PARKVIEW

Investigator Manual[i] (HRP-103)

Revised 10/30/2025

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Scope

Throughout this document “institution” refers to PARKVIEW HEALTH SYSTEM.

What is the purpose of this manual?

This document, INVESTIGATOR MANUAL (HRP-103), is designed to guide you through policies and procedures related to the conduct of Human Research that are specific to this institution.

General information regarding Human Research protections and relevant federal regulations and guidance is incorporated into the required human protections training. For additional information see below: “What training does my staff and I need in order to conduct Human Research?”

What is Human Research?

HUMAN RESEARCH PROTECTION PROGRAM PLAN (HRP-101) defines the activities that this institution considers to be “Human Research.” An algorithm for determining whether an activity is Human Research can be found in Human Research Determination (HRP-310), located in the IRB Policies & Procedures section of the IRB Web site. Use this document for guidance as to whether an activity meets either the DHHS or FDA definition of Human Research, keeping in mind that the IRB makes the ultimate determination in questionable cases as to whether an activity constitutes Human Research subject to IRB oversight.

You are responsible not to conduct Human Research without prior IRB review and approval (or an institutional review and determination of exempt Human Research). If you have questions about whether an activity is Human Research, contact the IRB Office who will provide you with a determination. If you wish to have a written determination, provide a written request to the IRB Office.

What is the Human Research Protection Program?

HUMAN RESEARCH PROTECTION PROGRAM PLAN (HRP-101) describes this institution’s overall plan to protect subjects in Human Research.

- The mission of the Human Research Protection Program.
- The ethical principles that the institution follows governing the conduct of Human Research.
- The applicable laws that govern Human Research.
- When the institution becomes “engaged in Human Research” and when someone is acting as an agent of the institution conducting Human Research.
- The types of Human Research that may not be conducted.
- The roles and responsibilities of individuals within the institution.

What training does my staff and I need to conduct Human Research?

This section describes the training requirements imposed by the IRB. You may have additional training imposed by other federal, state, or institutional policies.

Investigators and staff conducting research must complete the Collaborative Institutional Training Initiative (CITI) human subjects online training program.

The CITI site can be accessed at http://www.citiprogram.org/.

Training is valid for a three-year period, after which time the training must be repeated.

All members of the research team involved in the design, conduct, or reporting of the research must complete training. Members of the research team who have not completed human research protections training may not take part in aspects of the research that involve human subjects.

What financial interests do my staff and I need to disclose to conduct Human Research?

Individuals involved in the design, conduct, or reporting of research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards are considered to have an institution responsibility.

All individuals involved in the design, conduct, or reporting of research are required to disclose any applicable financial interests on the *IRB Conflict of Interest Disclosure xForm*:

- On submission of an initial review.
- At least annually as part of continuing review.
- Within 30 days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.

Individuals with reimbursed or sponsored travel by an entity other than a federal, state, or local government agency, higher education institution or affiliated research institute, academic teaching hospital, or medical center are required to disclose the purpose of the trip, the identity of the sponsor or organizer, the destination, and the duration of the travel.

Individuals subject to this policy are required to complete financial conflicts of interest training initially, at least every 3 years, and immediately when:

- Joining the institution
- Financial conflicts policies are revised in a manner that changes investigator requirements
- Non-compliant with financial conflicts policies and procedures

Additional details can be found in SOP (HRP-055) - Financial Conflicts of Interests.

How do I submit new Human Research to the IRB?

Complete *Protocol Submission xForm* and attach all requested supplements. Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for initial review, you must:

- Obtain the financial interest status ("yes" or "no") of each research staff.
- Obtain the agreement of each research staff to his/her role in the research.

How do I submit a request to use a Humanitarian Use Device (HUD) for clinical use?

This Institution utilizes the IRB to review and approve the use of a HUD before it can be used at a facility for clinical care. You can refer to HRP-323 - Criteria for Approval HUD for additional information regarding the criteria that the IRB uses to review and approve HUD uses. The clinical use of a HUD is not considered Human Research but must still be submitted for review and approval by the IRB prior to clinical use (with the exception of emergency use). An informed consent form is not required by the IRB for HUD use.

Complete *Protocol Submission xForm* and attach all requested supplements. Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for initial review, you must:

- Obtain the financial interest status ("yes" or "no") of each research staff.
- Obtain the agreement of each research staff to his/her role in the research.

When should I submit a request to rely on an External IRB?

For studies where this institution is a participating site (pSite), requests to rely on an external IRB should be submitted after the reviewing IRB has approved the study (e.g., lead site protocol), including consent templates and other document templates.

How do I request to rely on an external IRB?

Complete *Protocol Submission xForm*, choose Request for Deferral as the IRB review process you are requesting, and indicate which external IRB will serve as the IRB of record. Attach all requested supplements. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

How do I write an Investigator Protocol?

Use TEMPLATE PROTOCOL (HRP-503) as a starting point for drafting a new Investigator Protocol, and reference the instructions in italic text for the information the IRB looks for when reviewing research. Here are some key points to remember when developing an Investigator Protocol:

- The italicized bullet points in TEMPLATE PROTOCOL (HRP-503) serve as guidance to investigators when developing an Investigator Protocol for submission to the IRB. All italicized comments are meant to be deleted prior to submission.
- For any items described in the sponsor's protocol or other documents submitted with the application, investigators may simply reference the page numbers of these documents within the Investigator Protocol rather than repeat information.
- When writing an Investigator Protocol, always keep an electronic copy. You will need to modify this copy when making changes to the Investigator Protocol.
- If you believe your activity may not be Human Research, contact the IRB Office prior to developing your Investigator Protocol.
- Note that, depending on the nature of your research, certain sections of the template may not be applicable to your Investigator Protocol. Indicate this as appropriate.
- You may not involve any individuals who are members of the following populations as subjects in your research unless you indicate this in your inclusion criteria as the inclusion of subjects in these populations has regulatory implications.
    - Adults unable to provide legally effective consent
    - Individuals who are not yet adults (infants, children, teenagers)
    - Pregnant women
    - Prisoners
- If you are conducting community-based participatory research, you may contact the IRB Office for information about:
    - Research studies using a community-based participatory research design
    - Use of community advisory boards
    - Use of participant advocates
    - Partnerships with community-based institutions or organizations

How do I create a consent document?

Use TEMPLATE CONSENT DOCUMENT (HRP-502) to create a consent document.

Note that all long form consent documents and all summaries for short form consent documents must contain all the required and all additional appropriate elements of informed consent disclosure. Review the "Long Form of Consent Documentation" section in HRP-314a - Criteria for Consent, to ensure that these elements are addressed. When using the short form of consent documentation, the appropriate signature block from TEMPLATE CONSENT DOCUMENT (HRP-502) should be used on the short form.

If your research study meets the requirements for an exemption and there are interactions with subjects, you may use an abbreviated process for obtaining consent. Consent can be verbal,

but you must provide the following information to participants through an information sheet or written script:

- The subject is being asked to participate in a research study;
- A description of the procedure(s) the participant will be asked to complete;
- Participation is voluntary; and
- The investigator's name and contact information.

We recommend that you date the revisions of your consent documents to ensure that you use the most recent version approved by the IRB.

Do I need to obtain informed consent in order to screen, recruit, or determine the eligibility of prospective subjects?

The IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

> (1) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, OR
>
> (2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

The research protocol should include information about how potential subjects will be identified and recruited for the IRB to be able to determine whether informed consent for these activities is required.

Contact the IRB Office with additional questions or for further guidance regarding the requirement to obtain HIPAA authorization or a waiver to obtain HIPAA authorization for recruitment purposes.

What are the different regulatory classifications that research activities may fall under?

Submitted activities may fall under one of the following four regulatory classifications:

- Not "Human Subject Research": Activities must meet the institutional definition of "Human Research" to fall under IRB oversight. Activities that do not meet this definition of are not subject to IRB oversight or review. Review the IRB Office's HRP-310 - Human Research Determination for reference. Contact the IRB Office in cases where it is unclear whether an activity is Human Research.
- Exempt (from IRB Oversight): Certain categories of Human Research may be exempt from regulation but require IRB review. It is the responsibility of the institution, not the investigator, to determine whether Human Research is exempt from IRB review. Review the IRB Office's HRP-312 - Exemption Determination for reference on the categories of research that may be exempt.

- Review Using the Expedited Procedure: Certain categories of non-exempt Human Research may qualify for review using the expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review the IRB Administration's HRP-313 - Expedited Review for reference on the categories of research that may be reviewed using the expedited procedure.
- Review by the Convened (Full) IRB: Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

What are the decisions the IRB can make when reviewing proposed research?

The IRB may approve research, require modifications to the research to secure approval, table research, or disapprove research:

- Approval: Made when all criteria for approval are met. See "How does the IRB decide whether to approve Human Research?" below.
- Modifications Required to Secure Approval: Made when IRB members require specific modifications to the research before approval can be finalized.
- Tabled: Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum. When taking this action, the IRB automatically schedules the research for review at the next meeting.
- Disapproval: Made when the IRB determines that it is unable to approve research and the IRB cannot describe modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

How does the IRB decide whether to approve Human Research?

The criteria for IRB approval can be found in HRP-312 - Exemption Determination for exempt Human Research and HRP-314 - Criteria for Approval for non-exempt Human Research. The latter worksheet references other checklists that might be relevant. All checklists and worksheets can be found on the IRB Web site.

These checklists are used for initial review, continuing review, and review of modifications to previously approved Human Research.

You are encouraged to use the checklists to write your Investigator Protocol in a way that addresses the criteria for approval.

What will happen after IRB review?

The IRB will provide you with a written decision indicating that the IRB has approved the Human Research, requires modifications to secure approval, or has disapproved the Human Research.

- If the IRB has approved the Human Research: The Human Research may commence once all other institutional approvals have been met. IRB approval is good for a year unless otherwise noted in the approval letter.
- If the IRB requires modifications to secure approval and you accept the modifications: Make the requested modifications and submit them to the IRB. If all requested modifications are made, the IRB will issue a final approval. Research cannot commence until this final approval is received. If you do not accept the modifications, write up your response and submit it to the IRB.
- If the IRB disapproves the Human Research: The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in writing.

In all cases, you have the right to address your concerns to the IRB directly at an IRB meeting.

What are my obligations after IRB approval?

1) Do not start Human Research activities until you have the final IRB approval letter.
2) Do not start Human Research activities until you have obtained all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources.
3) Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
4) Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
5) Update the IRB office with any changes to the list of study personnel using the *Request for Modification xForm*
6) Personally conduct or supervise the Human Research. Recognize that the investigator is accountable for the failures of any study team member.
   a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB, and in accordance with applicable federal regulations and local laws.
   b) When required by the IRB ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
   c) Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
   d) Protect the rights, safety, and welfare of subjects involved in the research.
7) Submit to the IRB:
   a) Proposed modifications as described in this manual. (See "How do I submit a modification?")
      i) Single subject protocol exceptions should be submitted via the *Request for Modification xForm.*
   b) A continuing review application as requested in the approval letter. (See "How do I submit continuing review?")

c) A *Study Closure xForm* when the Human Research is closed. (See "How Do I Close Out a Study?")

8) Report any of the information items listed on the *Reportable New Information xForm* to the IRB within five business days of becoming aware of the items.
   a) Information that indicates a new or increased risk, or a new safety issue. For example:
      i) New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
      ii) An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk
      iii) Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
      iv) Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
      v) Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
      vi) Any changes significantly affecting the conduct of the research
   b) Harm experienced by a subject or other individual, which in the opinion of the investigator are **unexpected** and **probably related** to the research procedures.
      i) A harm is "unexpected" when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
      ii) A harm is "probably related" to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.
   c) Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB, or an allegation of such non-compliance.
   d) Audit, inspection, or inquiry by a federal agency and any resulting reports (e.g. FDA Form 483.)
   e) Written reports of study monitors.
   f) Failure to follow the protocol due to the action or inaction of the investigator or research staff.
   g) Breach of confidentiality.
   h) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
   i) Incarceration of a subject in a study not approved by the IRB to involve prisoners.
   j) Complaint of a subject that cannot be resolved by the research team.
   k) Premature suspension or termination of the protocol by the sponsor, investigator, or institution.
   l) Unanticipated adverse device effect (any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or

application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects).

9) Using the *IRB Conflict of Interest Disclosure xForm*, submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.
10) Do not accept or provide payments to professionals in exchange for referrals of potential subjects ("finder's fees.")
11) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments.")
12) See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do no override the baseline requirements of this section.
13) If the study is a clinical trial and supported by a Common Rule agency, one IRB-approved version of a consent form that has been used to enroll participants must be posted on a public federal website designated for posting such consent forms. The form must be posted after recruitment closes, and no later than 60 days after the last study visit. Please contact the study sponsor with any questions.
    a) If certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), the supporting Federal department or agency may permit or require redactions to the information posted. Contact the Federal department or agency supporting the clinical trial for a formal determination.
    b) Contact the supporting Federal department or agency sponsor with any other questions regarding consent form posting obligations.

What are my obligations as investigator when relying on an external IRB?

1) Obtain appropriate approvals from this institution prior to seeking review by another IRB.
2) Comply with determinations and requirements of the reviewing IRB.
3) Provide the reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB's determination prior to IRB review.
4) Notify the reviewing IRB when local policies that impact IRB review are updated.
5) Cooperate in the reviewing IRB's responsibility for initial and continuing review, record keeping and reporting and providing all information requested by the reviewing IRB in a timely manner.
6) Disclose conflicts of interest as required by the reviewing IRB and complying with management plans that may result.
7) Promptly report to the reviewing IRB any proposed changes to the research and not implementing those changes to the research without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
8) When enrolling participants, obtain, document and maintain records of consent for each participant or each participant's legally authorized representative.
9) Promptly report to the reviewing IRB any unanticipated problems involving risks to participants or others according to the requirements specified in the reliance agreement.

10) Provide the reviewing IRB with data safety monitoring reports in accordance with the reviewing IRB's reporting policy.
11) Report non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the reliance agreement.
12) Specify the contact person and providing contact information for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the reviewing IRB.
13) Determine which institutional requirements apply to your study and ensure all are met. Refer to HRP-309 - Ancillary Review Matrix.

How do I document consent?

Use the signature block approved by the IRB. Complete all items in the signature block, including dates and applicable checklists.

The following are the requirements for long form consent documents:

- The subject or representative signs and dates the consent document.
  - If the subject/representative is physically unable to sign the consent form, note this on the consent form and document the method used for communication with the prospective subject/representative and the specific means by which their agreement was communicated.
- The individual obtaining consent signs and dates the consent document.
- Whenever the IRB or the sponsor require a witness to the oral presentation, the witness signs and dates the consent document.
- For subjects or read who cannot read and whenever required by the IRB or the sponsor, a witness to the oral presentation signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the subject.

The following are the requirements for short form consent documents:

- The subject or representative signs and dates the short form consent document.
- The person obtaining consent signs and dates the summary.
- The impartial witness (fluent in both English and the language spoken by the subject/representative) to the oral presentation signs and dates the short form consent document and the summary. The witness and the interpreter may be the same person.
- Copies of the signed and dated consent document and summary are provided to the subject/representative.
- If the study is FDA regulated, obtain a translated copy of the IRB-approved English version of the long form consent promptly and submit to the IRB for review.
  - After IRB approval of the translated version, provide it to the subject or LAR as soon as possible.

How do I submit a modification?

Complete *Request for Modification xForm* and attach all requested supplements. Please note that research must continue to be conducted without inclusion of the modification until IRB approval is received.

How do I submit continuing review?

Complete *Continuing Review xForm* and attach all requested supplements.

If the continuing review involves modifications to previously approved research, submit those modifications as a separate request for modification using – Request for Modification xForm.

If the continuing review application is not received by the date requested in the approval letter, you will be restricted from submitting new Human Research until the completed application has been received.

If the approval of Human Research expires all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information. Continuing Human Research procedures is a violation of institutional policy. If current subjects will be harmed by stopping Human Research procedures that are available outside the Human Research context, provide these on a clinical basis as needed to protect current subjects. If current subjects will be harmed by stopping Human Research procedures that are not available outside the Human Research context, immediately contact the IRB chair and provide a written list of the currently enrolled subjects and why they will be harmed by stopping Human Research procedures.

How do I close out a study?

Complete *Study Closure xForm* and attach all requested supplements

If you fail to submit a *Study Closure xForm* to close out Human Research, you will be restricted from submitting new Human Research until the completed application has been received.

How long do I keep records?

Maintain your Human Research records, including signed and dated consent documents for at least three years after completion of the research. Maintain signed and dated HIPAA authorizations and consent documents that include HIPAA authorizations for at least six years after completion of the research.

If your Human Research is sponsored, contact the sponsor before disposing of Human Research records.

What if I need to use an unapproved drug, biologic, or device and there is no time for IRB review?

Contact the IRB Office or IRB chair immediately to discuss the situation. If there is no time to make this contact, see HRP-322 - Emergency Use for the regulatory criteria allowing such a use and make sure these are followed. Use TEMPLATE CONSENT DOCUMENT- Expanded Access (HRP-506) to prepare your consent document. You will need to submit a report of the use to the IRB within five working days of the use.

Include in the report a description of how the use meets the criteria outlined in HRP-322 - Emergency Use, a summary of the patient's diagnosis and treatment history, and date and time of the use. Attach to the report the consent document templates used (if applicable), approval of the use from the FDA (drugs and biologics), or concurrence letter from an independent physician that the use of the device is warranted and no other alternative treatments are/were available (devices).

If you fail to submit the report within five working days, you will be restricted from submitting new Human Research until the report has been received.

Emergency use of an unapproved drug or biologic in a life-threatening situation without prior IRB review is "research" as defined by FDA, the individual getting the test article is a "subject" as defined by FDA, and therefore is governed by FDA regulations for IRB review and informed consent. Emergency use of an unapproved device without prior IRB review is not "research" as defined by FDA and the individual getting the test article is not a "subject" as defined by FDA. However, FDA guidance recommends following similar rules as for emergency use of an unapproved drug or biologic.

Individuals getting an unapproved drug, biologic, or device without prior IRB review cannot be considered a "subject" as defined by DHHS and their results cannot be included in prospective "research" as that term is defined by DHHS.

FDA regulations require that any subsequent use of a test article at the institution have prospective IRB review and approval. If it is anticipated that this test article may be used again (for the same patient, a different patient, or for any indication), submit a protocol and consent document(s) to the IRB for review so that an approved protocol will be in place when the next need arises.

How do I submit a non-emergency expanded access request for an unapproved drug, biologic, or device to the IRB?

There are five different types of non-emergency use expanded access:

1. Individual patient expanded access use of an investigational drug

Individual patient drug expanded access requests should be submitted to the IRB as a new study. If the study team checked "Request for Authorization to Use Alternative IRB Review Procedures" on FDA Form 3926 (field 10.b.) or has a separate waiver request included with FDA Form 1571 for the purpose of obtaining concurrence from an IRB Chair or designee, this

information should be included in the application. Instead of uploading a protocol, the submission should include the following:

- A thorough patient history and treatment plan, included in the Form FDA 3926 or in a separate document that includes:
    - The proposed daily dose, route, and frequency of administration of planned treatment; duration of planned treatment; criteria for discontinuation of treatment; and planned dose modifications for adverse events;
    - The planned monitoring for adverse events, response to treatment, and changes in clinical status, as well as proposed modifications to the treatment plan to mitigate risks to the patient if appropriate;
    - The key details of the patient's history, including diagnosis and summary of prior therapy (including response to such therapy); the reason for request, including an explanation of why the patient lacks other therapeutic options; and information regarding a patient's relevant clinical characteristics (such as comorbid conditions and concomitant medications) that is necessary to assess the potential for increased risks of the drug; and
    - - A summary of known risks of the drug

Use TEMPLATE CONSENT DOCUMENT – Expanded Access (HRP-506) to prepare your consent document. A Continuing Review application must be submitted to the IRB at least annually, and any modifications or new information should be reported accordingly.

2. Compassionate Use (Individual patient/small group access) of a device

Requests for compassionate use of a device should be submitted to the IRB as a new study. See HRP-325 - Device Compassionate Use for the regulatory criteria allowing such a use and make sure these are followed. The FDA does not consider the compassionate use of an unapproved device to be a clinical investigation, however it is expected that informed consent be obtained. Use TEMPLATE CONSENT DOCUMENT - Expanded Access (HRP-506) to prepare your consent document.

Instead of uploading a protocol, the submission should include a summary of the conditions constituting the compassionate use, other relevant details of the case, approval from the device manufacturer, device/product manual, FDA authorization, and any other relevant information (i.e., patient-facing materials, etc..). Continuing review is not required for compassionate use, however if any problems occurred as a result of device use, these should be discussed in the follow-up report and reported to the IRB as soon as possible.

3. Intermediate-size patient population access of a drug
4. Expanded access for widespread use of a drug
5. Treatment use of a device

Requests for any of these three (3) types of expanded access use should be submitted to the IRB as a new study. Submissions should include the protocol, consent form, and other pertinent information (i.e., Investigator's Brochure, device/product manual, patient-facing materials, etc..). Use TEMPLATE CONSENT DOCUMENT (HRP-502) to prepare your consent document. A

Continuing Review application must be submitted to the IRB at least annually, and any modifications or new information should be reported accordingly.

How do I transfer responsibility to a new principal investigator?

Changes of PI often prompt changes to other parts of the study. Review all consent/assent forms, recruitment materials and other documents to make certain they have been updated to reflect the change. The current PI may transfer responsibility to a new PI by submitting a modification (See "How do I submit a modification?").

If the current PI is leaving the institution but will remain a study team member, please contact the IRB Office to determine if a reliance agreement is appropriate.

If the current PI is leaving the institution and plans to take research data or specimens with them, there are contractual agreements that may be needed in order to share individual level human subjects research data/specimens.

If a PI goes on an unanticipated leave or there is an abrupt departure from the institution, a modification should be submitted by a current member of the study team as soon as possible to update the PI. If a modification is not going to be submitted, complete and submit *Reportable New Information xForm*. The submission should include an explanation as to why a modification will not be submitted, whether the unanticipated leave is temporary (and for how long) or permanent, and who will be responsible for the conduct of the study during this time.

How do I get additional information and answers to questions?

This document and the policies and procedures for the Human Research Protection Program are available on the IRB Web Site at https://www.parkview.com/institutional-review-board

If you have any questions or concerns, about the Human Research Protection Program, contact the IRB Office at:

Shelly Murphy, Jennifer Dienelt (IRB Coordinators)
6509 Mutual Drive
Fort Wayne, IN 46825
Email: IRBCoordinators@parkview.com
260-266-8195

If you have questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program that cannot be addressed by contact the IRB Office, follow the directions in HUMAN RESEARCH PROTECTION PROGRAM PLAN (HRP-101) under "Reporting and Management of Concerns."

Appendix A-1 *Additional Requirements for DHHS-Regulated Research*[ii]

1. When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
2. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.
4. When seeking the informed consent of subjects, investigators should explain whether already collected data about the subjects will be retained and analyzed even if the subjects choose to withdraw from the research.
5. When research is covered by a certificate of confidentiality, researchers:
    a. May not disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
    b. May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.
    c. May not utilize third parties or entities to collect or store information (e.g., contractors, online platform vendors) that cannot or will not protect against the compelled disclosure of the personally identifiable information.
    d. May disclose information only when:
        i. Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding.

ii. Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;
iii. Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
iv. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human participants in research.

e. Researchers must inform participants of the protections and limitations of certificates of confidentiality (see language in TEMPLATE CONSENT DOCUMENT (HRP-502)).
    i. For studies that were previously issued a Certificate and notified participants of the protections provided by that Certificate, NIH does not expect participants to be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform participants.
    ii. If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer activity participating in the study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of a Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although the IRB may determine whether it is appropriate to inform participants.
f. Researchers conducting research covered by a certificate of confidentiality, even if the research is not federally funded, must ensure that if identifiable, sensitive information is provided to other researchers or organizations, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

Appendix A-2 *Additional Requirements for FDA-Regulated Research*

1. When a subject withdraws from a study:[iii]
    a. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
    b. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
    c. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
    d. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
    e. An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.
2. For FDA-regulated research involving investigational drugs:
    a. Investigators must abide by FDA restrictions on promotion of investigational drugs:[iv]
        i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
        ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
        iii. An investigator must not commercially distribute or test market an investigational new drug.
    b. Follow FDA requirements for general responsibilities of investigators[v]

i. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
ii. An investigator must, in accordance with the provisions of 21 CFR §50, obtain the informed consent of each human subject to whom the drug is administered, except as provided in 21 CFR §50.23 or §50.24 of this chapter.
iii. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.

c. Follow FDA requirements for control of the investigational drug[vi]
   i. An investigator must administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
   ii. The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
d. Follow FDA requirements for investigator recordkeeping and record retention[vii]
   i. Disposition of drug:
      1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
      2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
   ii. Case histories.
      1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
      2. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
   iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
e. Follow FDA requirements for investigator reports[viii]

i. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.
iv. Financial disclosure reports:
    1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
    2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

f. Follow FDA requirements for assurance of IRB review[ix]
    i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
    ii. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.
g. Follow FDA requirements for inspection of investigator's records and reports[x]
    i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
    ii. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
h. Follow FDA requirements for handling of controlled substances[xi]
    i. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

3. For FDA-regulated research involving investigational devices:
    a. General responsibilities of investigators.[xii]
        i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
    b. Specific responsibilities of investigators[xiii]
        i. Awaiting approval: An investigator may determine whether potential subjects would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
        ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
        iii. Supervising device use: An investigator must permit an investigational device to be used only with subjects under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
        iv. Financial disclosure:
            1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
            2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
        v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
    c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:[xiv]
        i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
        ii. Records of receipt, use or disposition of a device that relate to:
            1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.

2. The names of all persons who received, used, or disposed of each device.
3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
2. Documentation that informed consent was obtained prior to participation in the study.
3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
4. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

d. Inspections[xv]

i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).

ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

iii. Records identifying subjects: An investigator must permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not

obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

e. Prepare and submit the following complete, accurate, and timely reports[xvi]
    i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
    ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
    iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
    iv. Deviations from the investigational plan:
        1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
        2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
        3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
    v. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
    vi. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
    vii. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Appendix A-3 ***Additional Requirements for Clinical Trials (ICH-GCP)***

1. The clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice (GCP) and the applicable regulatory requirements. The rights, safety and well-being of the participants are the most important considerations and should prevail over interests of science and society.
2. Clinical trials should be scientifically sound for their intended purpose and based on adequate and current scientific knowledge and approaches.
    a. The available nonclinical and clinical information on an investigational product(s) should be adequate to support the proposed clinical trial.
    b. Clinical trials should be scientifically sound and reflect the state of knowledge and experience with the investigational product(s), including, if applicable, the condition being treated, diagnosed or prevented; the current understanding of the underlying biological mechanism (of both the condition and the investigational product); and the population for which the investigational product is intended.
    c. There should be periodic review of current scientific knowledge and approaches to determine whether modifications to the trial are needed, since new or unanticipated information may arise once the trial has begun.
3. Investigator's Qualifications and Training
    a. The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications.
    b. The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and/or in other information sources provided by the sponsor.
4. Resources
    a. The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of eligible participants within the recruitment period as agreed with the sponsor.
    b. The investigator should have sufficient time, an adequate number of available and qualified staff, and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
5. Responsibilities
    a. The investigator may delegate trial-specific activities to other persons or parties. The investigator may be supported by the sponsor in the identification of a suitable service provider(s); however, the investigator retains the final decision on whether the service provider intended to support the investigator is appropriate based on information provided to the sponsor. The investigator retains the ultimate responsibility and should maintain appropriate oversight of the persons or parties undertaking the activities delegated to ensure the rights, safety and well-being of the trial participants and reliability of the data. The level

of investigator oversight of the delegated activities should depend on the nature of the delegated activities and be proportionate to the importance of the data being protected and the risks to trial participant safety and data reliability.

b. The investigator should ensure that all persons or parties to whom the investigator has delegated trial-related activities are appropriately qualified and are adequately informed about the relevant aspects of the protocol, the investigational product(s), and their assigned trial activities (including activities conducted by staff provided by other parties in accordance with local regulatory requirements). Trial-related training to persons assisting in the trial should correspond to what is necessary to enable them to fulfill their delegated trial activities that go beyond their usual training and experience.
c. The investigator should ensure a record is maintained of the persons and parties to whom the investigator has delegated trial-related activities. Documentation of delegation should be proportionate to the significance of the trial-related activities. In situations where the activities are performed as part of clinical practice, delegation documentation may not be required.
d. Agreements made by the investigator/institution with service providers for trial-related activities should de documented.
e. The investigator/institution should permit monitoring and auditing by the sponsor, inspection by the appropriate regulatory authority(ies) and, in accordance with applicable regulatory requirements, review by IRB(s).

6. Communication with IRB
    a. Submission to the IRB may be made by the investigator/institution or sponsor in accordance with applicable regulatory requirements.
    b. Before initiating a trial, the investigator/institution should have a documented and dated approval from the IRB for the trial protocol, informed consent materials, participant recruitment procedures (e.g., advertisements), and any other trial-related information to be provided to participants.
    c. As part of the investigator's/institution’s or sponsor’s (in accordance with applicable regulatory requirements) submission to the IRB, a current copy of the Investigator's Brochure or basic product information brochure should be provided. If the Investigator's Brochure or basic product information brochure is updated during the trial, the IRB should receive the current version in accordance with applicable regulatory requirements.
    d. As the trial progresses, the investigator/institution or sponsor should provide any updates to the participant information to the IRB in accordance with applicable regulatory requirements.
    e. The investigator or sponsor should submit documented summaries of the trial status to the IRB in accordance with local regulatory requirements or upon request.
    f. The investigator or the sponsor should promptly communicate to the IRB and where applicable, to the institution any changes significantly affecting the conduct of the trial and/or increasing risk to participants.
7. Compliance with Protocol

a. The investigator/institution should sign the protocol, or an alternative contract, to confirm agreement with the sponsor.
b. The investigator/institution should comply with the protocol, GCP and applicable regulatory requirements.
c. The investigator should document all protocol deviations. In addition to those identified by the investigator themselves, protocol deviations related to their trial participants and their conduct of the trial may be communicated to them by the sponsor. In either case, the investigator should review the deviations, and for those deviations deemed important, the investigator should explain the deviation and implement appropriate measures to prevent a recurrence, when applicable.
d. The investigator should follow the protocol and deviate only where necessary to eliminate an immediate hazard(s) to trial participants. In case of deviations undertaken to eliminate immediate hazard to trial participants, the investigator should inform the sponsor promptly.
e. The investigator should report information on the immediate hazard, the implemented change and the subsequent proposed protocol amendment, if any, to the IRB and, where applicable, regulatory authorities.

8. Premature Termination or Suspension of a Trial
    a. If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial participants and should assure appropriate therapy and follow-up for the participants.
    b. Where the investigator terminates or suspends their involvement in a trial without prior agreement by the sponsors, the investigator should promptly inform the institution, where applicable, the sponsor, the IRB, and the regulatory authorities in accordance with applicable regulatory requirements and should provide a detailed explanation of the reasons.
    c. If the sponsor terminates or suspends a trial, the investigator/institution, or the sponsor, in accordance with applicable regulatory requirement(s), should promptly inform the IRB and the regulatory authorities and should provide an appropriate explanation.
    d. If the IRB terminates or suspends its approval of a trial, the investigator should inform the institution, where applicable, and the investigator/institution should promptly notify the sponsor.
9. Participant Medical Care and Safety Reporting
    a. Medical Care of Trial Participants
        i. A qualified physician or, where appropriate, a qualified dentist (or other qualified healthcare professionals in accordance with local regulatory requirements) who is an investigator or a sub-investigator for the trial, should have the responsibility for trial-related medical care and decisions.
        ii. Other appropriately qualified healthcare professionals may be involved in the medical care of trial participants, in line with their normal activities and in accordance with local regulatory requirements.
        iii. During and following participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a participant for

any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a participant when medical care is needed for intercurrent illness(es) of which the investigator becomes aware.

iv. The investigator should inform the participant's primary physician about the participant's involvement in the trial if the participant has a primary physician and agrees to the primary physician being informed.

b. Safety Reporting

i. Adverse events and/or abnormal test results required for safety evaluations (as outlined in the protocol) should be reported to the sponsor according to the reporting requirements and within the time periods specific in the protocol. Unfavorable medical events occurring in participants before investigational product administration (e.g., during screening) should be considered and reported to the sponsor if required by the protocol.

ii. All serious adverse events (SAEs) should be reported immediately (after the investigator reasonably becomes aware of the event) to the sponsor. The investigator should also include an assessment of causality. In accordance with applicable regulatory requirements, the protocol may identify SAEs not requiring immediate reporting, for example, deaths or other events that are endpoints. Subsequent information should be submitted as a follow-up report, as necessary.

iii. For reported deaths, the investigator should supply the sponsor, the IRB and, where applicable, the regulatory authority with any additional requested information (e.g., autopsy reports and terminal medical reports) when they become available.

iv. The investigator may delegate activities for safety reporting to qualified investigator site staff but retains the overall responsibility for safety of participants under their responsibility and compliance with the reporting requirements.

10. Informed Consent of Trial Participants

a. In obtaining and documenting informed consent (paper or electronic format), the investigator should comply with the applicable regulatory requirements and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. The informed consent process should include the following:

i. Prior to consenting and enrolling participants, the investigator should have the IRB's documented approval of the informed consent materials and process;

ii. The information should be as clear and concise as possible, use simple language and avoid unnecessary volume and complexity. This is to ensure that the trial participants or their legally acceptable representatives have an adequate understanding of the objectives of the trial, alternative treatments, potential benefits and risks, burdens, their rights, and what is

expected of the participants to be able to make an informed decision as to their participant in the trial.

iii. Varied approaches (e.g., text, images, videos and other interactive methods), may be used in the informed consent process including for providing information to the participant. The characteristics of the potential trial population (e.g., participants may lack familiarity with computerized systems) and the suitability of the method of obtaining consent should be taken into consideration when developing the informed consent materials and process. When computerized systems are used to obtain informed consent, trial participants may be given the option to use a paper-based approach as an alternative.

iv. Obtaining consent remotely may be considered where appropriate.

v. Whether the informed consent process takes place in person or remotely, the investigator should assure themselves of the identity of the participant (or legally acceptable representative) in accordance with applicable regulatory requirements.

b. The participant or the participant's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the participant's willingness to continue trial participation. The communication of this information and confirmation of the willingness to continue trial participation should be documented. New information that could impact a participant's willingness to continue participation should be assessed to determine if re-consent is needed (e.g., depending on the stage of the trial, consideration should be given to whether the new information is relevant only to new participants or to existing participants). If re-consent is needed (e.g., information on emerging safety concerns), new information should be clearly identified in the revised informed consent materials. Revised informed consent materials should receive the IRB's approval in advance of use.

c. Neither the investigator, nor the investigator site staff, should coerce or unduly influence a participant to participate or to continue their participation in a trial.

d. None of the information provided to the participant or the participant's legally acceptable representative during the informed consent process, should contain any language that causes the participant to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their service providers from liability for negligence.

e. The informed consent process should be conducted by the investigator or other investigator site staff delegated by the investigator, in accordance with applicable regulatory requirements. If the participant is unable to provide consent themselves (e.g., minors, patients with severely impaired decision making capacity), the participant's legally acceptable representative should provide their consent on behalf of the participant.

f. The information provided during the informed consent process and translations should be relevant, clear, simple, concise and understandable to the participant

or the participant's legally acceptable representative and the impartial witness, where applicable.

g. Before informed consent may be obtained, the investigator, or investigator site staff delegated by the investigator, in accordance with the protocol and conditions of IRB approvals, should provide the participant or the participant's legally acceptable representative ample time unless justified (e.g., in an emergency situation) and opportunity to inquire about trial details and to decide whether or not to participate in the trial. Questions about the trial should be answered to the satisfaction of the participant or the participant's legally acceptable representative.
h. Prior to trial participation, the informed consent form should be signed and dated by the participant or by the participant's legally acceptable representative, where appropriate, by an impartial witness and by the investigator or delegated investigator site staff who conducted the informed consent discussion. By signing the consent form, the investigator or delegated investigator site staff attests that the informed consent was freely given by the participant or the participant's legally acceptable representative and the consent information was accurately explained to and apparently understood by the participant or the participant's legally acceptable representative. The informed consent process may involve a physical or an electronic signature and date.
i. In emergency situations, when prior consent of the participant is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the participant is not possible and the participant's legally acceptable representative is not possible and the participant's legally acceptable representative is not available, enrollment of the participant should require measures described in the protocol and/or elsewhere, with documented approval by the IRB, to protect the participant's rights, safety and well-being and to ensure compliance with applicable regulatory requirements. The participant or the participant's legally acceptable representative should be informed about the trial as soon as possible, and consent as appropriate should be requested.
j. If a participant or the legally acceptable representative is unable to read, an impartial witness should be present (remotely or in-person) during the entire informed consent discussion. After the informed consent form and any other information is read and explained to the participant or the participant's legally acceptable representative, and they have orally consented to the participant's trial participation, and if capable of doing so, have signed and dated the informed consent form, the witness should sign and date the consent form. By signing the consent form, the witness attests that the consent information was accurately explained to, and apparently understood by, the participant or the participant's legally acceptable representative, and that informed consent was freely given by the participant or the participant's legally acceptable representative.
k. The informed consent discussion and the informed consent materials to be provided to participant should explain the following as applicable:

i. The purpose of the trial;
ii. That the trial involves research and summary of the experimental aspects of the trial;
iii. The trial's investigational product(s) and the probability for random assignment to the investigational product, if applicable;
iv. The trial procedures to be followed, including all invasive procedures;
v. What is expected of the participants;
vi. The reasonably foreseeable risks or inconveniences to the participant and, when applicable, the participant's partner, to an embryo, fetus, or nursing infant;
vii. The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this;
viii. The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks;
ix. The compensation and/or treatment available to the participant in the event of trial related injury;
x. Any anticipated prorated compensation to the participant for trial participation;
xi. Any anticipated expenses to the participant for trial participation;
xii. That the participant's trial participation is voluntary, and the participant may decide to stop taking the investigational product or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled;
xiii. The follow-up procedure for participants who stopped taking the investigational product, withdrew from the trial or were discontinued from the trial;
xiv. The process by which the participant's data will be handled, including in the event of the withdrawal or discontinuation of participation in accordance with applicable regulatory requirements;
xv. That by agreeing to participant in the trial, the participant or their legally acceptable representative allows direct access to source records, based on the understanding that the confidentiality of the participant's medical record will be safeguarded. This access is limited for the purpose of reviewing trial activities and/or reviewing or verifying data and records by the regulatory authority(ies) and the sponsor's representatives, for example, monitor(s) or auditor(s), and in accordance with applicable regulatory requirements, IRB;
xvi. That records identifying the participant will be kept confidential and, to the extent permitted by the applicable regulatory requirements, will not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential. The trial may be registered on publicly accessible and recognized databases, per applicable regulatory requirements;

xvii. That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue trial participation;
xviii. The person(s) to contact for further trial information and the trial participant's rights, and whom to contact in the event of suspected trial-related injury;
xix. The foreseeable circumstances and/or reasons under which the participant's trial participation may be terminated.
xx. The expected duration of the participant's trial participation;
xxi. The approximate number of participants involved in the trial;
xxii. That trial results and information on the participant's actual treatment, if appropriate, will be made available to them should they desire it when this information is available from the sponsor.

l. Prior to participation, the participant or the participant's legally acceptable representative should receive a copy (paper or electronic) of the signed informed consent form and any other informed consent materials provided, in accordance with applicable regulatory requirements. During trial participation, the participant or the participant's legally acceptable representative should receive a copy of the consent form updates and any other updated informed consent materials provided.
m. When a minor is to be included as a participant, age-appropriate assent information should be provided and discussed with the minor as part of the consent process, and assent from the minor to enroll in the trial should be obtained as appropriate. As process for re-consent should be considered if, during the course of the trial, the minor reaches the age of legal consent, in accordance with applicable regulatory requirements.
n. When a clinical trial includes participant who may only be enrolled in the trial with the consent of the participant's legally acceptable representative, the participants should be informed about the trial in a manner that facilitates their understanding and, if capable, the participant should sign and date the informed consent form or assent form as appropriate.

11. End of Participation in a Clinical Trial
    a. When a participant decides to stop treatment with the investigational product, stop trial visits or completely withdraw from a trial; is discontinued from the trial; or reaches the routine end of the trial, the investigator should follow the protocol and other sponsor instructions to determine appropriate follow-up measures. This may include instructions to avoid unnecessary loss of already collected critical data in accordance with applicable regulatory requirements.
    b. Although a participant is not obliged to provide a reason(s) for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the participant's rights. The investigator should consider if a discussion with the participant or the participant's legally acceptable representative is appropriate. This discussion

should focus on the reasons for withdrawal to determine if there are ways to address the concerns such that the participant could reconsider withdrawal without unduly influencing the participant's decision. The investigator or delegated investigator site staff should consider explaining to the participant the value of continuing their participation to minimize trial participants withdrawal. In this process, the investigator should ensure that it does not interfere with the participant's decision to refuse or withdraw participation at any time.

c. Where relevant, the investigator should inform the participant about the trial results and treatment received when this information is available from the sponsor after unblinding, with due respect to the participant's preference to be informed.

12. Investigational Product Management
    a. Responsibility for investigational product(s), including accountability, handling, dispensing, administration and return, rests with the investigator/institution. The sponsor may facilitate aspects of investigational product management (e.g., by providing forms and technical solutions, such as computerized systems, and arranging distribution of investigational product to trial participants).
    b. When the investigator/institution delegates some or all of their activities for investigational product(s) management to a pharmacist or another individual in accordance with local regulatory requirements, the delegated individual should be under the oversight of the investigator/institution.
    c. Where the investigator has delegated activities related to investigational product management or aspects of these activities have been facilitated by the sponsor, the level of investigator oversight will depend on a number of factors, including the characteristics of the investigational product, route and complexity of administration, level of existing knowledge about the investigational product's safety and marketing status.
    d. The investigator/institution and/or pharmacist or other appropriate individual, should maintain records of the product's delivery, the inventory, the use by each participant (including documenting that the participants were provided the doses specified by the protocol), and the return to the sponsor and destruction or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial participants. For authorized medicinal products, alternative approaches to the aforementioned may be considered, in accordance with local regulatory requirements.
    e. The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).
    f. The investigator should ensure that the investigational product(s) are used only in accordance with the approved protocol.
    g. When applicable, the investigator or a person designated by the investigator/institution should explain the correct use of the investigational product(s) to each participant and should check, at intervals appropriate for the trial, that each participant is following the instructions properly.

h. The investigational product may be shipped to the participant's location or supplied to/dispensed at a location closer to the participant (e.g., at a local pharmacy or local healthcare center). The investigational product may be administered at the participant's location by investigator site staff, the participant themselves, or a caregiver or a healthcare professional.
i. Investigational product management should be arranged and conducted in accordance with applicable regulatory requirements, and safeguards should be in place to ensure product integrity, product use per protocol and participant safety.

13. Randomization Procedures and Unblinding
    a. The investigator should follow the trial's randomization procedures, if any, and in the case of an investigator-blinded trial, should ensure that the treatment randomization code is broken only in accordance with the protocol. In the case of an emergency, to protect participant safety, the investigator should be prepared and capable from the start of the trial to perform unblinding without undue delay and hinderance. The investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, emergency unblinding to protect trial participant, unblinding due to an SAE) of the investigational product(s).
14. Records
    a. In generating, recording and reporting trial data, the investigator should ensure the integrity of data under their responsibility, irrespective of the media used.
    b. The investigator/institution should maintain adequate source records that include pertinent observations on each of the trial participants under their responsibility. Source records should be attributable, legible, contemporaneous, original, accurate and complete. Changes to source records should be traceable, should not obscure the original entry and should be explained if necessary (via an audit trail). The investigator should define what is considered to be a source record(s), the methods of data capture and their location prior to starting the trial and should update this definition when needed. Unnecessary transcription steps in between the source record and the data acquisition tool should be avoided.
    c. The investigator should be provided with timely access to data by the sponsor and be responsible for the timely review of data, including relevant data from external sources that can have an impact on, for example, participant eligibility, treatment or safety (e.g., central laboratory data, centrally read imaging data, other institution's records and, if appropriate, electronic patient-reported outcome (ePRO) data. The protocol may provide exceptions for access, for instance, to protect blinding.
    d. The investigator should ensure that data acquisition tools and other systems deployed by the sponsor are used as specified in the protocol or trial-related instructions.
    e. The investigator should ensure the accuracy, completeness, legibility and timeliness of the data reported to the sponsor in the data acquisition tools completed by the investigator site (e.g., case report form (CRF)) and in any other required reports (e.g., SAE reports). The investigator should review and endorse

the reported data at important milestones agreed upon with the sponsor (e.g., interim analysis).

f. Data reported to the sponsor should be consistent with the source records or the discrepancies explained. Changes or corrections in the reported data should be traceable, should be explained (if necessary) and should not obscure the original entry.
g. The investigator/institution should implement appropriate measures to protect the privacy and confidentiality of personal information or trial participants in accordance with applicable regulatory requirements on personal data protection.
h. Data reported to the sponsor should be identified by an unambiguous participant code that can be tracked back to the identity of the participant by the investigator/institution.
i. For systems deployed by the investigator/institution that maintain and retain trial data/information, the investigator/institution should ensure that such data are protected from unauthorized access, disclosure, dissemination or alteration and from inappropriate destruction or accidental loss.
j. When using computerized systems in a clinical trial, the investigator/institution should do the following:
    i. For systems deployed by the investigator/institution, ensure that appropriate individuals have secure and attributable access;
    ii. For systems deployed by the sponsor, notify the sponsor when access permissions need to be changed or revoked from an individual;
    iii. For system deployed by the investigator/institution specifically for the purposes of clinical trials, ensure the requirements for computerized systems in section 4 of ICH GCP Annex 1[xvii] are addressed proportionate to the risks to participants and to the importance of the data;
    iv. Where equipment for data acquisition is provided to trial participants by the investigator, ensure that traceability is maintained and participants are provided with appropriate training;
    v. Ensure that incidents in the use and operation of computerized systems, which in the investigator/institution's judgment may have a significant and/or persistent impact on the trial data or system security, are reported to the sponsor and, where applicable, to the IRB.
k. The investigator/institution should maintain the trial records as specified in Appendix C of ICH GCP Annex 1 and as required by the applicable regulatory requirement(s). The investigator/institution should have control of all essential records generated by the investigator/institution before and during the conduct of the trial.
l. The investigator/institution should retain the essential records for the required retention period in accordance with applicable regulatory requirements or until the sponsor informs the investigator/institution that these records are no longer needed, whichever is the longest. The investigator/institution should take measures to ensure availability, accessibility and readability and to prevent unauthorized access and accidental or premature destruction of these records.

m. The investigator/institution should keep the sponsor informed of the name of the person responsible for maintaining the essential records during the retention period; for example, when the investigator site closes or an investigator leaves the site.
n. Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial-related records.

15. Reports
    a. Upon completion of the trial, the investigator, where applicable, should inform the institution. The investigator/institution should provide the IRB with a summary of the trial's outcome, and, if applicable, the regulatory authorities with any required reports.

Appendix A-4 *Emergency/Disaster Preparedness Considerations for Investigators Conducting Human Research*

Investigators conducting human research should be aware of the following additional considerations associated with managing Human Research during an emergency/disaster scenario (e.g., extreme weather events, natural disasters, man-made disasters, infectious disease pandemics, etc.) related to investigators' ongoing interactions with research subjects and the institutional review board (IRB) in such cases.

During Emergency/Disaster Scenarios: Deciding Whether a Study-Specific Risk Mitigation Plan for Ongoing Research Is Needed

In general, investigators should develop a study-specific emergency/disaster risk mitigation plan for their research unless one of the following is true:

- Research does not involve in-person interaction with research subjects.
- Research can be conducted as written while adhering to additional institution-level and HRPP-level guidance and requirements regarding the emergency/disaster event.
- The research is externally sponsored, and the sponsor has developed a protocol-specific risk mitigation plan for the research.
- The research has been voluntarily placed on hold for recruitment and all research procedures (except for necessary follow-up procedures to be done consistently with additional institution-level and HRPP-level guidance and requirements regarding the emergency/disaster event).

Tools and Resources for Developing Study-Specific Emergency/Disaster Risk Mitigation Plans for Ongoing Research

Review HRP-351 - Protocol-Specific Emergency-Disaster Risk Mitigation Planning for general guidance on developing study-specific risk mitigation plans.

Voluntary Holds on Human Research Activities

Investigators may voluntarily elect to place all recruitment, enrollment and research procedures on temporary hold during emergency/disaster scenarios if doing so will better ensure the safety of research subjects and would not create any additional risks to the safety and welfare of research subjects. Such voluntary holds on research activity do not require IRB notification or review.

Submitting Study-Specific Emergency/Disaster Risk Mitigation Plans for IRB Review

If immediate modification of the research is necessary to eliminate an apparent immediate hazard to a subject, take action and notify the IRB within five business days following the standard pathway to submit reportable new information.

For all other study modifications made to ensure the ongoing safety of research subjects during emergency/disaster scenarios, submit a study amendment and all relevant new or modified study materials to the IRB.

Other Reportable New Information Considerations During Emergency/Disaster Scenarios

The IRB's list of reportable events includes two items for which additional clarification and guidance may be helpful during emergency/disaster scenarios:

- ***"Failure to follow the protocol due to the action or inaction of the investigator or research staff."*** Emphasis on action or inaction of the investigator or research staff has been added because this requirement does not include action or inaction of the research subject. For example, study teams may notice an increase in the number of subjects who do not arrive for scheduled research visits under emergency/disaster circumstances. Failure of a research participant to appear for a scheduled research visit is not noncompliance due to action or inaction by the investigator or research staff, and therefore does not require reporting to the IRB.
- ***"Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject."*** During emergency/disaster scenarios, there will be cases where there is sufficient time to receive IRB approval of any proposed modifications to previously approved research, and in such cases, investigators should follow standard IRB procedures for submitting modifications. However, there will be other cases where investigators must make more immediate changes to the protocol or investigational plan to minimize or eliminate immediate hazards or to protect the life and well-being of research participants. Such changes may be implemented without IRB approval, but are required to be reported to the IRB within five business days afterward in accordance with IRB policies and procedures for submitting reportable new information.

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[i] This document satisfies AAHRPP element I.1.A, I.1.C-I.1.F, I-3, I.4.C, I.5.C, I.5.D, I.6.B, I.7.A-I.7.C, I-9, II.2.A, II.2.C, II.2.G, II.2.E-II.2.E.2, II.2.F-II.2.F.3, II.2.I, II.3.C-II.3.C.1, II.3.E, II.3.F, II.3.G, II.4.A, II.4.B, II.5.A, II.5.B, III.1.A, III.1.B, III.1.D, III.1.E, III.1.F, III.2.A, III.2.C, III.2.D

[ii] http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html

[iii] http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf

[iv] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.7

[v] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60

[vi] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61
[vii] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62
[viii] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64
[ix] http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66
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[xvii] https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf