IRB-approved material to the relying site(s).

Incident reporting. The Hennepin Healthcare Principal Investigator is responsible for reporting the Hennepin Healthcare IRB in accordance with the Hennepin Healthcare requirements (133 GUIDANCE) for the overall study, the Hennepin Healthcare site, and on behalf of relying site(s). Relying site(s) are required to follow the Hennepin Healthcare reporting requirements in 133 GUIDANCE New information/Incident reporting, made available on the HRPO website: https://www.hhrinstitute.org/researcher-resources/ohsr/.

Study closure. The Hennepin Healthcare submits the study closure in Cayuse HE and provides the study closure documentation to the relying site(s).

IRB notifications to the relying site(s) and relying institution(s) are made in accordance with the reliance agreement and applicable study specific reliance plan.

Hennepin Healthcare reliance on external IRBs

Investigator-initiated request for IRB reliance

A request for IRB reliance must be initiated in the electronic IRB management system, Cayuse HE. Researchers may also contact HRPO to discuss a request to rely on an external IRB.

Initial HRPO determination

HRPO will review a reliance request submitted in Cayuse HE to confirm the following:

a. The institution is engaged in research
b. The research involves human subjects
c. The research is non-exempt
d. The research meets the criteria for external IRB reliance as described in 110 GUIDANCE Criteria for external IRB reliance and documented in 711 WORKSHEET Reliance review

If HRPO determines that the research does not meet all of the conditions 1a-d, HRPO will record its determination in Cayuse HE.

If HRPO determines that research meets all of the conditions 1a-d, review will proceed in Cayuse HE.

The study Principal Investigator and Primary Contact will receive automated communications in Cayuse and can access the status of their submission at any time

HRPO review of a request for IRB reliance

A request for IRB reliance application is reviewed by the HRPO Assistant Director and/or designee. The review will be conducted to assess the following 5 criteria (unless under the terms a reliance/authorization agreement, one or more of these criteria will be assessed by the IRB of record):

1. Institutional training of study investigators and support staff in the protection of human subjects in research
2. Qualifications of study investigators and support staff to conduct the study
3. Conflict of interest of study investigators and support staff
4. Local context considerations (state laws, community and/or institution-specific concerns)

5. Ancillary reviews required for this study

HRPO Assistant Director or other HRPO staff and the IRB Chair or designee will complete the IRB reliance pre-review and review

HRPO Assistant Director or other HRPO staff will record the reviewer's findings in Cayuse HE

HRPO approval to rely on external IRB

Upon completion of administrative review, the submission will be approved *(Rely on External IRB*) in Cayuse HE and the Principal Investigator will receive notification to proceed with submission to the external IRB for site approval.

HRPO acknowledgment of local site approval

Upon receipt in Cayuse HE of local site approval from the sIRB, the Principal Investigator will submit a Modification in Cayuse HE to notify HRPO of site approval. HRPO will acknowledge receipt of the site approval and enter the sIRB approval date.

Continuing review and ongoing reporting requirements

HRPO requires annual check-in submissions in Cayuse HE of continuing IRB approval from the IRB of record, as applicable, and ongoing personnel monitoring. Cayuse HE will send out automated email reminders of annual check-ins with guidance on other ongoing reporting requirements as described in 113 GUIDANCE *Notifications to HRPO for ceded studies.*

IRB authorization/reliance agreement

A reliance/authorization agreement[1] will be established between institutions to clearly establish roles and responsibilities and communication mechanisms. The 763 WORKSHEET *IRB authorization agreement* during the initial review of a request to rely on an external IRB or initial review of a relying site when Hennepin Healthcare has agreed to serve as sIRB. The reliance agreement will meet applicable OHRP and FDA regulatory requirements, as well as NIH sIRB policy, and will be attached to the study submission in Cayuse HE and provided to OHRP and/or FDA upon request.

Coordination and review of the terms of an IRB authorization agreement will be completed by the HRPO Assistant Director (or designee) with support from legal counsel and the Institutional Official, if needed. An IRB authorization agreement (and associated amendments to an IRB authorization agreement) will be signed by the Hennepin Healthcare Institutional Official.[2]

In cases where Hennepin Healthcare is serving as sIRB, a copy of the IRB authorization agreement with be provided to the relying site(s) and maintained in Cayuse HE.

In cases where Hennepin Healthcare is the prime awardee but relying on an external IRB, Hennepin Healthcare will maintain a copy of the reliance agreement between Hennepin Healthcare and the external IRB in Cayuse HE; documentation of the reliance agreement between the other relying site(s) and the external IRB will follow the process of the external IRB.

Note: Use of the SMART IRB Master Agreement is preferred for research under sIRB review, unless the research falls under an existing IRB authorization agreement.

Maintenance of records

All records related to reliance studies will be managed and stored in Cayuse HE and in accordance with institutional and regulatory record retention requirements.

[1] In cases where Hennepin Healthcare agrees to extend its FWA to an individual investigation, an individual investigator agreement (IIA) based on the OHRP sample IIA will be executed.

[2] A SMART IRB Letter of Acknowledgment/SMART IRB online reliance request/IREx reliance request will be completed by the HRPO Assistant Director (or designee) and does not require signature by the Institutional Official.

212 Criteria for IRB approval

PURPOSE

This SOP describes the criteria for IRB approval of non-exempt research involving human subjects submitted to the Hennepin Healthcare Human Research Protection Office (HRPO).

PROCEDURE

Human research submitted to the Hennepin Healthcare IRB (convened committee or expedited review) for approval will not be approved unless IRB review determines that all applicable criteria for approval are met.

The Hennepin Healthcare Institutional Review Board (IRB) complies with the requirements of US Food & Drug Administration (FDA) regulations 21 CFR Part 50 Protection of Human Subjects and 21 CFR Part 56 Institutional Review Boards, the US Department of Health & Human Services (HHS) regulations 45 CFR Part 46 Protection of Human Subjects, and International Conference on Harmonization (ICH) E6 and Good Clinical Practice (GCP) guidelines[3], as applicable, in addition to Minnesota law. Regardless of the source of research support and regulatory requirements, IRB criteria for approval include the three core principles described in The Belmont Report - *Ethical Principles and Guidelines for the Protection of Human Subjects*: respect for persons, beneficence, and justice as the basis for protecting the rights and welfare of human subjects in research.

The Hennepin Healthcare IRB uses a worksheet system to document that all IRB criteria for approval and any applicable regulatory requirements are met. An IRB analyst and IRB reviewer(s) complete the worksheet(s) to ensure that all criteria for approval and other applicable requirements have been identified and addressed. Detailed information about the criteria for approval and other applicable requirements are specified in the worksheets. See 203 SOP *Using worksheet with Cayuse HE* for an overview. The IRB also consults the 197 GUIDANCE Criteria for IRB approval as an additional reference to support IRB review.

214 Use of expert consultants

PURPOSE

This SOP describes the process that the Hennepin Healthcare HRPP may use to engage consultants with expertise in special areas to assist in the review of IRB submissions that require expertise beyond or in addition to the expertise provided by IRB members (45 CFR §46.107(e) & 21 CFR §56.107(f)).

PROCEDURE

The Hennepin Healthcare HRPP may engage consultants with expertise in special areas to assist in the review of IRB submissions that require expertise beyond or in addition to the expertise provided by IRB members (45 CFR §46.107(e) & 21 CFR §56.107(f)).

The IRB analyst will facilitate the process of obtaining consultant services. If the need for expert consult is identified during the pre-review process of submission, the IRB analyst may request expert consult at that time. If expert consult is warranted after pre-review, the IRB analyst will work with the assigned primary/designated reviewer to request the expert consult.

Expert consult may be completed by:

- IRB Members
- Employees of Hennepin Healthcare
- External experts, such as medical professionals outside Hennepin Healthcare

When evaluating relevant expertise, the HRPP will consider:

- professional credentials
- research experience

[3] Hennepin Healthcare IRB will apply the standards of the International Conference on Harmonisation-Good Clinical Practices ("ICH-GCP") E6 to the review of research when the sponsored agreement specifies adherence to ICH-GCP. Clinical trials subject to ICH-GCP (E6) will be conducted in accordance with the ethical principles that have the origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.

- scope of the review being requested

Individuals with a conflict of interest will not be permitted to provide expert consult.

For each consultation provided for an IRB submission, the expert consultant will complete the 714 WORKSHEET – *Expert consultant review*. The IRB analyst will share the completed worksheet with all relevant reviewers (including the full board for a submission that requires convened IRB review) by attaching it as a restricted comment in the Cayuse HE submission. For convened IRB submissions, the consultant may also be invited to attend the IRB meeting at which the submission is being reviewed, but do not vote with the IRB on the submission.

219 HRPO emergency preparedness and response plan

PURPOSE

This SOP establishes written procedures for initiating a response to an emergency impacting the Hennepin Healthcare Human Protection Program (HRPP) or HRPP operations. HRPP leadership includes the Hennepin Healthcare Institutional Official, Institutional Review Board (IRB) Chair, and Human Research Protection Office (HRPO) and Office of Education and Quality in Clinical Research (OEQCR) director/assistant director roles.

An emergency may include but is not limited to natural disasters, weather events, man-made disasters, and public health crises. This SOP establishes HRPO/IRB specific emergency planning and is intended to supplement, not replace, emergency response planning by Institutional leadership and/or Institution-wide response measures. HRPP-specific emergency response planning and measures are limited only to those functions of the HRPP not otherwise covered by institution-level plans.

This SOP is invoked once the Institutional Official (IO) has indicated an emergency has occurred or preparations are needed for an imminent emergency and human research at Hennepin Healthcare including the HRPP or HRPP operations, is or is likely to be adversely impacted.

Responsibilities

HRPP leadership is responsible for implementing and monitoring the procedures described in this SOP and evaluating the emergency plan periodically for adjustments, as necessary, to ensure continuity of operations.

HRPO and OEQCR leadership are responsible for evaluating educational materials and updating them as necessary, based on the outcome of the periodic evaluation of the emergency preparedness plan.

PROCEDURE

Assessing the nature of the risk and its potential impact on HRPP operations

Once an emergency is identified, HRPO leadership will determine the response based on the nature of the event and whether there are Institutional plans already in place to address the event. HRPP leadership will communicate with the research community as necessary regarding activation of an emergency preparedness plan and will proceed in accordance with institutional plans, as applicable.

Assessing whether the emergency may impact HRPP operations

IRB meetings: HRPO will leverage its existing review procedures (i.e., online and virtual platforms) to proceed with IRB meetings in the event that an in-person meeting that has been scheduled cannot be held.

If the emergency may prevent one or more IRB meetings from occurring as scheduled, HRPO will determine whether to cancel or reschedule meetings, being certain to identify currently approved human research that may expire prior to IRB review. If research protocols expire, the IRB will follow 250 SOP Continuing review/annual check-in.

HRPO submission processing and review: If HRPO staff will be unable to complete submission processing and review responsibilities, or if capacity will be limited, HRPO leadership will work with the staff to prioritize reviews. If research will expire, HRPO will follow Continuing review/annual check-in regarding lapses in continuing review.

Data and records: HHRI's electronic IRB system, Cayuse HE, is hosted in the Amazon Web Services (AWS) cloud, and should an outage occur, recovery is supported by the AWS infrastructure and the vendor's Disaster Recovery Plan. If any system outage at HHRI occurs, access to the electronic IRB system will not be impacted. In the event of an outage impacting the AWS region hosting the HHRI access, the continuity plan of the IRB electronic system vendor provides for restoring access via backup data with an estimate downtime of ~ 8 hours.

If electronic systems other than the electronic IRB system are unavailable, HRPO leadership will consult with HHRI Information Technology (IT) to implement alternative procedures to access information and/or identify estimate for duration of inaccessibility.

Post approval monitoring: HRPP leadership will adjust auditing and monitoring procedures overseen by OECQR or other institutional monitoring entities to protect the health and well-being of researchers and research participants

Assessing whether the emergency may impact investigators' ability to conduct research

In-person interactions with research subjects: If studies involve in-person interactions with research subjects, HRPP leadership will determine whether the studies may be conducted as written while adhering to emergency mitigation strategies.

Sponsored research: When studies have an external sponsor, HRPO leadership will confer with HHRI's Grants and Contracts office regarding sponsor mitigation plans.

Clinical care and/or research facility considerations: If an emergency impacts clinical care standards which may in turn impact research, HRPP leadership will clarify what does and does not require IRB approval. For example, in the case of a public health emergency, screening procedures to assess symptoms/exposure implemented by the healthcare system to address the public health emergency would not require IRB approval when performed within an approved clinical trial; however, conducting research procedures at an alternate clinical care location may require prospective IRB approval. Emergency response plans must be considered for each existing research location.

Safety monitoring: If research participants are unable to come to the research site for protocol-specified visits, HRPP leadership will establish a process, as appropriate, for researchers to implement alternative methods for safety assessments. This may include utilizing phone contact, virtual visits, alternative locations for assessment (including local labs or imaging centers) to assure the safety of research participants.

Considering necessary actions to address the impact of the emergency

HRPO leadership, in consultation with the IO and IRB Chair, as needed, will define the actions to take during the emergency to avoid or minimize pausing of research activities such as:

- Suspension of IRB reviews of new research that is non-interventional in nature or that presents no direct benefit to participants.
- Pausing some or all currently IRB-approved research activities, such as identifying studies for which recruitment and/or enrollment should be paused but ongoing study interventions may continue.
- Continuation of research activities via alternate mechanisms, such as implementing online or remote strategies for recruitment, consent, data collection, debriefing, and follow-up, or altering the timing of in-person visits and procedures.
- Initiation of reliance arrangements (when possible, in advance of an emergency) to rely upon an external IRB to provide IRB oversight. This option may be pursued for any emergency scenario but particularly in anticipation of a prolonged emergency event impacting the ability of the Hennepin Healthcare to continue and/or resume IRB review.
    - As needed, HRPO will leverage its existing IRB reliance process, including use of the SMART IRB Master Reliance Agreement, and relationships (e.g., Advarra) to establish IRB reliance for new and/or ongoing research as determined by the emergency response.
    - Research reviewed by an external IRB will stay under the review under the external IRB unless HHRI and the external IRB decide at the time of the IRB reliance to transfer IRB oversight to HHRI IRB when emergency response has ended OR on an individual study basis. Research transferred back to Hennepin Healthcare IRB will be overseen by the IRB Reliance Manager.
- Employment of strategies to exercise flexibility in IRB oversight:
    - For studies that are not federally regulated, the IRB may employ different but equivalent procedures in terms of protecting the rights and welfare of research participants. For example, the IRB may consider extending continuing review dates during the emergency, and/or allowing minor changes in research to be reported to the IRB at the

time of continuing review versus in advance of the change. Such procedural modification(s) will be recorded as part of the IRB review.

- For most minimal risk research regardless of funding, the IRB may consider more widespread use of waivers of documentation of consent using the existing *740 WORKSHEET Waiver or alteration of informed consent*.

Triaging research that may be subject to the emergency mitigation strategies

HRPP leadership will consider the types of research that may continue and the types of research that may need to be temporarily paused or postponed. This consideration may include:

- Research that presents a likelihood of direct benefit to participants (or conversely, research that includes interventions that may be harmful to subjects if discontinued) will not be postponed, to the extent possible.
- Research involving direct interactions or interventions that can continue via alternate mechanisms (such as remote visits) may continue.
- Research that may have an adverse impact on resources required to address the emergency will be postponed, if possible.

Research that is paused pursuant to this triage is not the same as IRB-initiated suspension and/or termination and does not require reporting to the FDA or OHRP under 45 CFR 56 or 21 CFR 56.

Developing education, training, and communications during an emergency

HRPP leadership will develop and disseminate targeted communications and education/training, as necessary. For example, researchers, IRB members, and departmental administrators may each have differing needs in regard to effectively responding to emergency mitigation strategies.

Communications will occur via standard communication routes, such as email and web-based platforms, as available. If standard routes are not available, HRPP leadership will consult the institutional plans in place to address communications. Communications will include instructions and expectations for impacted personnel.

HRPP leadership will determine the frequency and forum for presenting HRPP emergency preparedness and planning to the Hennepin Healthcare research community and other stakeholders.

References

- AAHRPP Element I.1.H
- AAHRPP Tip Sheet – Emergency Preparedness and Response
- HHRI HRPP Emergency Preparedness and Response Plan
- HHS Emergency Preparedness Plan

220 HRPO structure and composition

PURPOSE

It is the purpose of the Hennepin Healthcare Human Research Protection Program (HRPP) to have a qualified IRB Chair, IRB Chair designee, IRB members, consultants, and administrative staff to perform functions of the Hennepin Healthcare IRB for research that it oversees.

This SOP describes the general qualifications for the IRB Chair, IRB Chair designee, IRB members, consultants, and HRPO staff, and the procedures for how performance and composition are periodically evaluated. In addition, this SOP outlines required training, compensation, liability coverage, and HRPP support.

Structure and composition of the Human Research Protection Office (HRPO)

HRPO supports the Human Research Protection Program at Hennepin Healthcare by providing services such as managing the online submission system for Institutional Review Board (IRB) review and approval of human research, conducting pre-reviews, communicating compliance requirements to researchers, and coordinating IRB review activities. HRPO is comprised of the HRPO Director (1.0 FTE), Assistant Director (1.0 FTE), and IRB Analysts (1.1 FTEs).

- HRPO staff are employed by HHRI
- The HRPO Director reports to the HHRI COO
- The HRPO Assistant Director and Analysts report to the HRPO Director
- The HRPO Director and Assistant Director oversee day-to-day operations
- HRPO performance is reviewed on an annual basis by the HRPO/HHRI leadership

Structure and composition of the Institutional Review Board (IRB)

The IRB is composed in accordance with federal regulations; the IRB membership roster includes sufficient information about members' qualifications and experience to ensure appropriate representation at the meeting without conflict of interest for each protocol reviewed to ensure compliance with federal, state, and institutional regulations and guidelines governing human research.

Under the federal regulations, IRBs have the authority:

- To approve, require modifications to secure approval, or disapprove all human subjects research activities overseen and conducted under the auspices of Hennepin Healthcare
- To require that informed consent be obtained and documented in accordance with regulatory requirements unless the criteria for the waiver or alteration of such requirements has been satisfied and approved by the IRB. The IRB may require that information, in addition to that specifically mentioned in the regulations, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects
- To conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year
- To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants
- To observe, or have a third party observe, the consent process
- To observe, or have a third party observe, the conduct of the research

The IRB functions independently. Attempts to coerce or otherwise unduly influence the actions of the IRB are forbidden by policy and are to be reported as described in the section below: *Reporting and investigation of allegations of undue influence*.

IRB Chair: The IRB is overseen by the IRB Chair or designee:

- The Vice President of Medical Affairs may appoint a Vice Chair or alternate to serve as a designee for the IRB Chair.
- The IRB Chair and designees serve at the pleasure of the Vice President of Medical Affairs (VPMA) of HHS.
- The IRB Chair or designees will be removed from office if unable to fulfill the functions of the position as determined by the Vice President of Medical Affairs.
- Performance issues are discussed on a semi-annual basis with the Vice President of Medical Affairs.

IRB:

1) The IRB is responsible for ensuring that the rights and welfare of human research subjects are protected by reviewing and approving human research in a manner consistent with federal regulations, state and local laws, and institutional guidelines and policies. The IRB also considers the scientific merit of proposed research that has not been independently peer-reviewed.
2) The IRB is responsible for evaluating proposed human research and reviews initial submission and ongoing submissions.
3) The IRB serves at the pleasure of the Vice President of Medical Affairs.
4) The IRB is comprised of at least eight members with varying backgrounds and professions to promote complete and adequate review of research activities commonly conducted within HHS.
5) The IRB will be sufficiently qualified through the experience and expertise of its members and the diversity of their race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

6) As determined by IRB/HRPO leadership, an IRB member may serve as an alternate for another IRB member. Either the IRB member or alternate, but not both, will count as one IRB member for purposes of protocol review, determination of quorum, and vote.
7) Ex-Officio members will not count for purposes of determining quorum nor will they vote.
8) The IRB will consider each research site as it relates to community attitudes, information on conditions surrounding the conduct of research, and the continuing status of research.
9) The IRB will consider the community from which subjects are drawn to ensure the protection of their rights, and the appropriateness of the consent process.
10) In addition to possessing the professional competence necessary to review specific research activities to ensure compliance with standards of professional conduct and practice, IRB members will maintain knowledge to ascertain the acceptability of research activities in terms of federal regulations, applicable law, and institutional policies.
11) If the IRB regularly reviews research that involves a vulnerable category of subjects, it will have one or more members knowledgeable about and experienced in working with this population. Otherwise, a consultant will be used.
12) The IRB will have at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. It will also have at least one member who is not otherwise affiliated with HHS and who is not part of the immediate family of a person who is affiliated with HHS.
13) A member can be unaffiliated with HHS and have a primary concern in a nonscientific area. This member would satisfy two of the membership requirements.
14) The IRB will have at least one member who represents the perspective of research participants.
15) The IRB will make every nondiscriminatory effort to ensure that it does not consist entirely of men or entirely of women. Selections will not, however, be made on the basis of gender.
16) Membership composition is reviewed on an ongoing basis by IRB/HRPO leadership to ensure regulatory and guidance requirements are met. When an IRB member resigns, IRB/HRPO leadership will evaluate membership composition to ensure requirements are met.
17) With consultation of the IRB Chair and, if applicable, respective department head, IRB members, including Ex-Officio, will be appointed by the Vice President of Medical Affairs of HHS and will serve at the pleasure of the Vice President of Medical Affairs.
18) IRB members are appointed for indefinite terms.
19) IRB members must be able to appropriately review a minimum of one submission per month.
20) IRB members will be removed from the IRB if unable to fulfill the function of the position.
21) IRB member performance is reviewed on an annual basis by the Chair to ensure regulatory and guidance requirements are met.
    - An IRB membership form will be completed on an annual basis for all IRB members to confirm membership qualifications, COI status, and IRB authority of COI and mitigation.
    - The Annual Member Performance Evaluation will be emailed to members for completion and returned to the IRB Chair; the Chair will provide direct feedback to IRB members.
22) IRB members will report any undue influence to the IRB Chair, HRPO Director, or Institutional Official.

Ad hoc committees

IRB/HRPO leadership may create an ad hoc subcommittee on an as-needed basis.

An ad hoc subcommittee may make recommendations to the IRB.

Minutes of ad hoc subcommittee meetings will be prepared and retained by HRPO.

Consultants

HRPO or the IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available to it through its membership. Consultants may be affiliated or unaffiliated with HHS.

Consultants may present their assessments by phone, in writing, or in-person. All assessments will be documented and included with applicable HRPO and study records.

Consultants are not required to attend IRB meetings and do not vote.

Consultants are bound by the same confidentiality requirements as members.

IRB roster

An IRB member roster is maintained by HRPO and includes the following:

- Names of members
- Earned degrees of members
- The representative capacity of members (scientist or non-scientist; affiliated or non-affiliated; representative of a vulnerable population including prisoners)
- Indications of experience of members to describe each member's chief anticipated contributions to IRB deliberations
- Employment or other relationship between each IRB member and HHS
- Notation of ex-officio and alternate members

IRB membership shall be reported to OHRP in accordance with the Hennepin Healthcare Federalwide Assurance requirements.

Conflict of interest

The IRB must remain free from the influence of financial and other organizational interests. No individual with responsibility for the business and financial interests of the organization may serve on the IRB, for example, individuals such as staff from the Office of Grants and Contracts staff or other similar individuals. Individuals who are responsible for business development are prohibited from carrying out day-to-day operations of the review process.

The following are criteria to be used in determining whether an IRB member or consultant has a conflict of interest on any matter before a committee on which the member serves:

- A financial or managerial interest in a sponsoring entity or product or service, or in any direct competitor of the sponsor, product, or service being evaluated in the research [conflict of interest as defined by the HHRI Conflict of Interest Policy). The same definition is used for a researcher.
- Investigator status
- Involvement in the design, conduct, or reporting of the research
- A spouse or domestic partner, dependent children, and any other family member of the member or consultant who has a significant financial or managerial interest in a sponsoring entity or product, or in any direct competitor of the sponsor, product, or service being evaluated in the research or is involved in the design, conduct, or reporting of the research

A professional relationship such as membership in the same department or division as the investigator shall not usually be considered a conflict of interest

All IRB members shall comply with the HHRI Conflict of Interest (COI) policy and procedure for disclosure.

A conflict of interest of any IRB member with specific protocols shall be managed by all of the following:

- The member being excluded from completing a primary review
- The member being excluded from protocol review, discussion and voting, except to provide information as requested by the committee
- The member being absent from the meeting room for committee discussion and voting
- The member not being counted toward a quorum for that protocol and
- The conflict of interest being documented in meeting minutes

Review of exempt/expedited research, modifications, complaints, non-compliance, and other expedited/administrative review will be completed by the Chair or designee who is without a conflict of interest.

For consultant conflicts of interest, IRB/HRPO leadership will determine whether it is appropriate to ask about conflict of interest based on the issue in question.

- IRB/HRPO leadership will determine if the consultant has a conflict of interest based on the HHRI Conflict of Interest (COI) policy (no disclosure form needs to be completed). If COI exists, it will be will be documented and included with applicable HRPO and study records.
- Consultants with a conflicting interest may provide information but the conflict of interest shall be disclosed to IRB members. A conflict of interest of any consultant with specific protocols shall be managed by all of the following:
    - Such consultants are excluded from discussion except to provide information requested by the IRB.
    - Such consultants are absent from the meeting room for committee discussion and voting.

Training

The following resources shall be provided to all new IRB members:

- Electronic access to HRPO SOPs
- Orientation to the HRPO website resources
- Orientation and ongoing support to the Cayuse Human Ethics (HE) electronic management system

All IRB members and HRPO administrative staff must complete the Hennepin Healthcare-required CITI Program courses

Upon initial appointment, all IRB members and HRPO staff will complete a 301 FORM

For continuing education, all IRB members and HRPO administrative staff must complete ongoing Hennepin Healthcare-required education for research involving human subjects and participate in educational topics presented at IRB meetings

Compensation for IRB members

a) Compensation for the IRB Chair (and designee(s) if appointed) is provided by HHS

b) IRB members receive no compensation

c) Parking is provided to IRB members that are not employees of HHS

Liability coverage for IRB members

Individuals serving on the IRB are entitled to the same defense and indemnity for their activities on behalf of the IRB as are Hennepin Healthcare System employees.

Reporting and investigation of allegations of undue influence

If the IRB Chair or designee, IRB member, or HRPO staff person feels that the IRB has been unduly influenced by any party, they must make a confidential report to the HRPO Director or Institutional Official (IO), or via HHS Ethics hotline, depending on the circumstances. The HRPO Director, IO, or other designated party as appropriate, will ensure that an investigation is conducted and if the allegation is determined valid, that corrective action is taken to prevent additional occurrences.

HRPO support

a) Compensation for HRPO staff is provided by HHRI

b) HRPO completes the budgetary process under HHRI, including identification, justification, and acquisition of needed resources

222 IRB member responsibilities for non-exempt human research

PURPOSE

This SOP describes responsibilities for members of the Hennepin Healthcare Institutional Review Board (IRB) and process of review for submissions in the electronic IRB management system submissions that are subject to IRB oversight.

PROCEDURE

IRB members are expected to commit to a minimum of a 1-year term and, during that time, to fulfill certain duties. IRB members are expected to attend at least 80% of the convened IRB meetings per year.

IRB members shall be versed in the federal regulations governing human subject protections, biomedical and behavioral human research, research ethics, and institutional policies relevant to the protection of human subjects.

Non-scientific members

(a) Non-scientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise.
(b) Non-scientific members are not asked to serve as primary reviewers of research reviewed by the convened IRB.
(c) Non-scientific members should advise the IRB when additional expertise in a non-scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.

Scientific members

(a) Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of clinical practice.
(b) Scientific members are expected to serve as primary reviewers of research reviewed by the convened IRB; however, non-scientific members may be asked to assist in review of certain research requiring their representative capacity (such as review of research which required review by the prisoner representative).
(c) Scientific members should advise the IRB when additional expertise in a scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.

IRB Chair

(a) In addition to the responsibilities as a member, the Chair moderates convened meetings of the IRB.

(b) The Chair may serve as a designated reviewer or may delegate to one or more experienced IRB member(s) (designees) review of research eligible under expedited review procedures.

(c) The Chair is empowered to suspend human research when deemed urgent to protect the rights and welfare of participants. (see 261 SOP Suspensions and terminations)

Designated reviewers

(a) The IRB Chair and IRB members, as designated by the IRB Chair and as identified on the IRB roster as a *designated reviewer*, are empowered to perform IRB reviews using expedited review procedures.
(b) IRB members not assigned as designated reviewers may be asked to assist in review of certain research requiring their representative capacity (such as review of research which required review by the prisoner representative).

223 IRB member addition & removal

PURPOSE

This SOP describes the process by which members are appointed or removed from the Hennepin Healthcare Institutional Review Board (IRB).

PROCEDURE

IRB member appointments and removals are considered on an as needed basis as determined by the IRB Chair in consultation with the HRPO Director. Existing members may request to end their membership at any time.

The Hennepin Healthcare Vice President of Medical Affairs (VPMA) has the authority to approve an appointment to the IRB and a removal when not requested by the member as recommended by the IRB Chair.

Appointing a new member to the IRB

Once approved by the VPMA and prior to activating a new appointment to the IRB, HRPO staff will:

1. Assign required CITI coursework to the new member (see 501 MANUAL Conducting Human Research, section 1.6 *What training and education is required to conduct human research*?)
2. Confirm completion of CITI coursework
3. Add the new member to the *HRPO_IRBmembers_TrainingsAndEducation* spreadsheet to track education throughout their membership [Dropbox (HHRI)\HRPP Admin\HRPO admin\IRB Member Resources & Training\HRPO and IRB Member Training and Education Tracking]
4. Collect and save the member's current CV or resume [iDRIVE: *IRB Membership CV/Resumes*]
5. Collect and save a completed 301 FORM [Dropbox (HHRI) > HRPP Admin > HRPO Admin > *301 FORM completed*]
6. Draft an IRB Member Appointment letter and route to the HRPO director and IRB Chair once items 1-5 are complete

The IRB chair will route the final IRB Member Appointment letter to VPMA and notify HRPO staff once the appointment is confirmed.

Once the appointment is confirmed, HRPO staff will:

1. Update the roster spreadsheet to include the new IRB member (add to the Active Members and add to the Start & End Dates (Members) tabs) [Dropbox (HHRI)\IRB\Roster]
2. Create a user profile for the new IRB member and add member to the roster in Cayuse HE
3. Schedule a one-on-one meeting with the new IRB member to review:
    - meeting workflow
    - submission review
    - navigating Cayuse HE
    - resources for IRB members

NOTE: This step may be done before a confirmed appointment, depending on the IRB meeting schedule and the availability of the new IRB Member.

4. Schedule one observation of a convened IRB meeting for the new member (this must happen before participating as a voting member). Additional observations may be done, if deemed appropriate or necessary by the IRB chair or new IRB member.

Removing a member from the IRB

Once HRPO has been notified regarding removal of a member from the IRB, HRPO staff will:

1. Move the IRB member's CV or resume to the *Previous IRB Members* folder [iDRIVE: *IRB Membership CV/Resumes*]
2. Update the roster to remove the IRB member from the *Active Members* section and add an END DATE to the *Start & End Dates (Members)* tab [Dropbox (HHRI)\IRB\Roster]
3. Remove the IRB member from the roster in Cayuse HE
4. Hide the row of the IRB member in the *HRPO_IRBmembers_TrainingsAndEducation* spreadsheet [Dropbox (HHRI)\HRPP Admin\HRPO admin\IRB Member Resources & Training\HRPO and IRB Member Training and Education Tracking]

230 Convened meetings

PURPOSE

It is the policy of the Hennepin Healthcare Human Research Protection Program to have properly convened meetings to permit appropriate research review to ensure compliance with federal, state, and institutional regulations and guidelines governing human subject research. In addition, it is the policy of the Hennepin Healthcare Human Research Protection Program to have required documentation of pertinent discussions and decisions on research protocols and activities. This SOP describes the requirements of properly convened IRB meetings, documentation of discussions and findings of the convened meetings and reviews conducted by expedited procedures, and communications between the Hennepin Healthcare Human Research Protection Office (HRPO) and investigator.

PROCEDURE

Location of IRB convened meetings

IRB meetings shall be held shall be held via ZOOM or other HHRI-approved virtual meeting platform. When meetings are not held virtually, they shall be held in-person as determined within a private Hennepin Healthcare conference room or other designated space.

Convened meetings schedule

The annual schedule for convened meetings is established by IRB/HRPO leadership in December for the following calendar year.

Convened meetings are typically scheduled for the first and third Monday at noon each month. The annual schedule is managed in Cayuse HE and posted on the HRPO website.

Scheduled meetings are subject to change and may be cancelled, added, or rescheduled by IRB/HRPO leadership for holidays, a lack of quorum, in response to the number of protocol submissions, or for issues regarding the rights and welfare of any subject.

Board members shall confirm attendance at convened meetings via email requests with the IRB analyst.

Attendance during convened meetings will be tracked by an IRB analyst in the meeting details space of Cayuse HE.

Agenda and other materials for convened IRB meetings

Approximately a week before a scheduled meeting, an IRB analyst will summarize agenda items. During the week before the meeting, an IRB analyst will review specific agenda items with the IRB Chair, as necessary.

Agendas are typically finalized a week prior to a convened meeting.

An IRB analyst verifies study materials and generates the agenda for a convened meeting. All board members (including attending alternate members) receive notifications via Cayuse HE with the agenda for a convened meeting and review responsibilities.

Once the agenda is finalized, all materials to be reviewed at convened meetings are made available electronically in Cayuse HE to all IRB members (including attending alternate members) for review, including:

- meeting agenda
- report of Expedited Actions
- previous IRB minutes for review
- all materials related to a study submission, as applicable, including:
    - reviewer worksheets and any additional institutional/federal guidance
    - full protocol, application, or a protocol summary containing the relevant information to determine the proposed research fulfills the criteria for approval
    - proposed consent document
    - recruitment materials
    - investigator brochure (when one exists), which is reviewed by at least the primary reviewer

Materials to support review of studies (e.g., review worksheets, job aids, institutional/federal guidance) are also made available via the HRPO website.

The primary reviewer's completed worksheets will be available in the submission in Cayuse HE once the review is complete, but no later than at the time of the meeting at which the reviewed protocol is considered.

Confidentiality of materials and discussion

All information that attendees have access to as part of convened meetings shall be held as confidential. A confidentiality notice shall be placed on all meeting agendas.

Any printed submission materials shall be maintained by attendees as confidential.

Quorum and voting requirements

Prior to a convened meeting, an IRB analyst will confirm whether the appropriate members required for protocol review and discussion have affirmed their attendance; any anticipated attendance issues will be resolved prior to convening a meeting.

A majority (> 50%), quorum of voting members (each eligible member has one vote) must be present at convened meetings. Member(s) calling in and present on a telephone conference call and/or on ZOOM or other HHRI-approved virtual meeting platform is/are considered part of quorum.

Quorum will be confirmed using the 710 WORKSHEET *Convened Meeting Requirements*, which is completed by an IRB Analyst and saved in the Meeting Details space in Cayuse HE. All attendance information will be included in meeting minutes.

If a quorum fails during a convened meeting, the committee will not take further action or vote until quorum is restored. If required members (e.g., non-scientific) leave the meeting and quorum is lost, votes cannot be taken until the quorum is restored, even if a majority of members are still present.

Quorum may be lost when committee members with a conflict of interest, including a member who is an investigator on a submission being reviewed, must leave the meeting for a vote.

When the convened IRB reviews research involving prisoners, the prisoner representative must be included in the quorum and a majority of voting committee members (exclusive of the prisoner representative) must have no association with the prison involved.

When the convened IRB reviews research involving subjects likely to be vulnerable to coercion or undue influence, at least one member knowledgeable about or experienced in working with such subjects must be included in the quorum.

Approval of any action requires a majority vote of the quorum. All votes will be recorded to confirm quorum in Cayuse HE.

- No proxy votes (written or telephone) are allowed.
- Any Ex-Officio member is neither a voting member nor a member for purposes of a quorum.
- Only one member of a member/alternate member combination may vote on any issue.

Investigator presentations to the IRB

For initial submissions requiring convened IRB review, the principal investigator or designee shall present a brief summary of the protocol to the convened IRB at the assigned meeting.

IRB/HRPO leadership may waive this requirement.

Primary reviewer presentation and discussion

Following protocol presentation by the principal investigator (or designee), the primary reviewer shall summarize his/her review, and IRB members shall have the opportunity to address questions/concerns with the principal investigator (or designee) and the primary reviewer. When the primary reviewer will be absent from the IRB meeting, pending questions shall be discussed with the Chair prior to the meeting.

Once the principal investigator (or designee) leaves the meeting, the protocol is open for further discussion.

A vote will not take place until the PI (or designee) has left the meeting.

Voting

The required criteria for approval will be used for review of all submissions of research, including initial review, continuing review, and review of a modification to previously approved research when the modification affects a criterion for approval.

After discussion of a submission, the committee will vote upon a decision.

IRB decisions include the following:

- **Approved**: the submission is approved as submitted requiring no modifications or clarifications
- **Minor stipulations:** minor modifications and/or clarifications that are prescriptive, specific, and not impacting criteria for approval are required and must be addressed point by point by the investigator; may be converted to approval by subsequent expedited review of responsive materials (without subsequent review by the convened committee).

  During convened IRB review, the IRB may indicate whether a specific IRB member must review the PI's response to stipulations. When a specific IRB member is not identified, the IRB analyst (who is also a member of the IRB) will review the PI's response. The IRB analyst may request assistance from another IRB member, when additional expertise is necessary.
- **Deferred:** substantive modifications and/or clarifications are required and must be addressed point by point by the investigator and subsequently reviewed by the convened IRB prior to the decision on submission approval
- **Disapproved:** the full board identified major issues with the study or submission and disapproved the research. For an initial submission that is disapproved, the PI has an opportunity to submit a written request for reconsideration with sufficient justification within 10 working days of receiving a notice of disapproval. For disapproved renewal or modification submission, the research team will need to create a new submission to proceed.
- **Suspended**: for a previously approved research protocol, all or some of the activity of the research protocol is suspended and must be reconsidered by the IRB in order to be reactivated. The PI has an opportunity to submit a written request for reconsideration with sufficient justification within 10 working days of receiving a notice of suspension.
- **Terminated**: for a previously approved research protocol, all activity of the research protocol is terminated by the IRB. The PI has an opportunity to submit a written request for reconsideration with sufficient justification within 10 working days of receiving a notice of termination.
- **Not reviewed:** when an agenda item is not voted on by the convened IRB for reasons such as a lack of time, lack of necessary expertise or lack of quorum.

Convened IRB meeting minutes

All meeting information shall be stored in the Meeting Details space in Cayuse HE, which will be used to generate meeting minutes for each convened meeting.

IRB meeting minutes will be electronically available to all IRB members, approximately 5 days prior to the next convened IRB meeting.

Convened IRB meeting minutes are completed by the IRB analyst and then distributed to the HRPO director and IRB chair for review (typically within 1-2 business days). The IRB analyst incorporates requested revisions based on feedback from the HRPO director and IRB chair. IRB determination letters are sent for all submission on the meeting agenda, after the HRPO director and IRB chair approve the minutes. When either the IRB chair or HRPO director are not available to review minutes, letters may be sent after final approval of just one. The minutes are shared with all IRB members in the next convened IRB meeting agenda (also available in the meeting details space of the next convened IRB meeting). All members are given an opportunity to provide feedback or comments prior to or during the next convened IRB meeting discussion. After the opportunity for feedback, the IRB analyst will either approve the minutes in Cayuse HE or incorporate changes requested and then approve the minutes in Cayuse HE.

Meeting minutes are confidential and securely maintained via the Cayuse HE system.

Meeting minutes shall contain at a minimum, the following:

The following elements are entered into the NOTES section of the Meeting Details space:

- Date, time, and location of meeting

- Documentation of attendance of members, including the documentation of attendance of Ex-Officio and alternate members
- Documentation of which members, if any, participated in the convened meeting via an alternative mechanism, such as telephone or video conferencing.
- Attendance of staff, guests, study coordinators, investigator(s) or designee, and others
- Member absences during the meeting or loss of quorum (if any)
- Description of IRB member education provided (if any)
- Announcements/discussion items (if any)
- Previous IRB minutes and expedited actions, summary of questions or comments from IRB members on those items, and necessary actions (if any)

The following elements are entered into the MAKE DECISION function of each separate submission:

- decision made (such as approved, minor stipulations, etc.)
- result date
- expiration date (*for initial and renewal submissions*) and the continuing review assignment, if a determination is made that it must be required more frequently than annually
- IRB member who motioned and IRB member who seconded the decision made
- number of votes for, against, abstained
- name(s) of any IRB member(s) recused from voting

  The names of members who leave the meeting because of a conflict of interest along with the fact that a conflict of interest is the reason for the absence must be documented in the RECUSED section of the MAKE DECISION

- protocol specific determinations as required by local policy and/or applicable regulations concerning the following:
  - waiver or alteration of informed consent or consent documentation
  - waiver or alteration of HIPAA Authorization
  - drug or device determinations
  - approval to include certain vulnerable populations as subjects, such as:
    - pregnant women, human fetuses, and neonates
    - prisoners
    - children
    - subjects with diminished capacity
  - IRB approval of a COI and mitigation plan
- the study risk level determination (*for initial submissions*)
- required revisions to the submission and the basis for those revisions (when the decision minor stipulations)
- the basis for deferral of research (when the decision is deferred)
- the basis for disapproving research (when the decision is disapproved)
- summary of the meeting discussion, including but not limited to:
  - summary of review provided by the primary reviewer and/or other IRB members, including topics such as drug or device determinations, inclusion of vulnerable populations, or COI mitigation plan
  - summary of any substantive issues raised
  - for device studies, the rationale for Significant Risk/Nonsignificant Risk device determinations and subsequent approval or disapproval decisions
- summary of discussion of controverted issues and their resolution (if any)
- links to reviewer worksheets completed as part of the review.

Expedited actions report

A report of expedited actions will be generated by Cayuse HE regularly and electronically available to committee members; the report will provide a summary of all expedited actions that have been completed between the date of the last meeting and the date of the next upcoming meeting.

NOTE: A subsequent approval of a submission for which the convened IRB's initial decision is *Minor stipulations* will be listed under *Full Expedited Reviews.*

Reports of expedited actions are confidential and securely maintained via the Cayuse HE system.

Expedited actions are made available to IRB members in the agenda (also available in the meeting details space of the next convened IRB meeting). The date range includes all submissions approved since the last convened IRB. All members are given an opportunity to provide feedback or comments prior to or during the next convened IRB meeting discussion. IRB members are asked if they have any questions or comments before proceeding with other agenda items.

Communication to investigators and other stakeholders

For a submission requiring review at a convened IRB meeting, the Principal Investigator and Primary Contact will receive an email communication from an IRB analyst with meeting information, including date, location, and time for their presentation, if applicable.

The Principal Investigator and Primary Contact will receive automated email communications via Cayuse HE regarding all committee decisions, stipulations, findings, basis for deferral or suspension, and other applicable committee communication related to review at a convened meeting.

HRPO will provide to the HHRI Office of Grants and Contracts, as requested, convened meeting agendas, minutes, expedited action reports, or any other IRB report. Per 270 SOP, HRPO will generate monthly IRB reports for the Hennepin Healthcare Vice President of Medical Affairs and HHRI Institutional Official.

Guest attendance at a convened meeting

Guests are allowed to attend convened meetings with the permission of IRB/HRPO leadership.

Guests may request to attend a convened meeting by contacting HRPO.

Guests must agree to maintain the established confidential standards.

232 IRB meeting minutes

PURPOSE

This SOP describes the process by which Human Research Protection Office (HRPO) manages IRB meeting minutes in the electronic IRB management system, Cayuse Human Ethics (HE).

PROCEDURE

The IRB meeting minutes provide documentation of the Hennepin Healthcare IRB's discussions, decisions, and findings. Electronic copies of IRB meeting minutes, as well as the agenda and other pertinent materials associated with an IRB meeting are maintained within Cayuse HE. Reviewer worksheets are maintained in individual submissions in Cayuse HE in accordance with the 203 SOP (Using Worksheets in Cayuse HE).

Recording minutes

The IRB analyst facilitating an IRB meeting is responsible for documenting discussions, decisions, and findings during the meeting and will record the following:

- IRB member attendance, which will include:
  - The times of any members joining after the start the meeting, leaving before the end of the meeting, or stepping away during discussion

  - When an alternate member replaces a regular member
  - Attendance of members or alternate members who participate through teleconference
- Attendance of any guests, such as investigators, presenters, and/or expert consultants
- The start and stop time for the meeting
- A description of announcements shared with IRB members
- A description of IRB member education provided
- Confirmation for approval of the previous meeting minutes and expedited actions, and any requested revisions
- The IRB decision, for each submission reviewed during the meeting, including a rationale for the basis of requiring stipulations or disapproving a submission; each submission (e.g., Initial, Renewal, Modification, Incident) will be discussed and voted on individually
- Summary of the discussion of controverted issues and resolution
- Summary of discussion for each submission
  Recommendations or stipulations documented in the reviewer worksheet (which are typically submitted prior to the meeting) may deviate from board decisions after a discussion at a convened meeting. In the event that recommendations in the reviewer worksheet are not consistent with the conclusions resulting from the board discussion, the minutes will document the final decisions and determinations
- Voting results include number for, opposed, and abstaining. This will include only voting members present in the meeting at the time vote is called. These votes, along with notation of those members who recused themselves for a conflicting interest, will be recorded
- Determination of the level of risk (minimal, greater than minimal) will be documented at review of an initial submission.
- The IRB approval expiration date will be indicated for initial and renewal submissions
- Findings required by regulation and protocol-specific findings (e.g., waiver or alteration of informed consent and/or authorization, inclusion of subparts, waiver or partial waiver of HIPAA authorization, participants with diminished capacity to consent)
- Links to all reviewer worksheets completed by the primary reviewer for each submission

Approving minutes

The IRB analyst facilitating an IRB meeting is responsible for preparing the draft minutes and will provide a draft version of the minutes to the IRB chair and/or HRPO director. The draft version will typically be sent out within 24 hours after the meeting.

- The IRB chair and HRPO director/HRPO Assistant director (or one of these individuals, when both are not available) will review the draft minutes and any requested revisions will be incorporated.
- Once any necessary revisions have been made, IRB determination letters will be sent to investigators (via Cayuse HE).

A link to draft minutes is available to all IRB members via the agenda for the subsequent IRB meeting. Prior to an IRB meeting, IRB members review the draft minutes; during the IRB meeting, the IRB chair (or designee) will invite IRB members to share questions or comments about the minutes.

- Any questions or comments will be documented in the current meeting's minutes.
- The IRB analyst will correct the draft minutes if revisions are necessary.
- The IRB analyst approves minutes in Cayuse HE, where they remain available to all IRB members.

239 Administrative withdrawals and closures

PURPOSE

The Hennepin Healthcare Human Research Protection Office (HRPO) has discretion to administratively withdraw or administratively close study records in Cayuse HE. This SOP describes criteria for administrative withdrawal and administrative closure. Studies that are administratively withdrawn or closed cannot proceed with human research activities and cannot be re-opened in Cayuse HE.

PROCEDURE

HRPO will consider exceptions to response times described in this policy on a case-by-case basis if circumstances prohibit a PI response within the established timelines. The PI (or designee) must respond within 5 calendar days to an HRPO email notification regarding administrative withdrawal, closure, or unresolved submission status to request an extension.

Administrative withdrawals

Initial submissions: in-draft

HRPO may administratively withdraw a study record in Cayuse HE when an *Initial* submission remains in draft mode after 180 calendar days of creation or last routing action or when requested by the PI (or designee) (e.g., duplicate submission, submission in error, Principal Investigator is no longer affiliated with Hennepin Healthcare).

Administrative closures

Initial submissions with decision: *No engagement in research / No human subjects research*

For an *Initial* submission that receives a decision: *No engagement in research* or *No human subjects research*, IRB oversight is not applicable and HRPO will administratively close the study record.

Initial submissions with decision: Minor Stipulations / Return to PI / Deferral

For an *Initial* submission that receives a decision: *Return to PI*, *Deferred*, or *Minor stipulations*, the PI is responsible to ensure that a response to comments and/or stipulations is submitted via Cayuse HE within 180 calendar days. HRPO will administratively close the study record after 180 calendar days of such a decision when the PI does not respond to an email notification from HRPO regarding administrative closure.

***Renewal* submissions with decision: Minor Stipulations / Return to PI / Deferral**

For a *Renewal* submission that receives a decision: *Return to PI*, *Deferred*, or *Minor stipulations*, the PI is responsible to ensure that a response to comments and/or stipulations is submitted via Cayuse HE within 30 calendar days. If no response is submitted after 30 calendar days of such a decision and the PI does not respond to an email notification from HRPO regarding unresolved submission status, the study is subject to a noncompliance determination by the IRB; if the noncompliance is not resolved accordingly, the study is subject to additional IRB determinations and actions, including administrative closure.

Expired IRB approval

For a study subject to continuing review approval by the Hennepin Healthcare IRB, the PI is responsible to ensure that IRB approval does not expire. If a *Renewal* submission is not certified via Cayuse HE within 30 calendar days of the IRB approval expiration date and the PI does not respond to an email notification from HRPO regarding unresolved submission status, the study is subject to a noncompliance determination by the IRB; if the noncompliance is not resolved accordingly, the study is subject to additional IRB determinations and actions, including administrative closure.

240 Pre-review

PURPOSE

This SOP describes the process by which Human Research Protection Office (HRPO) conducts a pre-review of submissions in the electronic IRB management system, Cayuse Human Ethics (HE).

PROCEDURE

Pre-review is an initial assessment of a submission. The purpose of pre-review is to:

- Ensure that the application is eligible for review by the Hennepin Healthcare IRB
- Identify the applicable regulatory oversight
- Determine the appropriate level of review
- Promote compliance, consistency, and efficiency of IRB reviews

- Allow IRB review to focus on the criteria for approval, ethical principles, and required determinations

The process of pre-review begins when an IRB Analyst is assigned a submission in Cayuse HE. When pre-review is complete, the analyst assigns the appropriate level of review and reviewer and the submission moves forward in the Cayuse HE workflow. Completion of pre-review does not guarantee IRB approval.

For a submission requiring convened IRB review, the process of pre-review must be completed at least 2 weeks prior to a scheduled IRB meeting.

HRPO staff generally carry out these procedures. Other individuals may be designated to support pre-review, as appropriate.

Conducting a pre-review

The pre-reviewer will read and evaluate the provided information, using the appropriate guidance materials, as necessary. The following table provides an overview of procedures for each submission type:

Submission Type	Before being assigned for final review, the pre-reviewer will review the submission to ensure that the following have been provided:	The pre-reviewer will also review the submission for the items below, which must be resolved before a final IRB determination:
Initial	- Appropriate smartform selections/responses - Relevant study materials (such as protocol, consent, data collection forms, and subject facing materials) - A data and safety monitoring plan - Sufficient documentation for any drug or device determinations (such as criteria for relevant IND or IDE exempt category, Investigator's Brochure, or documentation of IND or IDE # as described in 717 WORKSHEET FDA- Drugs and IND requirement and 718 FDA – Devices and IDE requirement) - Documentation of approval from any required ancillary reviews	- Personnel training that has not been completed or has expired - Completeness of study materials
Modification	- Appropriate changes made to the smartform - Modifications requested are consistent with changes made throughout study materials, as necessary - Documentation of approval from any required ancillary reviews	- Personnel training current for any newly added personnel
Renewal	- Appropriate smartform selections/responses - No outstanding modification or incident submissions to be resolved prior to renewal - Enrollment numbers consistent with reporting from previous continuing review and approved total	- Current personnel training for all study personnel - Accurate responses to reporting dates, based on previous continuing review
Incident	- Appropriate smartform selections/responses - Necessary documentation/detail has been provided	
Closure	- Appropriate smartform selections/responses - No outstanding modification or incident submissions to be resolved	N/A – Closure submissions are not subject to IRB review

Communication to the researcher. When a submission is assigned to a pre-reviewer, the Principal Investigator (PI) (and Primary Contact (PC) if assigned) will receive notification. If pre-review indicates that clarification, additional information and/or materials are required, the submission will be returned to the PI with comments.

Researcher response. All clarifications and new information must be documented in the Cayuse HE submission as (1) response to comments and (2) edits to the submission forms and/or uploaded materials, as appropriate.

Exempt and expedited determinations. As part of pre-review, the assigned analyst will assess whether the submission qualifies for exemption from IRB oversight or expedited review, using the appropriate guidance materials and determination worksheets. When a submission qualifies for exemption or expedited review, the pre-reviewer may also serve as the designated reviewer to complete the review process using the applicable review worksheets if he/she is an IRB member with appropriate expertise.

Documenting the pre-review outcomes. Clarifications and revisions requested will be documented via comments in the smartform submission. For an initial submission, the pre-reviewer will begin the 708 WORKSHEET to identify applicable oversight. For a follow- on submission, the pre-reviewer will open the most recently completed 708 WORKSHEET to identify applicable oversight. The 708 WORKSHEET will also document which reviewer worksheets are necessary.

241 Level of review assignment

PURPOSE

This SOP describes the assignment of the level of IRB review for research involving human subjects submitted to the Hennepin Healthcare Human Research Protection Office (HRPO) and criteria and process for administrative withdrawals.

PROCEDURE

For research that meets the definition of human research and is not ceded to another IRB, HRPO will assign the submission in Cayuse Human Ethics (HE) to one of the following types of review using regulatory criteria as outlined in 45CFR46 and 21CFR56:

- convened IRB
- expedited
- exempt

242 Convened IRB review

PURPOSE

This SOP describes the initial review by a convened IRB of research involving human subjects submitted to the Hennepin Healthcare Human Research Protection Office (HRPO).

PROCEDURE

All submissions that are not eligible under expedited review procedures (45 CFR 46.110 or 21 CFR 56.110) will be reviewed by the convened IRB with the following exception:

> Emergency use of test articles (emergency IND) notifications may be reviewed and confirmed by IRB Chair or designee as outlined in 21 CFR 56.104(c).

For investigator-initiated clinical research, the initial submission must include documentation that the Office of Education & Quality in Clinical Research (OEQCR) has completed an assessment of the research. The OEQCR process will be conducted in accordance with OEQCR SOPs and must be completed prior to placing a submission on the IRB agenda.

- At the discretion of HRPO leadership, any initial submission with important deficiencies may be required to complete an OEQCR assessment.
- Submissions that have not completed a required EOQCR assessment will be returned to the investigator.

Pre-review

HRPO staff will conduct an IRB pre-review for all submissions that require convened IRB review; pre-review ensures that a submission includes all required and relevant elements and identifies the applicable regulatory oversight.

Assignment for review

Upon completion of pre-review, HRPO staff will add the submission to the agenda for the next available IRB meeting. This assignment is subject to a cut-off time of up to 2 weeks prior to the scheduled meeting, the number of submissions that have already been assigned to the scheduled meeting, and available expertise.

Upon addition to an IRB meeting agenda, HRPO staff will review the relevant information and assign the submission to an IRB member with relevant expertise, availability, and without conflict of interest to serve as a primary reviewer for in-depth review. All submission documents will be available to the primary reviewer for review in Cayuse HE. The primary reviewer will track and complete the primary reviewer process in Cayuse HE, adding comments in the submission and uploading completed reviewer worksheets, as applicable.

During the review process, the primary reviewer shall determine whether the primary reviewer needs additional expertise to assist in the submission review. If necessary, the primary reviewer will inform the IRB analyst. The IRB analyst will contact a consultant(s).

HRPO staff will monitor the status of primary reviews to ensure they are completed prior to the convened meeting.

All submission and primary review documents will be available to IRB members for review in Cayuse HE.

Convened IRB review

Quorum will be confirmed prior to a meeting in accordance with the 710 WORKSHEET. If any unanticipated absences occur, the IRB analyst will consult the 710 WORKSHEET during the convened meeting to ensure quorum is met. If quorum is not met – for the meeting or during review of a submission; items will be tabled for a future agenda.

During review of an initial submission at the convened meeting, the principal investigator and/or designee shall present a brief summary of the protocol. The primary reviewer will summarize their review. If the primary reviewer will be absent from the IRB meeting, pending questions may be discussed with the Chair prior to the meeting. The IRB Chair and members will have the opportunity to address questions/concerns with the principal investigator and/or designee and the primary reviewer. Once all questions have been answered, the principal investigator and/or designee will be dismissed from the meeting. Once the principal investigator and/or designee leave the meeting, the submission is open for discussion. Additional information, consultation, and revision may be requested.

Use of a consultant (if applicable) and key information provided from the consultation (including any potential conflict of interest of the consultant) shall be documented in the Cayuse HE meeting record.

For submissions that have a recorded conflict of interest, documentation of resolution including the management plan from the HHRI Conflict of Interest Committee must be included for IRB review; the convened IRB has the final authority to decide whether the conflict of interest and its management, if any, allow the research to be IRB-approved. IRB members annually acknowledge the authority of the IRB over conflict of interest and its management.

For research involving a drug and/or device, IRB review will include additional considerations and determinations made in accordance with HRPO reviewer worksheets of drug and device studies:

- For those submissions that involve either a drug or device, the convened IRB will confirm that an IND or IDE has been obtained or the submission meets the criteria for an IND or IDE exemption.
- For those submissions that are subject to IDE regulation (involving investigational devices and requiring a significant or nonsignificant risk determination), the convened IRB will review and determine risk by vote. Risk determinations of device studies shall not be made using expedited review procedures.

When a submission indicates a radiation safety issue, documentation of resolution from the Radiation Safety and Radioactive Materials Committee must be obtained prior to being assigned to the convened IRB. Documentation of approval will be available in the submission.

When a submission indicates a biosafety issue, documentation of resolution from the Institutional Biosafety Committee must be obtained prior to being assigned to the convened IRB. Documentation of approval will be available in the submission.

IRB approval period

The date of IRB approval of a submission shall be the date of the IRB meeting at which the submission was *Approved* or A*pproved with minor stipulations*. Expiration will be set one year minus one day* from this date, or sooner if deemed appropriate by the

IRB. For approvals with minor stipulations for initial submissions, no research activities involving human subjects may be initiated until HRPO confirms that the minor stipulations have been met to update the submission as *Approved* with an accompanying approval letter.

*For example, an initial or renewal submission approved by the convened IRB on 01/15/2023 with annual continuing review will receive an expiration date of 01/**14**/2024.

243 Initial review of expedited research

PURPOSE

This SOP describes expedited initial review of research involving human subjects submitted to the Hennepin Healthcare Human Research Protection Office (HRPO).

PROCEDURE

Expedited review criteria

The expedited review procedure may be used on any submission that meets the criteria below. A copy of the current criteria is included in 45 CFR 46.110(b) and 21 CFR 56.110(b). Criteria for expedited review include all of the following:

- The research presents no more than minimal risk to subjects. A list of characteristics of studies involving no more than minimal risk has been prepared and is updated from time to time by the Secretary of Health and Human Services and by the Food and Drug Administration.
- The identification of the subjects or their responses will not reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- The research is not classified.
- The research activities fit into one or more of the categories below (1-7):

  (1) clinical study of a drug or medical device that does not require full committee review [an investigational new drug (IND) or an investigational device exemption (IDE) is not required];

  (2) collection of blood samples by finger stick, heel stick, ear stick, or venipuncture [(a) from healthy, nonpregnant adults who weigh at least 110 pounds; for these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected; for these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week)];

  (3) prospective collection of biological specimens for research purposes by noninvasive means;

  (4) collection of data through noninvasive procedures routinely employed in clinical practice, excluding procedures involving general anesthesia, sedation, x-rays, or microwaves;

  (5) research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis);

  (6) collection of data from voice, video, digital, or image recordings made for research purposes; and

  (7) research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies

Pre-review

HRPO staff will conduct an IRB pre-review for all submissions that require convened IRB review; pre-review ensures that a submission includes all required and relevant elements and identifies the applicable regulatory oversight.

Assignment for review

Expedited review must be conducted by the IRB Chair or designated IRB member or alternate with no conflict of interest. The following criteria are considered when determining whether an IRB member/alternate is qualified to conduct expedited reviews: length of IRB service, training regarding expedited review procedures, research experience/expertise, and/or work with the research subjects being studied.

If expedited review is used for research involving prisoners, the review will be conducted in accordance with 45 CFR 46 Subpart C and HRPO SOPs and Worksheets and documented in the Cayuse HE submission record (see 256 SOP Research involving prisoners).

All submission documents will be available to the expedited reviewer(s) for review in Cayuse HE.

The expedited reviewer(s) will track and complete their process in Cayuse HE, adding comments in the submission and uploading completed reviewer worksheets, as applicable. The reviewer(s) shall confirm whether the research qualifies for the expedited review process [45 CFR 46.110(b) and 21 CFR 56.110(b)]. If the submission does not meet criteria for expedited review, the submission will be returned to the investigator with a request to revise the submission accordingly.

Significant/nonsignificant risk determinations of device studies cannot be made using the expedited review procedure.

During the review process, the reviewer(s) shall determine whether he/she needs additional expertise to assist in the submission review. If necessary, the reviewer(s) will inform the IRB analyst. The IRB analyst will contact a consultant(s).

The reviewer(s) may exercise all authority of the IRB except that the reviewer(s) may not disapprove the research. A research submission may be disapproved only after review in accordance with the convened IRB review procedure.

For those submissions that have a recorded conflict of interest, approval shall not be granted until documentation of resolution from the HHRI Conflict of Interest Committee has been attached to the submission in Cayuse HE. Conflict of interest management plans will be reviewed by expedited procedures to decide whether the conflict of interest and its management, if any, allow the research to be approved.

All IRB members will be informed of research submissions that have been approved under the expedited procedure through a report of expedited actions available in the meeting details space in Cayuse HE for each convened IRB meeting.

IRB approval period

The date of approval entered in Cayuse HE for a submission will be used to establish a continuing review date. The date of IRB approval of a submission shall be the result date of the IRB review during which the submission was *Approved* or A*pproved with minor stipulations*. Expiration will be set one year minus one day* from this date, or sooner if deemed appropriate by the IRB.

Continuing review may be completed using the expedited review procedure.

*For example, an initial or renewal submission approved by the IRB on 01/15/2023 with annual continuing review will receive an expiration date of 01/**14**/2024.

244 Exempt research

PURPOSE

This SOP describes the initial review of research involving human subjects submitted to the Hennepin Healthcare Human Research Protection Office (HRPO) that is exempt from ongoing IRB oversight.

PROCEDURE

Exempt reviews may be carried out by an IRB member designated to conduct exempt reviews. Eligibility for an exempt determination is made in accordance with HRPO 160 GUIDANCE *Criteria for exemption from IRB oversight*. Exempt research fulfills Hennepin Healthcare Research Institute's ethical standards.

HRPO staff will assess eligibility for exemption as part of the pre-review process. The pre-reviewer may obtain a consultation from an IRB member if there is uncertainty about whether the submission is eligible for exemption. Research that is not eligible for exemption will undergo expedited review or review by the convened IRB.

When a submission is determined to qualify for exemption from IRB oversight, the IRB Analyst/ Reviewer will complete HRPO worksheets in accordance with 203 SOP Using worksheets with Cayuse HE.

Research that meets criteria as described in 45 CFR 46.101 or 21 CFR 56.104, as applicable, is exempt from ongoing IRB oversight.

Research that is submitted for exemption shall be reviewed by an IRB member or alternate with appropriate expertise to review exempt research and with no conflict of interest.

The reviewer(s) may not disapprove the research. A research submission may be disapproved only after review in accordance with the convened IRB review procedure.

All submission documents will be available to the reviewer for review in Cayuse HE. The reviewer will track and complete his/her review in Cayuse HE, adding comments in the submission and uploading completed reviewer worksheets, as applicable. The reviewer shall determine the research to be exempt if it meets the regulatory criteria.

For any exempt research that indicates a conflict of interest, approval shall not be granted until documentation of resolution from the HHRI Conflict of Interest Committee has been attached to the submission in Cayuse HE. Conflict of interest management plans will be reviewed by expedited procedures to decide whether the conflict of interest and its management, if any, allow the research to be approved.

IRB members are informed of research that has been determined to be exempt through a report of expedited actions available in the Cayuse HE Meetings module.

245 Emergency research

PURPOSE

This SOP describes the process of reviewing emergency use of an investigational product in accordance with FDA regulatory requirements.

PROCEDURE

Emergency use criteria

Emergency use is defined per 21 CFR 56.102(d) as the *use of a test article on a human subject in a life-threatening situation in which:*

- *No standard acceptable treatment is available*
  AND
- *There is not sufficient time to obtain IRB approval*

When the conditions described in 21 CFR 56.102(d) are met and for which the investigator/clinician has completed an emergency use submission to the Hennepin Healthcare IRB within 5 working days, an initial *emergency use of a test article* is allowed an **exemption,** per 21 CFR 56.104(c), from the 21 CFR 56 prospective IRB review requirement.

Any subsequent use of the test article at Hennepin Healthcare is subject to convened IRB review. The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. If such a circumstance arises, the Hennepin Healthcare IRB may apply emergency use criteria for a subsequent use.

Informed consent must be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by 21 CFR 50 and informed consent must be appropriately documented, in accordance with and to the extent required by 21 CFR 50.27, unless exception to informed consent requirements for emergency use of a test article are met (21 CFR 50.23).

Emergency use involving an investigational drug or biologic or device is subject to applicable FDA regulatory requirements (e.g., IND or IDE).

NOTE: Under the emergency use regulations, the authority of a physician to provide emergency medical care is not limited, to the extent the physician is permitted to do so under applicable federal, state, and institutional regulations.

Emergency use review

HRPO staff will conduct an initial assessment of a submission for emergency use (i.e., five-day report) to verify it includes all relevant elements. After the initial assessment is complete, HRPO staff will assign the submission to the IRB Chair or designated IRB member/alternate with appropriate expertise (as described in 243 SOP, *Assignment for review*) and with no conflict of interest to complete the review process.

The review process will be tracked and completed in Cayuse HE, including the addition of comments in the submission, as applicable, and attachment of a completed 788 WORKSHEET *Emergency use of a test article* to confirm the submission qualifies for exemption under FDA regulations.

Emergency use notifications

The IRB does not provide "IRB approval" for an emergency use submission. The investigator/clinician will receive an acknowledgement to confirm criteria have been met for exemption from the IRB requirement.

If the submission does not qualify for exemption, the submission will be returned to the investigator/clinician with additional instructions.

All IRB members will be informed of emergency use submissions via a report of expedited actions available in the meeting details space in Cayuse HE for each convened IRB meeting.

247 Recruitment and screening of potential participants

PURPOSE

This SOP describes the process by which the Hennepin Healthcare Institutional Review Board (IRB) conducts review of recruitment strategies for research involving human subjects.

PROCEDURE

The IRB will evaluate the investigator's plan for screening and recruitment of human subjects in research to ensure appropriateness and an equitable selection of participants. The 501 MANUAL Conducting Human Research, section 5. *Recruiting and screening potential participants* provides supporting information for this SOP.

The IRB will evaluate the investigator's materials for recruitment to ensure appropriateness. Materials to recruit subjects should include information that would help them determine their eligibility and interest. The IRB will not allow recruitment materials that are misleading, inaccurate, exculpatory, coercive, or unduly influential.

The investigator is responsible for describing recruitment in the study submission for IRB review and approval. Any change or addition to approved recruitment must be submitted via a *Modification* submission and approved by the IRB prior to implementation. Minor changes to previously approved recruitment for a study subject to convened IRB review may be reviewed by the expedited IRB review procedure.

Considerations for various methods of recruiting potential participants

If a study involves sending recruitment letters, the IRB will consider the following:

- The recruitment letter should identify how the investigator is affiliated with the institution and how they obtained access to the individual's information. The letter should come from the individual's clinic/care team; if the study team does not have a patient care relationship with prospective participants, the study team should collaborate with the clinic/provider care team to have recruitment letters signed/sent out by the clinic/provider group.
- If the study involves follow-up via telephone, the initial recruitment letter must describe the follow-up so individuals are made aware of an unsolicited phone call and provide instructions for individuals to opt out of future contact (for example, return postcards or instructions of how to inform the study team). The IRB will also review the script to be used by research staff when calling potential participants.
- If letters will be re-sent to individuals who do not initially respond, the initial letter must describe this possibility so individuals are aware of additional mailings and provide instructions for individuals to opt out of future contact (for example, return postcards or instructions of how to inform the study team).

- An investigator cannot guarantee that a mailing will be opened by the intended recipient. Therefore, for research of a sensitive nature, the IRB will evaluate whether special efforts must be made to protect the privacy and confidentiality of potential participants and appropriate precautions to avoid any real or perceived breach of confidentiality.

When the study team will approach potential participants in-person, the IRB will consider the following:

When another provider assists with recruitment (for example, sharing information about the study with their participant population), the referring physician must document permission to be contacted by the study team in the electronic medical record.

Accessing Epic medical records to screen potential participants

Under the revised Common Rule [45CFR46], the IRB may approve research that involves obtaining information or biospecimens to screen, recruit, or determine eligibility of prospective subjects for a research study without informed consent, i.e., a waiver of informed consent for these types of activities is not required. This is applicable if (1) the information is obtained through oral or written communication with the subject or the subject's legally authorized representative, or (2) identifiable private information or identifiable biospecimens are obtained by accessing records or stored identifiable biospecimens. The HIPAA Privacy Rule permits use of PHI for reviews preparatory to research, however, the Hennepin Healthcare IRB considers this part of the overall research plan and requires IRB review prior to the review activity commencing. It is not permissible to begin the research by gathering preliminary data via lookups in clinical information systems or reviewing clinic appointment logs or other records of clinical care prior to IRB approval of a study.

The Hennepin Healthcare IRB serves as the Privacy Board to oversee compliance with the HIPAA Privacy Rule pertaining to research. The study submission must adequately describe the screening and recruitment process and must also address the criteria for a partial HIPAA waiver, when applicable; the IRB will review such requests in accordance with the 741 WORKSHEET HIPAA waiver or alteration of authorization for research.

248 Recruitment materials

PURPOSE

This SOP describes the process by which the Hennepin Healthcare Institutional Review Board (IRB) conducts review of recruitment materials.

PROCEDURE

The IRB will evaluate recruitment materials to ensure appropriateness and an equitable selection of participants.

Final versions of recruitment materials for research involving human subjects (e.g., materials that are intended to be seen or heard by prospective subjects to solicit their participation in research) must be reviewed and approved by the IRB. Recruitment materials should be included as part of an *Initial* study submission in Cayuse HE. Changes to approved materials must be submitted to the IRB through via a *Modification* submission for approval prior to implementation. When new materials or minor changes to previously approved materials may be easily compared to previously approved materials for a study subject to convened IRB review, they may be reviewed by the expedited IRB review procedure.

Review and approval of a listing with a study's basic information (e.g., clinicaltrials.gov) is not required.

When advertisements, such as videos or postings on social media, TV, radio, or websites, are used, the IRB will consider the following:

- The investigator may need to confirm necessary approvals for posting materials in public spaces
- Researchers may submit a script or storyboard prior to producing final media
- The IRB must review and approve the media in its final form prior to use

Considerations for approval

Advertisements and other recruitment materials shall be reviewed to assure that materials do **NOT**:

- state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

- make claims, either explicitly or implicitly, that the investigational drug, biologic, or device is safe or effective for the purposes under investigation.
- make claims, either explicitly or implicitly, that the investigational article is known to be equivalent or superior to any other drug, biologic, or device.
- use terms such as “new treatment”, “new medication”, or “new drug” without explaining that the test article is investigational.
- promise “free medical treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.
- contain Information in the advertisement or use a method of communications that is coercive.
- use any language that is exculpatory.
- overemphasize the payment or the amount to be paid (if payment is provided).

Information provided in advertisements and other recruitment materials shall be limited to the information the prospective subjects need to determine their *eligibility* and *interest*. When appropriately worded, the following items **may be included** in advertisements:

- The name and address of the clinical investigator or research facility
- The condition under study
- The purpose of the research
- In summary form, the criteria that will be used to determine eligibility for the protocol
- A brief list of participation benefits, if any
- The time or other commitment required of the subjects
- The location of the research and the person or office to contact for further information

249 Compensation for study participation

PURPOSE

This SOP describes the process by which the Hennepin Healthcare Institutional Review Board (IRB) conducts review of compensation for participation in research.

PROCEDURE

The IRB will evaluate compensation, as applicable, provided to subjects for their participation in research to ensure appropriateness.

Considerations for approval

- Compensation to research subjects for participation in research is not considered a benefit for the purposes of the risk/benefit analysis.
- All information concerning compensation, including the amount, type, and schedule of payment(s), must be described as part of the informed consent process, e.g., included in an informed consent document or supporting material.
- Compensation to research subjects for participation should be based primarily on their time, effort, and inconvenience.
- The amount and schedule of all payments should be described in the *Initial* submission for IRB approval; if changes are made to the IRB-approved compensation plan, a *Modification* submission must be approved prior to implementation of the change.
- The IRB will consider whether the compensation plan (e.g., amount of payment and the proposed method and timing of disbursement) may be coercive or present undue influence.
- Any credit for payment must accrue as the study progresses and must not be contingent upon the subject completing the entire course of the study.
- Unless it creates undue inconvenience or coercion, compensation to subjects who withdraw from the research may be made at the time they would have completed the research (or completed a phase of the research) had they not withdrawn.
- While the entire payment to subjects must not be contingent upon completion of their research activities, payment of a small proportion as an incentive for completion of the research is acceptable, providing that such incentive is not coercive.

- Sponsors may not provide discounts as compensation or incentive for participation in a study.
- If the amount of compensation may exceed the threshold for tax purposes, researchers should inform participants that they will be required to provide their social security number and that their compensation is subject to tax rules; researchers should explain limitations on confidentially via third-party payment processes.
- The IRB prohibits incentives, finder's fees (payments to professionals in exchange for referrals of potential subjects), or bonuses of any type in exchange for referral of potential participants or tied to the rate or timing of enrollment, which may encourage recruiters to put inappropriate pressure on prospective participants.

250 Continuing review/administrative check-in

PURPOSE

This SOP describes continuing review or administrative check-in processes for previously approved research.

PROCEDURE

Researchers must respond to the requirement for continuing review or administrative check-in using Cayuse HE. Cayuse HE generates automatic, continuing review reminders beginning 3 months prior to the renewal due date and 2 months prior to the administrative check-in due date. Researchers must complete a *Renewal* submission in Cayuse HE in accordance with continuing review or administrative check-in due dates.

Continuing review

Continuing review is required if any of the following apply:

- Research is initially subject to review and approval by the convened IRB
- Research is subject to the pre-2018 Common Rule
- Research is regulated by the FDA, DoJ, or Consumer Product Safety Commission (regardless of risk and review type (e.g., expedited or convened IRB)
- The IRB has imposed a continuing review requirement (e.g., research approved under the revised Common Rule) documented

Except for research approved under the revised Common Rule, the need for continuing review exists as long as the research remains active for follow-up of subjects, even when the research is permanently closed to enrollment of new subjects and all subjects have completed all research-related interventions. In addition, continuing review occurs when the remaining research activities are limited to data analysis unless there is no access to identifiable data and the study meets all criteria for study closure.

For research approved under the revised Common Rule, continuing review is not required for:

- Research that is eligible for expedited review
- Exempt research conditioned on limited IRB review
- Research that has completed all interventions and now only includes analyzing data, even if the information or biospecimens are identifiable
- Research that has completed all interventions and now only includes accessing follow-up clinical data from clinical care procedures.

The IRB has the authority to require continuing review for research approved under the revised Common Rule; this requirement and rationale must be documented in the decision function of Cayuse HE study record. [45 CFR 46.109(f), 46.110; 46.115(a)(8) revised Common Rule]

Research submissions determined to be exempt do not have a continuing review requirement.

The criteria for IRB approval as described in HRPO SOPs applies to continuing review of research.

When a renewal submission is eligible for review under an expedited category, continuing review may be done via expedited review when the researcher or IRB has not identified additional risks or concerns. All other renewal submissions shall be reviewed by the convened IRB.

Continuing review of research shall be conducted at intervals appropriate to the determination of the degree of risk, but not less than once per year.

For research initially approved via expedited review where continuing review is required

Once a submission is approved, the interval for continuing review shall be annual or more frequently as determined by the reviewer.

The first period of continuing review for research starts on the date the submission was approved (with or without minor stipulations).

Approval expiration and requirements shall be included in the approval letter.

A designated IRB reviewer will be assigned for continuing review approval of all expedited research; the reviewer will evaluate the *Renewal* submission in Cayuse. Expedited review and approval is completed via Cayuse HE in accordance with HRPO SOPs and worksheets.

When annual reapproval is granted under expedited review (without minor stipulations), the next expiration date will be set from the effective approval date. When annual reapproval is granted under expedited review with minor stipulations, the next expiration date will be set from the approval with minor stipulations and not the final effective approval date.

For research initially approved via convened IRB

Projects will be assigned annual continuing review at the time of initial approval unless the IRB determines that a project should be assigned to a more frequent continuing review period. The IRB shall consider the degree of risk, study population, and/or other factors pertaining to the protection of human subjects such as the experience of the researcher, the IRB's previous experience with that researcher, the projected rate of enrollment, and/or whether the study involve novel therapies when establishing a continuing review period more frequent than annual (e.g., monthly, quarterly, semi-annually).

The first period of continuing review starts on the date of the meeting at which the IRB approved the submission (with or without minor stipulations).

Approval expiration and requirements shall be included in the IRB meeting minutes and approval letter.

The convened IRB reviews and approves continuing review submissions for all renewals not eligible for review under expedited review. A primary IRB reviewer will be assigned for continuing review approval of all non-expedited research; the reviewer and IRB members will evaluate the *Renewal* submission in Cayuse HE in accordance with HRPO SOPs and worksheets. Non-expedited review and approval is completed via Cayuse HE in accordance with HRPO SOPs and worksheets. Worksheets completed by the primary reviewer prior to the IRB meeting will serve as a discussion tool during the IRB meeting.

The primary reviewer or convened IRB will determine whether there is a need for additional information from the investigator or additional expertise in review. If necessary, the primary reviewer and/or HRPO will contact the investigator or consultant(s), as applicable.

The primary reviewer or convened IRB may determine that verification is needed from sources other than the investigator that no material changes have occurred since previous review. The following criteria shall be used to determine the necessity of additional verification:

- Inconsistencies resulting from review of information;
- Inconsistencies with a data safety monitoring board report; and/or
- Inconsistencies resulting from a review/audit

For IRB continuing review approvals, a vote will be taken after discussion in accordance with HRPO SOPs.

When annual reapproval is granted, the IRB meeting date will dictate the next expiration date, unless reapproval is granted with a more frequent time period. When annual reapproval is granted with minor stipulations, the next expiration date will be set from the date of the IRB meeting and not the final effective approval date.

Following submission of continuing review in accordance with HRPO requirements and satisfactory review by the fully convened IRB or designated reviewer via expedited review, IRB approval will be renewed.

Expired IRB approval

If an investigator fails to provide continuing review in accordance with HRPO requirements and approval has expired, all research activities involving human subjects must stop, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection of private identifiable information. Interventions and interactions for current subjects should continue only when the IRB finds an overriding safety concern or ethical issue involved such that it is in the best interest of individual subjects; new enrollment may not occur. The PI will be notified via Cayuse HE of approval expiration and conditions regarding human subject activities. Such expiration of approval (failure of annual reapproval) is not reported to OHRP as a suspension of approval under DHHS regulations; however, the study is subject to a noncompliance determination by the IRB. If the noncompliance is not resolved accordingly, the study may be subject to additional IRB determinations and actions, including administrative closure.

Renewal submissions with minor stipulations

If a *Renewal* submission receives a *Minor stipulations* decision, activities related to the stipulations (provided in the IRB determination letter) must temporarily stop until subsequent IRB approval is obtained. For example:

- When a stipulation requires that an individual renew expired CITI coursework or complete other education, the individual must not engage in any human research activities until OEQCR certification is submitted and approved by the IRB.
- When a stipulation requires updates to a consent form, new enrollment must halt until the revised consent form submitted and approved by the IRB.

A study will appear expired in Cayuse HE if IRB approval is not provided prior to the study's expiration date. If IRB approval expires for a study with a *Renewal* submission that has received a *Minor stipulations* decision, human research activities may continue except for those related to the stipulations. Once all issues related to an IRB decision of *Minor stipulations*, *Return to PI*, or *Deferral* have been resolved, the submission will receive the decision: Approved and an IRB approval letter will be generated to complete the submission.

Administrative check-in

For research initially approved by expedited review where continuing review is NOT required or research determined to be exempt, an administrative check-in is required at the following frequency:

- For research where a student, resident, or fellow serve as PI, administrative check-in is required 1 year from the initial approval every 1 year thereafter
- For all other research, administrative check-in is required 3 years from the initial approval every 3 years thereafter

Administrative check-in submissions will be reviewed and processed by HRPO staff.

251 Incidents/New information

PURPOSE

Regulations require an institution to establish and follow written procedures for ensuring prompt reporting and review of information that represents unanticipated problems involving risk to subjects or others (UPIRTSO), serious or continuing non-compliance, and suspensions and terminations of IRB approval to ensure the rights and welfare of research participants are protected. This SOP describes the general review procedure for promptly reportable incidents/new information to the Hennepin Healthcare IRB.

PROCEDURE

HRPO staff will assign reviewer(s) in Cayuse Human Ethics (HE) to conduct review of all *Incident* submissions that meet reportable criteria in accordance with HRPO SOPs and reviewer worksheets. All HRPO SOPs and reviewer worksheets are electronically available.

Researchers report incidents/new information via an *Incident* submission in Cayuse HE. HRPO provides guidance documents that outline reporting criteria and timelines.

The HRPO Director or designee will assign the level of review (e.g., expedited, convened IRB) for an *Incident* submission in accordance with the 504 MANUAL *IRB Analyst pre-reviews*.

Expedited review

The designated reviewer determines whether there is a need for additional information from the investigator or additional expertise in review. The reviewer may contact the investigator via Cayuse HE or request consultant(s) expertise, as necessary.

Convened IRB review

IRB reviewers determine whether there is a need for additional information from the investigator or additional expertise in review. The assigned reviewer may contact the investigator via Cayuse HE or request consultant(s) expertise, as necessary.

For *Incident* submissions reviewed by the convened IRB, the Principal Investigator may be asked to attend and provide relevant information for discussion.

After discussion of an *Incident* submission, the convened IRB will vote on an IRB action. Possible actions will include, but are not limited to, the following:

- Determination of UPIRTSO;
- Determination of serious and/or continuing non-compliance;
- Suspend;
- Refer the matter to the IRB Chair;
- Refer the matter to the IRB for discussion and further action; and/or
- Notify current subjects of new information (required when new information might relate to willingness to continue to participate)
- Other actions may include, but not limited to, the following:
- Modify the protocol;
- Modify the consent;
- Provide additional information to past subjects;
- Require current subjects to re-consent to participate;
- Modify continuing review assignment;
- IRB member or designee to monitor the research;
- IRB member or designee to monitor the consent process; and/or
- Request additional information
- Provide additional information to investigators
- Required additional education/re-education of investigators and/or research support personnel
- Request a discretionary audit(s)

External IRB reliance

Incidents/information that meet reportable criteria for studies relying on external IRB as determined by HRPO staff, will be administratively reviewed, and triaged to the IRB Chair and other reviewers, if applicable, as identified in the 711 WORKSHEET Reliance review.

252 Modifications to previously approved research

PURPOSE

This SOP describes the review of proposed changes to previously approved human research – modification submissions – prior to implementation to ensure that the modification to the research continues to meet the criteria for approval.

PROCEDURE

Submission of modifications

Researchers conducting human subject research approved by the Hennepin Healthcare IRB are required to submit proposed changes in approved research, including planned protocol exception requests, for review and approval prior to initiation of the change except where necessary to eliminate apparent immediate hazards to subject(s). Researchers submit all requests for modification(s) to previously approved research via the electronic IRB management system, Cayuse Human Ethics (HE).

The following steps are taken to ensure that modifications to previously approved research will not be initiated without IRB review and approval (except when necessary to eliminate apparent immediate harm to the subject):

- Researcher and research team training by the Office for Education and Quality in Clinical Research (OEQCR)
- Guidance available in the 501 Manual, HRPO website and Cayuse HE
- Specific directives included in approval letters
- Post-approval reviews

Review via expedited procedure

The expedited review procedure may be used to review minor modifications in previously approved research during the period (of one year or less) for which approval is authorized.

Minor modifications are modifications that do not adversely affect the overall assessment of the risks and benefits of the research and do not substantially change the specific aims/design of the research. A modification cannot be deemed minor if it involves the addition of procedures that involve more than minimal risk or that do not fall into federal categories (1) – (7) of research that can be reviewed by expedited procedures.

Modifications (minor changes) to previously approved research will be subject to the expedited review process in accordance with HRPO SOPs before the modification can be implemented.

The reviewer(s) may exercise all authority of the IRB except that the reviewer(s) may not disapprove modifications. A modification to a research protocol may be disapproved only after review in accordance with the convened IRB review procedure.

All IRB members are advised of modifications to previously approved research that have been approved under the expedited procedure through a monthly report of expedited actions.

Addition of a relying institution for a single IRB study relying on the Hennepin Healthcare IRB may be reviewed via expedited procedures, with limited exceptions.

Review via convened IRB

When a proposed modification is not minor, the modification request will be reviewed and approved via convened IRB review in accordance with HRPO SOPs before the modification can be implemented.

Considerations for approval

During modification review, the IRB determines whether the research with the proposed changes continues to meet the regulatory criteria for approval and any other applicable requirements are met.

Modifications to exempt studies are evaluated to determine whether changes alter the original exempt determination.

Reviews and applicable determinations are made using the Reviewer worksheet(s).

Modifications to previously approved research that were initiated without IRB review and approval to eliminate apparent immediate hazards to the subject(s) must be promptly reported to the IRB in accordance with the Hennepin Healthcare requirements for promptly reportable information and will be reviewed, in accordance with HRPO SOPs, by the expedited review procedure or convened IRB to ensure the continued welfare of subject(s).

253 Noncompliance

PURPOSE

The Hennepin Healthcare HRPP mission includes enforcing the requirement to promptly investigate allegations of noncompliance and determine (1) whether each allegation of noncompliance has a basis in fact; (2) whether it is serious and/or continuing; (3) the management of the serious or continuing noncompliance; and (4) report such noncompliance to the appropriate institutional officials and required regulatory authorities. These procedures apply to all research activities subject to the jurisdiction of the Hennepin Healthcare IRB/HRPP.

PROCEDURE

For definitions (e.g., Continuing noncompliance, Noncompliance, Serious noncompliance), see 501 MANUAL Conducting Human Research - GLOSSARY

Reporting noncompliance

The following are required to report an allegation of noncompliance:

- HRPP personnel and IRB board members
- Investigator(s)
- Research support personnel

Anyone may report an allegation of noncompliance.

An allegation of noncompliance may be reported in the IRB electronic management system, Cayuse Human Ethics (HE), directly to HRPP personnel, or through the Hennepin Healthcare System Compliance Hotline (1-800-609-9773) or Compliance Reporting Website. All information that supports the allegation will be reported by verbal or written communication or in Cayuse HE. An allegation of noncompliance may be reported anonymously through the website or the hotline.

The timeframe of reporting noncompliance should be in accordance with HRPO requirements described in HRPO guidance

Research under the oversight of an external IRB will be reported to the external IRB in accordance with the external IRB reporting policy and in accordance with HRPO 113 Guidance on ongoing reporting when relying on an external IRB.

Review of noncompliance submissions

Allegations of noncompliance will be reviewed by the IRB Chair or HRPO Director (or designee) and level of review determined and assigned. IRB review of and determination of noncompliance will be made in accordance with HRPO 251 SOP.

Noncompliance allegations and supporting documentation will be reviewed by at least one of the following:

- IRB Chair
- HRPO Director or designee
- Convened IRB

When a noncompliance report/allegation is submitted via Cayuse HE, it will be available to the IRB Chair, HRPO Director (or designee), and/or the convened IRB, as appropriate, for review. For noncompliance that is not submitted via Cayuse HE, all documents and information gathered as a part of the investigation will be distributed electronically to reviewer(s), including the IRB, if involved in the review process. The following materials will be reviewed, as applicable, including, but not limited to:

- Description of the event(s) that precipitated the report of allegation of noncompliance
- Current protocol
- Current consent
- Continuing review report(s)
- Serious adverse event reports
- Drug/device accountability reports
- Post-approval review/Audit report(s)
- Communications with principal investigator or other personnel

The reviewing entity:

- May request additional information, tailored to the nature of the allegation.
- Will after initial review, determine whether the allegation has no basis in fact, in which case it will record its decision and take no further action.
- Will after initial review, determine whether the allegation has basis in fact and if so, whether it is serious and/or continuing.

After initial review, if it is determined that the allegation has a basis in fact:

- The IRB Chair may in his or her discretion:
  (1) Suspend approval of the research pending further investigation;
  (2) Authorize a discretionary audit;
  (3) Refer the matter to the IRB for discussion and further action;
  (4) Notify the department chair; and/or
  (5) Notify the Hennepin Healthcare Institutional Official.
- The HRPO Director may in his or her discretion:
  (1) Refer the matter to the IRB Chair; and/or
  (2) Refer the matter to the convened IRB for discussion and further action.
- The convened IRB may in its discretion:
  (1) Suspend approval of the research pending further investigation
  (2) Authorize a discretionary audit; and/or
  (3) Terminate approval of the research.

If at any point during review/investigation, it is determined that the allegation cannot be investigated adequately, the allegation will be referred to the Hennepin Healthcare Institutional Official.

If at any point during review/investigation, it reasonably appears that serious and/or continuing noncompliance is likely and/or that study subjects are at risk if the protocol were to continue, the IRB Chair may suspend, or the convened IRB may suspend or terminate approval of the research.

If at any point during review/investigation it is determined that the noncompliance is serious and/or continuing:

- The principal investigator will receive notification via Cayuse HE of the concerns and requested to respond in writing to each of the concerns within 10 working days of notification. A shorter time period may be imposed based on the degree of risk to subjects. Investigation of such research will be tailored to the nature of the problem.
- The principal investigator's response will be reviewed by the reviewing entity and the principal investigator may be asked to answer questions in-person.
- At the conclusion of the investigation of such research:

The IRB Chair and the IRB has the authority to suspend or terminate approval of research that is reasonably believed to be involved with serious and/or continuing noncompliance.

The IRB will act on any finding of serious and/or continuing noncompliance. Outcomes may include, but are not limited to the following:

- If study subjects are at risk if the research were to continue, the IRB may:
  (i) Suspend approval of the research; or
  (ii) Terminate approval of the research;
- Notify current subjects (required when such information might relate to their willingness to continue participation);
- Require modification(s) to the protocol and consent;
- Require re-consent of subjects;

- Provide additional information to past subjects;
- Monitor the research;
- Monitor the consent process;
- Modify the continuing review schedule;
- Require additional education or training for investigator and research support personnel;
- Restrict use of data collected under the protocol;
- Withdraw or limit the privileges of the investigator to conduct further human research;
- Refer finding to other officials within the institution, as applicable;
- No further action.

Documentation and communication of actions

The review and any action taken by the IRB Chair, HRPO Director, and/or convened IRB will be documented in the Cayuse HE study record and, as applicable, meeting minutes.

For a determination of serious and/or continuing noncompliance, the findings and outcome (including modifications and/or corrective actions) of the investigation will be entered into Cayuse HE promptly to generate a notification to the principal investigator of the IRB determination.

HRPO will communicate suspension or termination of IRB approval in accordance with HRPO SOPs.

IRB communication of a finding of serious and/or continuing noncompliance, UPIRTSO, suspension, or termination of research to the PI's department head and other institutional stakeholders, and external entities, as appropriate, will be conducted in accordance with HRPO SOPs and institutional requirements and obligations. The Institutional Official will promptly notify (no longer than 30 days from IRB determination of serious and/or continuing noncompliance, UPIRTSO, suspension, or termination of research) the required regulatory authorities and sponsor/grantor and conform with any special program reporting.

For research relying on an external IRB, the terms of the reliance agreement will guide reporting responsibilities.

254 UPIRTSOs

PURPOSE

The Hennepin Healthcare IRB is responsible for determining whether an event meets the definition of an unanticipated problem involving risks to subjects or others (UPIRTSO) and for reporting according to the SOP *Institutional reporting of non-compliance, UPIRTSOs, suspensions and termination*. This SOP describes UPIRTSO reporting and review.

PROCEDURE

For definitions (e.g., Serious Adverse Event, UPIRTSO), see 501 MANUAL Conducting Human Research - GLOSSARY

Reporting UPIRTSOs

For research under the review and oversight of the Hennepin Healthcare IRB, researchers are required to report unanticipated problems via the electronic IRB system, Cayuse HE, in accordance with HRPO 133 GUIDANCE.

For research under the review and oversight of an external IRB, researchers are required to report UPIRTSOs in accordance with reporting requirements of the external IRB and HRPO 113 Guidance.

The reporting requirements for UPIRTSOs apply if it occurs during the conduct of the study, after subject withdrawal or completion, or after study completion.

Review of UPIRTSO submissions

All UPIRTSOs submitted to HRPO will be reviewed by the IRB Chair or HRPO Director (or designee), and level of review determined and assigned. IRB review of and determination of a UPIRTSO will be made in accordance with HRPO 251 SOP.

UPIRTSO submissions will be reviewed by at least one of the following:

- IRB Chair
- HRPO Director or designee
- Convened IRB

Reviewers will have access to all submission materials for review via Cayuse HE. If at any point during review, additional information is needed, the investigator will be contacted to provide the requested information. If at any point during review, additional expertise is needed, a consultant shall be contacted for his or her input.

If at any point during review, it reasonably appears that study subjects are at increased risk if the protocol were to continue:

- The IRB Chair may in his or her discretion:
  (1) Suspend approval of the research pending further investigation; and/or
  (2) Refer the matter to the convened IRB for discussion and further action.
- The IRB HRPO Director may in his or her discretion:
  (1) Refer the matter to the IRB Chair; and/or
  (2) Refer the matter to the convened IRB for discussion and further action.
- The IRB may in its discretion;
  (1) Suspend approval of the research;
  (2) Terminate approval of the research.
  (3) Require notification of current subjects of new information (required when new information might relate to willingness to continue to participate)
  (4) Other actions include those described in section 3 of the 713 Worksheet.

Documentation and communication of actions

IRB review and determination will be documented in the Cayuse HE submission record, and, as applicable, in the convened IRB meeting minutes.

For a determination of UPIRTSO, the findings and outcome (including modifications and/or corrective actions) of the investigation will be entered into Cayuse HE promptly to generate a notification to the principal investigator of the IRB determination. The maximum time allowed between the submission of a UPIRTSO and notification to the PI is 30 calendar days.

The IRB determination letter will specify required changes, suspension, or termination of the research, as applicable.

If the IRB determination is suspension or termination, the process for requesting reconsideration will be provided in accordance with HRPO SOPs.

IRB communication of a finding of serious and/or continuing non-compliance, UPIRTSO, suspension, or termination of research to the PI's department head and other institutional stakeholders, and external entities, as appropriate, will be conducted in accordance with HRPO SOPs and institutional requirements and obligations. As required, the Institutional Official will promptly notify (typically within 30 days from IRB determination of serious and/or continuing noncompliance, UPIRTSO, suspension, or termination of research) the required regulatory authorities and sponsor/grantor and conform with any special program reporting.

For research relying on an external IRB, the terms of the reliance agreement will guide reporting responsibilities.

255 Participant complaints and concerns

PURPOSE

The Hennepin Healthcare HRPP is committed to the protection of research participants. Research participants are encouraged to express any concerns or complaints regarding the involvement in a research study. This SOP addresses how complaints, concerns and suggestions reported directly or indirectly to Hennepin Healthcare Institutional Review Board (IRB) are addressed.

PROCEDURE

All consent documents must contain contact information for participants to call to voice concerns or complaints.

Consent documents must include the investigator's contact information for any questions, complaints and/or concerns the participant or legal representative may have about the research or related matters.

Consent documents must include contact information for HRPO for the reporting of questions, complaints and/or concerns. Information about how to report complaints or concerns is also provided on the HRPO website, along with a link to submit complaints, concerns, or questions via an online survey.

Responding to participant concerns or complaints

Concerns or complaints reported to HRPO will be documented and triaged as described below.

Concerns or complaints received by the investigator or other members of the study team must be timely addressed and resolved in a manner that protects the rights and welfare of the participant. In certain cases, participant complaints must also be reported to the IRB via an Incident submission in Cayuse HE in accordance with the 113 *Notifications to HRPO for ceded studies* or 133 GUIDANCE *New information/Incident reporting*.

Complaints submitted via an Incident submission in Cayuse HE will be processed in accordance with HRPO *251 SOP Incident-new information review*.

Triaging participant concerns or complaints

Concerns or complaints that are reported to HRPO by the complainant directly or forwarded from a complaint received by another entity (other than the PI) will be documented in a database maintained by OEQCR.

The HRPO Director or designee will attempt to find a suitable resolution and response to the complaint or concern in a timely manner. As necessary and appropriate, complaints may be brought to the IRB Chair, other HRPP leadership, Principal Investigator, or other party for discussion and recommendation of resolution.

Documentation of resolution of the concern or complaints will be entered into the OEQCR database.

If the concern or complaint involves possible non-compliance or unanticipated problem, the complaint will be handled according to 253 SOP Non-compliance or 254 SOP UPIRTSOs.

256 Research Involving prisoners

PURPOSE

This SOP describes specific human research requirements that are required for research involving prisoners.

PROCEDURE

For definitions (e.g., *Prisoner*, *Minimal risk (research involving prisoners)*, see 501 MANUAL Conducting Human Research - GLOSSARY

Federally funded research involving prisoners will be reviewed and approved in accordance with the requirements of 45 CFR 46 Subpart C.

For non-federally funded research involving prisoners, the Hennepin Healthcare IRB will apply equivalent protections. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46, Subpart C will be applied to the greatest extent possible in consideration of the nature of the research.

Hennepin Healthcare is "engaged" in research involving prisoners when both of the following circumstances apply:

- The Hennepin Healthcare investigator obtains data through intervention or interaction with a prisoner, or identifiable private information about a prisoner; AND
- The Hennepin Healthcare investigator knows that one or more of the data subjects includes a person whose circumstances meet the regulatory definition of "prisoner" under 45 CFR 46.303(c).

In addition, Hennepin Healthcare is engaged in research involving prisoners if Hennepin Healthcare is the primary awardee of DHHS funds to conduct prisoner research, even where all activities involving prisoner subjects are carried out by another institution.

IRB submission

For research proposing to enroll prisoners, the study team completes the IRB application and provides protocol-specific information related to research with prisoners. When research is conducted in detention or correctional facilities, the IRB submission must also include documentation of approval or permission to conduct the research from the facilities involved in the research.

IRB review

For all research involving prisoners, an IRB member who qualifies as a prisoner representative must be present at the convened meeting of the IRB and during the presentation, discussion, and vote of any study which involves prisoners. A majority of the IRB members (exclusive of prisoner members) must have no association with the prison involved, apart from their membership on the IRBs.

The prisoner representative:

- Must be a voting member of the IRB. (This individual may be listed as an alternative member who becomes a voting member when needed).
- Must review research involving prisoners, focusing on the requirements in Subpart C or equivalent protections. The prisoner representative must receive all review materials pertaining to the research (same as primary reviewer).
- Must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved. Attendance may be by phone, video-conference, or webinar, as long as the representative is able to participate in the meeting.
- Must present their review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.

The Hennepin Healthcare IRB must make the required determinations when reviewing an application involving prisoner research and will use the 732 WORKSHEET Research involving prisoners (Subpart C) to document the determinations required by the regulations along with protocol specific findings justifying those determinations.

Continuing review must occur using the same procedures for initial review, including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above). (If no subjects have been enrolled, the research may receive continuing review using the expedited procedure under expedited category #8).

Modifications involving more than a minor change reviewed by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).

Minor modifications to research involving prisoners may be reviewed using the expedited procedures described below, based on the type of modification.

Research involving prisoners may not receive exempt review.

Review by expedited procedures

Research **involving interaction** with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied. If expedited review is used for research involving interaction with prisoners, the prisoner representative on the IRB must be one of the designated reviewers and must concur with the determination that the research involves no greater than minimal risk. The review will be conducted in accordance with 45 CFR 46 Subpart C and HRPO SOPs and Worksheets and documented in the Cayuse HE submission record.

Review of modifications and continuing review must use the same procedures for initial review using this expedited procedure including the responsibility of the prisoner representative.

Research that **does not involve interaction** with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied. If expedited review is used for research involving prisoners with no interaction (e.g., existing data, record review), the prisoner representative on the IRB is not required to be a reviewer. The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair.

Review of modifications and continuing review must use the same procedures as initial review.

OHRP Certification for DHHS funded or supported research

After the IRB completes its review and issues approval, the PI must certify to the Secretary of Health and Human Services (through OHRP) that the IRB has made the findings required under 45 CFR 46.305(a), including the finding that the proposed research represents one of the permissible categories of research under 45 CFR 46.306(a)(2). The PI is responsible to submit a completed Subpart C Certification Form to OHRP. Following OHRP's review of the certification, if OHRP determines that the research involves one of the permissible categories, OHRP will send a letter authorizing the involvement of prisoners in the proposed research. Once OHRP has determined that the proposed research falls within the categories of research permissible for involvement of prisoners, the PI must submit documentation to the IRB via a *Modification* submission (in Cayuse HE). If OHRP determines that the proposed research does not involve one of the permissible categories, it will state in the letter to the institution that such research involving prisoners cannot proceed.

The PI notifies HRPO upon receipt of the OHRP completed review of the Subpart C Certification via a *Modification* submission in Cayuse HE.

The PI may not initiate research involving prisoners until the certification process is complete authorizing the involvement of prisoners in the proposed research.

When a participant becomes a prisoner while enrolled in a study not approved to enroll prisoners

For studies originally reviewed and approved by the IRB without prisoners as participants, if the study team learns that a participant has become a prisoner during the study, all research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-participant must cease.[4]

The study team must submit an *Incident* submission to inform the Hennepin Healthcare IRB of the individual's change in status. The *Incident* submission will include:

- Current status of the participant's involvement in study activities.
- Length of incarceration (if known) and whether the individual's incarceration is expected to be temporary.
- Whether the participant is receiving a research intervention for which cessation due to incarceration may imperil the participant's health.
- If it is in the subject's best interests to continue on the study as a prisoner.
- Plan for continuation or cessation of study activities involving the participant.

[4] OHRP allows one important exception: In special circumstances in which the principal investigator asserts that it is in the best interests of the participant to remain in the research project while incarcerated, the IRB Chair may determine that the subject may continue to participate in the research until the requirements of Subpart C are satisfied.

The Hennepin Healthcare IRB must make the final determination whether the subject may continue as a participant in a research study that was not previously reviewed by the IRB according to Subpart C. IRB approval for inclusion of prisoners is not required if research procedures will not occur during the incarceration period.

When Subpart C applies, the IRB will:

- Confirm that the incarcerated subject meets the definition of a prisoner.
- Terminate enrollment of the incarcerated subject or review the research study under Subpart C if it is feasible for the incarcerated subject to remain in the study.
- Before terminating the enrollment of the incarcerated subject, the IRB should consider the risks associated with terminating participation in the study.
- If the incarcerated subject cannot be terminated for health or safety reasons, the IRB will provide a determination, i.e.:
    - Keep the subject enrolled in the study and review the research under Subpart C. If some of the requirements of Subpart C cannot be met, but it is in the best interests of the subject to remain in the study, keep the subject enrolled and inform OHRP of the decision along with the justification for doing so.
    - Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use, off-label use, etc.

When Subpart C does not apply, the IRB will provide equivalent protections by:

- Confirming that the subject meets the definition of a prisoner.
- Deciding whether it is in the best interests of the incarcerated subject to remain in the study or to terminate enrollment.
- Also deciding whether it is feasible for the subject to remain in the study.
- If it is in the best interests of the subject to remain in the study, keep the subject in the study and review the research at next meeting of the convened IRB.

If a subject is incarcerated temporarily while enrolled in a study, the IRB will determine the following:

- If the temporary incarceration has no effect on the study, keep the subject enrolled.
- If the temporary incarceration has an effect on the study, the IRB will review the involvement of the prisoner under the above criteria for an individual who becomes a prisoner while enrolled in a research study.

Planned emergency research

Waiver of informed consent in certain emergency research is not applicable to research involving prisoners (61 FR 51531, October 2, 1996).

Multisite research

Hennepin Healthcare does not serve as sIRB for research involving prisoners.

Research involving prisoners that is under the oversight of an external IRB must comply with the requirements of that IRB and applicable policies and law.

Research subject to Department of Defense (DoD) regulations

See 281 SOP Department of Defense-sponsored research

Research subject to Department of Justice (DoJ) regulations

See 282 SOP Department of Justice-sponsored research

See also: 501 MANUAL Conducting Human Research **Section 7.3.** ***Research involving prisoners***

260 Compliance activities

PURPOSE

The Hennepin Healthcare HRPP will conduct post-approval audits in support of their mission to ensure compliance with federal, state, and institutional regulations and guidelines governing human subject research. and to promote quality in research. This standard operating procedure (SOP) describes HRPP compliance activities.

PROCEDURE

Post-approval audits

Post-approval audits will be conducted under the auspices of the Office of Education & Quality in Clinical Research (OEQCR) in accordance with OEQCR SOPs (refer to 20 OEQCR Compliance SOP Post-Approval Audits). Copies of audit results and any follow-up letters sent to principal investigators and written responses will be forwarded to HRPO.

For studies relying on an external IRB, communication to the OEQCR about requested for-cause audits or other issues from an external IRB will be sent to: EQ@hhrinstitute.org and the OEQCR Director. Audit reports will be forwarded to the IRB Reliance Manager (IRBreliance@hhrinstitute.org) for reporting to the external IRB in accordance with the reliance agreement governing the research.

Not-for-cause audits

OEQCR will conduct not for cause audits in accordance with its SOPs

OECQR will notify HRPO of the outcome of not for cause audits in accordance with its SOPs

OECQR will communicate to the investigator the obligation to separately submit an Incident in Cayuse HE for such findings that meet the promptly reportable requirements in HRPO 133 GUIDANCE. In the case of studies relying on an external IRB, audit reports will be forwarded to HRPO and HRPO will report to the external IRB in accordance with the reliance agreement governing the research.

For cause audits: investigations of complaints, potential noncompliance, and potential undue harm to subjects

HRPP may initiate a for-cause audit if there is a reasonable indication that conduct of research involves potential serious or continuing non-compliance, potential undue harm to subjects, or other negative impact on the safety and welfare of human subjects. Examples include, but are not limited to, the following:

- Research conducted by an investigator who previously failed to comply with federal, state, or institutional regulations
- Research where information suggests that possible material changes occurred without approval
- Research with significant protocol violations reported
- Research with serious adverse events (SAEs) of major concern or a large number of SAEs reported
- Research with complaints or reports suggesting non-compliance from subjects, research support personnel, or other source
- Research relying on an external IRB where the external IRB requests Hennepin Healthcare conduct a for-cause audit, in accordance with the reliance agreement

The process of investigating complaints, potential non-compliance, and potential undue harm to subjects includes the following:

- The complaint, report, and/or information will be triaged by the IRB Chair or designee, and he/she will assign the reviewing entity. All supporting information will be reviewed by at least one of the following:

  (1) IRB Chair or designee

  (2) Convened IRB

- After initial review:

(1) The IRB Chair may suspend approval of the research pending further investigation;

(2) The designee may refer the matter to the Chair;

(3) The matter may be referred to the convened IRB for discussion and further action; and/or

(4) The IRB Chair, designee, or convened IRB may authorize a for-cause audit.

(a) An audit team will be activated and the audit will proceed in the same manner as for post-approval reviews under the auspices of OEQCR and/or an ad hoc audit team drawing on resources appropriate to the particular problem will be constructed, activated, and will proceed in a manner appropriate to the particular problem.

(b) Inclusion of a consultant with the audit team may be requested.

- The for-cause audit process will include the following:

(1) The IRB Chair or designee will contact the principal investigator at an appropriate point and inform him/her of the for-cause audit. An auditor will follow up with written notification with specific details.

(2) For-cause audits will be scheduled as soon as possible.

(3) Unless directed otherwise by the IRB Chair or designee, the audit date will be set at the first agreeable date between the principal investigator and auditor(s).

(4) Study subject records will be reviewed based on the complaint. This may include only specified subjects, a random sample of subjects, or all consented subjects.

(5) An OEQCR audit questionnaire may be used.

(6) HRPP 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.

(7) Post-audit procedures will include the following:

(a) A post-audit summary will be reviewed/discussed with the IRB Chair and/or designee. This summary will include the findings and outcome of the audit as well as any recommendations or requirements.

(b) HRPP will provide written communication to the principal investigator summarizing the findings and outcome of the audit as well as any recommendations or requirements that must be met. This may include, but not limited to, a follow-up audit to reexamine deficits identified for corrective action, suspension, and/or review by the convened IRB,

(c) The principal investigator will have two weeks to provide to HRPP a corrective action plan, as needed.

(d) The IRB Chair and/or designee will review the corrective action plan and decide if further review and actions are required.

(e) Audit documentation will be added to the study record in Cayuse HE and available for convened IRB review.

(8) In the case of a for-cause audit requested by an external IRB, the OEQCR will coordinate with HRPO to ensure the external IRB has (a) communicated the expected timing of the audit and required completion date; (b) communicated what information and source documents should be reviewed, and (c) how the audit observations should be communicated back to the external IRB, including whether a standard report template should be used.

Assessment of compliance

The IRB Chair or designee will review all post-approval review and audit findings and assess compliance patterns across human subject research. Findings of potential noncompliance will be investigated in accordance with HRPO SOPs.

When a pattern is identified that needs to be rectified, solutions will be generated by the IRB Chair, and any other appropriate personnel to increase compliance. Such solutions may include, but are not limited to, the following:

- Additional education requirements for investigators and/or research support personnel
- Provision of additional resources to conduct the study
- Re-audit of the study demonstrating compliance issues on initial audit at a later time
- Additional audits for studies of the same principal investigator to assess compliance issues on initial audit

261 Suspensions and terminations

It is the purpose of the Hennepin Healthcare Institutional Review Board (IRB) to review and oversee research involving human subjects to protect the rights of study subjects and ensure compliance with federal, state, and institutional regulations and guidelines governing human research. Consistent with federal regulations, the Hennepin Healthcare IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with regulations, the requirements or determinations of the Hennepin Healthcare IRB or that has been associated with unexpected serious harm to subjects. This SOP describes suspension and termination of IRB approved research.

PROCEDURE

For definitions (e.g., *Suspension of IRB approval*, *Termination of IRB approval*), see 501 MANUAL Conducting Human Research - GLOSSARY

Criteria for suspension and/or termination of approval

Approval of research may be suspended or terminated when:

- The research is not being conducted in accordance with IRB approval requirements.
- The research has been associated with unexpected serious harm to subjects.
- There is new information that may have an effect on the rights and welfare of subjects.

Authorization of suspension and/or termination of approval

The following are authorized to suspend approval of research on a non-urgent or urgent basis, subject to notification and review as delineated:

- IRB Chair
- HRPO Director (or designee)
- Convened IRB

The following is authorized to terminate approval of research on a non-urgent or urgent basis, subject to notification and review as delineated:

- Convened IRB

Considerations of suspension and/or termination of approval

When approval is suspended or terminated, the IRB Chair, HRPO Director, or Convened IRB will consider actions to protect the rights and welfare of currently enrolled subjects and determine whether any of the following actions are required:

- Subjects currently on active treatment must be withdrawn from the study and whether those procedures take into account the rights and welfare of the subjects and may require additional actions such as:
  (1) Making arrangements for clinical care outside of the research
  (2) Transferring subjects to an investigator at another research site
  (3) Allowing continuation of some research activities under the supervision of an independent monitor
- Subjects must be informed of the suspension or termination and if so, the procedure for informing the subjects
- Follow-up of subjects for safety reasons
- Review any reports of new information submitted by researchers

Documentation and communication of actions

Any review or action taken by the IRB Chair or HRPO Director will be documented in the study record in the electronic IRB management system (Cayuse HE) and reported to the IRB at the next convened meeting.

Any review or action taken by the Convened IRB will be documented in the meeting minutes.

Any suspension or termination of approval will be promptly communicated to the principal investigator in writing along with the reason for the action and include, as applicable:

- Any requirement(s) associated with the suspension or termination (e.g., notification to subjects)
- Any requirements that is/are required in order for the IRB to reinstate approval (in the case of suspension)

Any options to request reconsideration of suspension or termination of IRB approval will be promptly reported to the Institutional Official and regulatory authorities in accordance with the HRPO 262 SOP *Institutional reporting of non-compliance, UPIRTSOs, suspensions and termination.*

262 Institutional reporting of non-compliance, UPIRTSOs, suspensions, and terminations

PURPOSE

The Hennepin Healthcare Human Research Protection Program (HRPP) mission includes enforcing the requirement to promptly report (1) serious and/or continuing non-compliance, (2) unanticipated problems involving risks to subjects or others, and (3) suspensions or terminations of previously approved research to officials and regulatory agencies, and other oversight agencies as appropriate. This SOP describes the reporting process for institutional reporting to oversight agencies.

PROCEDURE

Federal mandatory regulatory reporting references:

https://www.hhs.gov/ohrp/compliance-and-reporting/guidance-on-reporting-incident/index.html

https://www.fda.gov/science-research/report-problems-fda/mandatory-irb-reporting-fda-contacts

Circumstances that require reporting outside the institution

- An IRB determination of serious or continuing non-compliance
- An IRB determination of an unanticipated problem involving risks to subjects or others (UPIRTSO)
- An IRB determination to suspend or terminate previously approved research

The report

The Hennepin Healthcare Institutional Official will draft and finalize the report. Other institutional reviewers, such as legal or compliance may be recommended by the Institutional Official (IO) and will occur, if applicable, prior to report finalization by the IO. The Hennepin Healthcare IO will submit the final report to required federal officials.

If the circumstance involves a suspension or other action pending further investigation, the report will be a preliminary notification and identified as such. Upon receiving the final findings and outcomes of the investigation, a final report will be promptly forwarded to the required regulatory authorities and sponsors/grantor.

Reporting is not required when federal agencies have already been notified through other mechanisms, such as reporting by the investigator, sponsor, or another organization. Hennepin Healthcare may supplement such reporting when deemed appropriate by the Institutional Official.

For research relying on an external IRB, the terms of the reliance agreement will guide reporting responsibilities.

The contents of the report will include the following:

- The nature of the event
- The findings of the organization
- Actions taken by the IRB or institution
- Reasons for the IRB's or institution's actions

- Plans for continued investigation or action

The report will be promptly submitted to the following, as applicable:

- OHRP, when the research is covered by DHHS regulations
- FDA, when the research is FDA-regulated
- Department of Defense (DoD) Component Office of Human Research Protections (COHRP), within 30 days of the IRB's determination, if subject to DoD regulations.
- Other federal agencies when the research is overseen by those agencies, and they require reporting separated from that to OHRP

Copies of the report will be distributed as follows:

- Applicable research industry sponsor or grantor/funder
- Other sites involved in the research, when appropriate
- Principle investigator, when appropriate
- HRPO
- Office for Education & Quality in Clinical Research (EQ) Director
- Others as deemed appropriate by the Institutional Official, such as:
    - Physician Chief or supervisor of the investigator
    - Privacy Officer, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from a covered entity
    - Information Security Officer, if the event involved violations of information security requirements of that organization

The HRPO Director and IO will establish reporting compliance within 30 working days of the determination.

Circumstances requiring reporting to AAHRPP

When members of the Hennepin Healthcare HRPP become aware of any of the following, the Association for the Accreditation of Human Research Protection Program (AAHRPP) must be notified as soon as possible, but not later than 48 hours after becoming aware:

- Any negative actions by a government oversight office, including OHRP determinations, FDA Warning Letters, FDA 483 Inspection
- Reports with official action indicated, FDA Restrictions placed on IRBs or investigators, and corresponding actions taken under non-US authorities related to human research protections
- Any litigation, arbitration, or settlements initiated related to human research protections
- Any external press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the HRPP.

270 Communication of actions

PURPOSE

This SOP describes how the Hennepin Healthcare Human Research Protection Office (HRPO) communicates IRB actions related to the protection of human subjects and compliance with federal, state, and institutional regulations and guidelines governing human subject research.

PROCEDURE

Human Research Protection Office (HRPO) will generate monthly IRB reports for distribution as follows:

- The Hennepin Healthcare Vice President of Medical Affairs and HHRI Institutional Official will receive IRB meeting minutes
- Reports may be distributed to other Hennepin Healthcare individuals, upon request

HRPO will manage and monitor all communication to Principal Investigators regarding status for all submission types in the IRB electronic management system, Cayuse Human Ethics (HE). Communications in Cayuse HE include:

- System-wide messages
- Meeting messages
- IRB analyst messages
- IRB reviewer messages
- Notification of submission receipt
- Notification of return to PI
- Notification of IRB exemption
- Notification of IRB approval
- Notification of IRB approval with minor stipulations letters
- Notification of IRB deferral
- Notification of IRB disapproval
- Notification of UPIRTSO
- Notification of serious or continuing noncompliance
- Notification of IRB suspension
- Notification of IRB termination
- Notification of study approval expiring
- Notification of study approval expired
- Notification of study withdrawal
- Notification of study closure
- Notification of no further action

271 Request for reconsideration of IRB actions

PURPOSE

This SOP describes the process established by HRPP for investigators to request reconsideration of IRB actions.

PROCEDURE

The principal investigator has the right to request reconsideration of an IRB action to disapprove an initial submission or to suspend or terminate IRB approval of research involving human subjects.

The PI must submit a written request for reconsideration that provides sufficient justification within 10 working days of receiving the notice of IRB action and, in addition, may request an opportunity to appear before the IRB to discuss the reasons for disapproval, suspension, or termination.

The IRB Chair will review the request and may do one of the following:

- Create an ad hoc subcommittee to evaluate the request and make a recommendation to the IRB or
- Have the IRB evaluate the request.

The IRB will vote on the request for reconsideration.

281 Department of Defense-sponsored research

PURPOSE

This SOP describes specific human research requirements that are required for Department of Defense (DoD)-sponsored research.

PROCEDURE

Hennepin Healthcare does not conduct the following research:

- Human participant research involving the testing or chemical or biological agents, including research for prophylactic, protective, or other peaceful purposes involving chemical or biological agents.

- Classified research as defined in DoDI 3216.02, Section 3.13.
- Research that intentionally involves DoD personnel

DoD regulations and requirements

For research that is supported or conducted by the Department of Defense (DoD):

Definitions

Minimal Risk (Part 219 of Title 32, CFR): The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests., This definition of minimal risk does not include the inherent occupational risks that certain subjects face in their everyday life, such as those: (1) Encountered by Service members, law enforcement, or first responders while on duty; (2) Resulting from or associated with high-risk behaviors or pursuits; or (3) Experienced by individuals whose medical conditions involve frequent tests or constant pain.

Research involving a human being as an experimental subject: An activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as an experimental subject is a subset of research involving human subjects.

Prisoner: As defined in 45 CFR 46 subpart C, but explicitly includes military personnel in either civilian or military custody or detainment.

Education

Initial and continuing research ethics education will be completed by all personnel who conduct, review, approve, oversee, support, or manage human subjects research in accordance with Hennepin Healthcare's HRPP policies.

Specific DoD educational requirements or certification may be required as determined and communicated through the terms and conditions of the sponsored awarding documents.

HRPP and research personnel will be notified of the requirements for DoD training by the HHRI Office for Grants & Contracts as determined and communicated through the terms and conditions of an award.

Scientific merit

For non-exempt research, the IRB will consider the scientific merit of the research. Consultants may be used to assist in the evaluation of scientific merit in accordance with HRPO SOPs.

Research monitor

A research monitor is not required. Researchers may remove the requirement for a research monitor from existing open studies through a modification approved by an IRB.

Conflict of interest

For research that has a reported conflict of interest, approval will not be granted until documentation of resolution from the HHRI Conflict of Interest Committee has been received and approved by the IRB in accordance with HRPO SOPs. The IRB will ensure that informed consent forms for applicable research include a disclosure of any remaining conflicts of interest if required to comply with the requirements of the DoD component as determined and communicated through the terms and conditions of the award.

Research-related injury

The HHRI Office of Grants and Contracts will confirm that the disclosure for research-related injury follows the requirements of the DoD component as determined and communicated through the terms and conditions of the award. These requirements will also be disclosed in the informed consent document.

Research involving US military personnel as research participants

When the research involves DoD-affiliated personnel, the following additional protections to minimize undue influence are required as determined and communicated through the terms and conditions of the award: DoD-affiliated personnel, military and civilian supervisors, officers, and others in the chain of command:

- Are prohibited from influencing their subordinates to participate in research involving human participants.
- Must not be present at any human participant recruitment sessions or during the consent process for any DoD-affiliated personnel.
- May participate in separate human participant research recruitment session.

For greater than minimal risk research involving DoD personnel, when recruitment and consent occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:

- Must not have a conflict of interest with the research or be a part of the research team.
- Must be present during human participant recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials.
- Should be available to address DoD-affiliated personnel's concerns about participation.

When research involves U.S. military personnel, the following limitations on dual compensation are required as determined and communicated through the terms and conditions of the award:

- An individual may not be compensated for research if the subject is involved in the research during duty hours.
- An individual may be compensated for research if the subject is involved in the research when not on duty.
- Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.
- Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

Research involving an *experimental subject*

When research involves "experimental subjects," the following will apply:

If consent is to be obtained from the experimental subject's legal representative, the research must intend to benefit the individual subject. The determination that research is intended to be beneficial to the individual experimental subject must be made by the IRB.

A waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering.

- The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:
  - The research is necessary to advance the development of a medical product for the Military Services.
  - The research may directly benefit the individual experimental subject.
  - The research is conducted in compliance with all other applicable laws and regulations.
- For classified research, waivers of consent are prohibited.

The IRB may waive or alter some elements of informed consent for research involving human beings as experimental subjects, so long as it preserves the informed consent of the participant (i.e., the consent indicates that participation in the research is voluntary and the participant/representative is informed of research risks). Such waiver or alteration of some elements of information consent will be made in accordance with HHRI SOPs and reviewer worksheets.

If the research subject does not meet the definition of "experimental subject," the IRB may waive the consent process in accordance with HRPO SOPs.

Research involving pregnant women, prisoners, and children

- When research involves pregnant women, prisoners, and children, it is subject to the DHHS Subparts B, C, and D:

- For purposes of applying Subpart B, the phrase "biomedical knowledge" will be replaced with "generalizable knowledge."
- The applicability of Subpart B is limited to research involving pregnant women as subjects in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involves fetuses or neonates as subjects.
- For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, written approval from the DOHRP must be obtained through the COHPR prior to research starting.
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
- Research involving children as human subjects must comply with Subpart D of Part 46 of Title 45.
- Research involving prisoner in addition to the allowable categories of research on prisoners in Subpart C, two additional categories are permissible (DoDI 312.02, section 3.9(c):

  - Epidemiological research is permitted when:

    ii. The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.

    iii. The research presents no more than minimal risk.

    iv. The research presents no more than an inconvenience to the subject.

    v. Prisoners are not a particular focus of the research.

  b. Human participant research involving prisoners that would otherwise meet exemption criteria may be conducted but must first be approved by an IRB and meet the requirements of Subpart C and DoDI 3216.02.

- When a previously enrolled subject becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C, the researcher must promptly notify the IRB and the DoD Office for Human Research Protections (DOHRP). The DOHRP must concur with the IRB before the research participant can continue to participant while a prisoner.
- Research involving a detainee or prisoner of war as a human subject is prohibited. (DoDI 3216.02 section 3.9 (g)). This prohibition does not apply to activities covered by investigational new drug or investigational device provisions of FDA regulations, when the purpose is for diagnosis or treatment of a medical condition in a patient. Such treatment may be offered to detainees or prisoners of war with their informed consent when the medical products are subject to FDA regulations, and only when the same product may be available to DoD-affiliated personnel consistent with established medical practices.

Planned emergency research

When conducting emergency medicine research, exception from consent in emergency medicine research is prohibited unless approval from the DOHRP on behalf of the Secretary of Defense for a waiver is obtained. HRPO will coordinate with the Office of Grants and Contract and the Principal Investigator to obtain and document approval of the waiver from the DoD Office for Human Research Protections (DOHRP)/ DoD Component Office of Human Research Protections (COHRP), as applicable.

Multisite research

When conducting multi-site research, a formal agreement between organizations will be established to specify the roles and responsibilities of each party consistent with the terms and conditions of the award.

Additional DoD review

After the IRB completes its review and issues approval, the PI submits documentation of IRB approval, the risk level, and the expiration date of the research to the DoD Component sponsoring or supporting the study. The DoD may also request additional documentation to verify compliance with federal and DoD policies, including minutes related to the research.

If the study involves surveys performed on DoD personnel, such surveys must typically be submitted, reviewed, and approved by the DoD. After the research protocol is reviewed and approved by the IRB in accordance with HRPO SOPs, the PI, with assistance from the Office of Grants and Contracts, identifies any requirements for an additional level of DoD review and submits the surveys and all required documentation relevant to the survey research review to the requesting DoD Component. This approval will be obtained by in accordance with the terms and conditions of the award.

If the study involves the following types of research, a DoD component-level administrative review (CLAR) must be conducted:

- The research requires a waiver of informed consent pursuant to 10 USC 980, Subsection (b).
- The research is required to be approved by the DOHRP (in addition to the COHRP) in accordance with DoDI 3216.02.
- The research is fetal research, as described in 42 USC 289g-289g-2.
- The following types of research do not occur at Hennepin Healthcare but in the event a request to do is submitted, the DoD CLAR will be conducted:
    - Large scale genomic data (LSGD) is collected from DoD-affiliated personnel. LSDG includes data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data; etc.
    - DoD supported or funded human participants research in a foreign country, unless conducted by a DoD overseas institution, or only involves DoD-affiliated personnel who are US citizens.

The PI, with assistance from the Office of Grants and Contracts, identifies any requirements for an additional level of DoD review and submits all required documentation relevant to research to the requesting DoD Component for the CLAR.

The PI notifies HRPO upon receipt of relevant DoD HRPO authorization, DoD CLAR, and/or DoD survey review approval, as applicable, via a *Modification* submission in Cayuse HE.

The PI may not initiate the study until the human research protection officer within the sponsoring DoD Component reviews and approves the IRB approval and other submitted documentation.

Reporting to the DoD

The following will be promptly (within 30 days) reported to the DoD human research protection officer by the Hennepin Healthcare Institutional Official. The appropriate process for making required disclosures to DoD will be addressed in the terms and conditions of the award:

- Any determination(s) of serious or continuing non-compliance for DoD research
- Any determination of an unanticipated problems involving risks to subjects or others for DoD research
- Any suspension or termination of DoD-supported research
- Reports of audits by another federal or state agency, official governing body of a Native American or Alaskan native tribe, other official entity, or foreign government of DoD research
- When the organization is notified by any Federal department, agency or national organization that any part of the human research protections program is under investigation for cause involving a DoD-supported research protocol
- Any other reporting as required by the terms and conditions of the award

The Principal Investigator of research supported or conducted by DoD has additional reporting obligations (within 30 days) to the COHRP as described in DoDI 3216.02 section 3.6:

- Any problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD-supported research
- When significant changes to the protocol are approved by the IRB, including:
    - Changes to key investigators or institutions
    - Change of reviewing IRB
    - Decreased benefit or increased risk to subjects in greater than minimal risk research
    - Addition of vulnerable populations as subjects
    - Addition of DoD-affiliated personnel as subjects
- The results of the IRB's continuing review, if required
- Change in status when a previously enrolled subject becomes pregnant, or when the investigator learns that a previously enrolled subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46, Subpart B
- Change in status when a previously enrolled subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 32 CFR 219, Subpart C
- Closure of a DoD-supported study

Record retention and DoD inspection

Study records will be made accessible to DoD representatives in accordance with the terms and conditions of the award and Hennepin Healthcare policies.

See also: 501 MANUAL Conducting Human Research **Appendix C.** ***Additional requirements for Department of Defense (DoD) research***

282 Department of Justice-sponsored research

PURPOSE

This SOP describes specific human research requirements that are required for Department of Justice (DoJ)-sponsored research.

PROCEDURE

The review of research will be conducted and electronically documented, as required by DoJ requirements.

For research conducted within the Bureau of Prisons

- Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.
- The requirements of 28 CFR 512 will be followed.
- The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
- The research design must be compatible with both the operation of prison facilities and protection of human participants. The researcher must observe the rules of the institution or office in which the research is conducted.
- The researcher must assume responsibility for actions of any persons engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.
- Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the requirements of 28 CFR 512.
- All research proposals will be reviewed by the Bureau Research Review Board.
- The researcher must have academic preparation or experience in the area of study of the proposed study.
- When submitting a research protocol, the applicant shall provide the following information:
  - A summary statement, which includes:
    - Names and current affiliations of the researchers
    - Title of the study
    - Purpose of the study
    - Location of the study
    - Methods to be employed
    - Anticipated results
    - Duration of the study
    - Number of participants (staff or inmates) required and amount of time required from each
    - Indication of risk or discomfort involved as a result of participation
  - A comprehensive statement, which includes:
    - Review of related literature
    - Detailed description of the research method
    - Significance of anticipated results and their contribution to the advancement of knowledge

  - Specific resources required from the Bureau of Prisons
  - Description of all possible risks, discomforts, and benefits to individual participants or a class of participants and a discussion of likelihood that the risks and discomforts will actually occur
  - Description of steps taken to minimize any risks
  - Description of physical or administrative procedures to be followed to:
    - Ensure the security of any individually identifiable data that are being collected for the study
    - Destroy research records or remove individual identifiers from those records when the research has been completed
  - Description of any anticipated effects of the research study on organizational programs and operations
  - Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules
  - A statement regarding assurances and certification required by federal regulations, if applicable
  - The project must have an adequate research design and contribute to the advancement of knowledge about corrections. Consultants may be used to assist in the evaluation of scientific merit.
- The selection of participants within any one organization must be equitable.
- Incentives may not be offered to help persuade inmate participants to participate. However, soft drinks and snacks to be consumed at the test setting may be offered.
- Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both:

    1. No longer in Bureau of Prisons custody
    2. Participating in authorized research being conducted by Bureau employees or contractors

- A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
- Except as noted in the consent statement to the participant, the researcher must not provide research information that identifies a participant to any person without that participant's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
- Except for electronic data records maintained at an official DoJ site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic records system.
- If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project. Required elements of disclosure include the following:
  - Identification of the researchers
  - Anticipated uses of the results of the research
  - A statement that participation is completely voluntary and the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable)
  - A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law; for example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization
  - A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility

For research funded by the National Institute of Justice (NIJ)

- All projects are required to have a privacy certificate approved by the NIJ human subject protection officer.

- Under a privacy certificate, researchers and research staff do not have to report child abuse unless the participant signs another consent document to allow child abuse reporting.
- All researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.
- The confidentiality statement on the consent document must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.

Submission and reporting to DoJ

Reporting will be conducted in accordance with the terms and conditions of the funding agency award.

See also: 501 MANUAL Conducting Human Research **Appendix D.** ***Additional requirements for Department of Justice (DoJ) research***

290 IRB records retention

PURPOSE

This SOP describes the Hennepin Healthcare Human Research Protection Office (HRPO) record retention practices for documentation pertaining to IRB review and oversight to comply with federal, state, and institutional regulations and guidelines governing human research.

PROCEDURE

For IRB submissions, HRPO will maintain records related to IRB submissions for at least three years after IRB closure of the research.

HRPO will not maintain records for IRB submissions that have been withdrawn by an action or inaction of the principal investigator.

HRPO will maintain records related to membership and meeting activities (e.g., rosters, agendas, meeting attendance, minutes) for 3 years after their origination date or *no longer in effect* date.

Records shall be accessible for inspection at reasonable times and in a reasonable manner for authorized representatives of sponsors, federal agencies, or other authorized individuals.

Retention practices for hard-copy records

Hard-copy records shall be stored safely and confidentially by the following:

- Study files are stored in file cabinets in the Human Research Protection Offices; these offices are monitored and secured by HRPO staff.
- All other records are filed in binders and stored in the Human Research Protection Offices; these offices are monitored and secured by HRPO staff.
- Records shall not be removed from their location without permission of HRPO staff.
- Archived study files may be sent (not sooner than three years after IRB closure or termination) to a designated third-party service for hard-copy records storage and destruction and shall be handled in a safe and confidential manner.
- Archived study files shall be destroyed (not sooner than seven years after IRB closure or termination) by a secure shredding process supervised by a designated third-party service for hard-copy records storage and destruction.

Retention practices for electronic records

Effective January 2021, HRPO supports 100% electronic management for IRB records using an IRB electronic management system, Cayuse Human Ethics (HE), to generate, track, and store all IRB (and CRC) records pertaining to research involving human subjects overseen by the Hennepin Healthcare IRB. All records for non-exempt studies with an active status as of January 4, 2021 will be migrated to Cayuse HE. Cayuse HE stores all records in the cloud and can be accessed securely from any web-based

location. Cayuse HE provides a complete audit history of all submissions and IRB (and CRC) determinations throughout the lifecycle of a study and eliminates HRPO's use of hard-copy records.

Effective January 2021, HRPO will use Cayuse HE to manage and retain records related to IRB (and CRC) membership and meeting activities (e.g., agendas, meeting attendance, minutes)

IRB (and CRC) records not captured in Cayuse HE will be managed via a secure HHRI-approved file management system (such as Dropbox) and/or the HHRI web platform.

Any records available in electronic format prior to January 2021 will be managed as electronic records.

VERSION HISTORY

version date	Summary of substantive revisions
25 AUG 2023	203 Using worksheets in Cayuse HE Added new worksheets to table (752, 763) 211 Single IRB review: Hennepin Healthcare as sIRB and reliance on external IRBs Revised to describe Hennepin Healthcare as sIRB and use of 763 WORKSHEET 212 Criteria for IRB approval Added footnote (per AAHRPP Step 1 Application feedback (I.1.D) and AAHRPP Tip Sheet: *FOLLOWING THE GUIDELINE OF THE INTERNATIONAL CONFERENCE ON HARMONISATION – GOOD CLINICAL PRACTICE (E6))* 230 Convened meetings Added description of documents that are provided and reviewed by IRB for convened IRB reviews (per AAHRPP Step 1 Application feedback (II.2.E)) 232 IRB meeting minutes Minor edit to who may review draft minutes 240 Pre-review Added reference to 717 & 781 WORKSHEETS (per AAHRPP Step 1 Application feedback (I.7.A)) 242 Convened IRB review Clarified that expiration date setting is 1 year *minus 1 day* 243 Initial review of expedited research Removed description of prisoner research reviewed via expedited review and added reference new 256 SOP *Research involving prisoners* (per AAHRPP Step 1 Application feedback (II.4.A)) Clarified that expiration date setting is 1 year *minus 1 day* Removed description of emergency use reviewed via expedited review (see 245 SOP *Emergency use*) 244 Exempt research Minor edit (per AAHRPP Step 1 Application feedback (Element II.2.B)) NEW – 245 Emergency use (per AAHRPP Step 1 Application feedback (I.7.C)) 250 Continuing review/administrative check-in Minor edit (per AAHRPP Step 1 Application feedback (II.2.E)) NEW – 256 Research involving prisoners (per AAHRPP Step 1 Application feedback (II.4.A)) 270 Communication of actions Added notification types 281 Department of Defense-sponsored research Minor edits and additional content describing DoD review and reporting (per AAHRPP Step 1 Application feedback (I.1.A, I-2, I-3, II.2.B)
13 FEB 2023	203 Using worksheets in Cayuse HE Added new worksheets to table (711-A, 757, 788) NEW - 209 OHRP registrations 210 IRB jurisdiction Revised title of SOP from *Determination of IRB jurisdiction* to *IRB jurisdiction* Added specific detail to address AAHRPP Element I.1.C(1)(b) Incorporated content moved from 220 IRB SOP Added reference to A2 APPENDIX *HRPP Components*

	212 Criteria for IRB approval Added reference to relevant federal regulations and guidelines, *The Belmont Report, and* 197 GUIDANCE Criteria for IRB approval 214 Use of expert consultants Minor wording change 220 HRPO structure and composition Change title of SOP from *Jurisdiction, structure, and composition* to *HRPO structure and composition* Move content related to jurisdiction of HRPO/IRB to 210; add specific detail to address AAHRPP element I.1.C and I.9. 222 IRB member responsibilities for non-exempt human research Update Designated reviewer section to align with 243 IRB SOP 223 IRB member addition & removal Update reference to education requirements to remove 401 Checklist and replace with Section 1.6 of 501 Manual 232 IRB meeting minutes Add language to Recoding minutes section to explicitly call out consideration of participants with diminished capacity to consent [AAHRPP II.5B.1(i)] 250 Continuing review/administrative check-in Minor revision to specifically call out additional factors considered by the IRB [AAHRPP II.2.E(1)(a)(v)] 251 Incident/New Information Added information regarding expedited and convened IRB review processes and IRB actions 255 Participant complaints and concerns Add reference to new online compliant form. NEW - 200-A1 APPENDIX Compliance statement NEW – 200-A2 APPENDIX HRPP Components
31 OCT 2022	Origination of SOP compilation format 201 Resource gallery management Update to reflect SOP compilation format and streamlined process to manage Resource Gallery documents 203 Using worksheets with Cayuse HE Added reference to 724-A, 720-A, and updates to clarify when 727 is required for expedited research; added language to clarify use of worksheets during convened IRB review 211 Reliance on external IRBs Minor updates to reflect process for IRB reliance and actions taken in Cayuse HE and reference to related resources 212 (formerly 245) Criteria for IRB approval Content moved into separate SOPs on specific topics; revised to provide general criteria for approval and reference to worksheets system NEW – 219 HRPO emergency preparedness and response plan NEW – 222 IRB member responsibilities for non-exempt human research NEW – 223 IRB member addition & removal 230 Convened meetings Added description of *Full expedited* review type NEW – 232 IRB meeting minutes

NEW – 239 Administrative withdrawals and closures

244 Exempt research
Added reference to 160 GUIDANCE *Criteria for exemption from IRB oversight*

NEW –247 Recruitment and screening of potential participants

NEW –248 Recruitment materials

NEW –249 Compensation for study participation

250 Continuing review/administrative check-in
Update to the frequency for Admin Check In; added section: renewal submission with minor stipulations

252 Modifications to previously approved research
Update to incorporate review of protocol exception requests; update to incorporate review via modification for relying site for research under sIRB review; update to remove detail addressed in applicable reviewer worksheet

NEW –255 Participant complaints and concerns

260 SOP Compliance activities
Added reference to specific OEQCR SOP

281 Department of Defense-sponsored research
Update to reflect revisions to DOD INSTRUCTION 3216.02 (April 15, 2020)