Fred Hutch Cancer Center

Institutional Review Board

Investigator Manual[1]

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[1] This document satisfies AAHRPP element I.1.A, I.1.C-I.1.E, 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

Contents

What is the purpose of this manual?

This document is designed to guide you through policies and procedures related to the conduct of research that are specific to research reviewed by the Fred Hutch Institutional Review Board (IRB).

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 is required to conduct Human Research?

What is Human Research?

The Human Research Protection Program plan 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 *HRP-262 - FORM - Not Human Research Determination*, located on the IRB web site. PIs may not independently determine that a research project does not involve "human research" (also referred to as "human subjects research"), with the exception of research that exclusively involves de-identified information or biospecimens obtained from an IRB pre-reviewed source.

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. Fred Hutch requires investigators to submit for a formal determination of Not Human Research.

What is the Human Research Protection Program?

The *Human Research Protection Program policy* 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 is required to conduct Human Research?

HRP-062 - POLICY - Training describes the training requirements imposed by the IRB. You may have additional training imposed by other federal, state, or institutional policies.

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 Research": Certain categories of Research may meet the criteria for a Not Human Research (NHR) determination. By Fred Hutch policy, it is the responsibility of the institution, not the investigator, to determine Research meets the criteria for Not Human Research, with the exception of research that exclusively involves de-identified information or biospecimens obtained from an IRB pre-reviewed source. Review the *HRP-262 - FORM - Not Human Research Determination* for reference on the categories of research that may be NHR.
- Exempt: Certain categories of Human Research may be exempt from regulation but require IRB review. By Fred Hutch policy, it is the responsibility of the institution, not the investigator, to determine whether Human Research is exempt from IRB review. Review *HRP-275 - FORM - Exempt* 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-276 - FORM - Expedited Review* for reference on the categories of research that may be reviewed using the expedited procedure.
- Review by the Convened IRB: Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

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

The *Individual Conflict of Interest and Conflict of Commitment Policy* describes the conflict of interest policy for investigators and study staff. For the IRB's purposes, any conflict subject to a Conflict Management Plan must be disclosed during the IRB review process.

Who may submit to the IRB?

The Principal Investigator of a study automatically has the authority to submit to the IRB in the system.

In addition, a PI may designate a PI proxy to submit on their behalf: This is equivalent to the PI granting signatory authority.

- PI proxy assignment is done on a study-by-study basis. If one individual manages all of a PI's submissions, that individual must be assigned as the PI proxy for each study.
- More than one PI proxy may be assigned on any given study.
- The PI may update the PI proxies at any time.

When the PI or PI proxy submits to the IRB in the system, they will be asked to attest to the accuracy of the submission, the conduct of the research, and, in the case of the proxy, confirm they have the authority to submit.

For awareness, the PI will receive an email notification any time a PI proxy submits something on their behalf.

The PI retains full responsibility for oversight of the study and all submissions made by the proxy.

How do I submit a new study to the IRB?

Complete the New Study SmartForm in the electronic IRB system, Hutch IRB, and attach all the IRB Application and all requested supplements, have the SmartForm submitted by the PI or a designated PI Proxy by clicking the "Submit" activity. The IRB Application you will attach depends on the type of submission: *HRP-250 - FORM - IRB Application (Contact)*, *HRP-251 - FORM - IRB Application (No Contact)*, or *HRP-262 - FORM - Not Human Research Determination*.

All documents must be submitted as Word documents because this allows the system to enable the Compare feature for future document revisions. The only exception is if you do not have a PDF copy such as for an industry-sponsored protocol or Investigator Brochure.

Maintain electronic copies of all information submitted to the IRB in case revisions are required. Before submitting the research for initial review, you must provide assurances for the following:

A. All of the information provided in the submission is complete and correct;
B. The submission accurately indicates whether the PI or any study team members have a conflict management plan;
C. The PI will conduct this research in accordance with requirements in the *HRP-103 - Investigator Manual* (this document);
D. No research activities will begin until after final IRB approval is received.

In addition, if you are submitting as a PI proxy, you must affirm that the PI is aware of the submission and has given you permission to submit on their behalf.

How do I request to rely on an external IRB?

Complete the New Study SmartForm in the electronic IRB system, indicate that an External IRB will serve as the IRB of Record and attach *HRP-892 - FORM - External IRB Supplement* and all requested supplements. Have the SmartForm submitted by the PI or a designated PI Proxy by clicking the "Submit" activity. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

How do I request that this IRB serve as the IRB of record (sIRB) for my collaborative or multi-site research study?

On the New Study SmartForm in the electronic IRB system, indicate if the study is a multi-site or collaborative research study, then select "Yes" to the question "Will your IRB act as the single IRB of record for other participating sites?" Complete the rest of the New Study SmartForm and attach the IRB Application form and all applicable supplements, including *HRP-254 - FORM - Multi-Center Supplement*. The IRB Application you will attach depends on the type of submission: *HRP-250 - FORM - IRB Application (Contact)* or *HRP-251 - FORM - IRB Application (No Contact)*. Have the SmartForm submitted by the PI or a designated PI Proxy by clicking the "Submit" activity.

Participating sites are added by executing the "Add Participating Site" activity.

NOTE: A study involving multiple Cancer Consortium sites should be marked as a multi-site study in Hutch IRB. The *HRP-254 - FORM - Multi-Center Supplement* is not required if all sites this IRB is reviewing are within the Cancer Consortium.

How do I create a consent document?

Use one of the consent templates to create a consent document:

- Consent for Clinical Research
- Consent for Minimal/Low Risk Studies
- Minimal Risk (Consent R)
- Public Health Sciences Consent for Research
- Public Health Sciences Consent for Minimal Risk Studies
- Assent for Participants Aged 7-13
- Short Form Consent to Participate in a Research Study

Note that all consent documents must contain all of the required elements of consent and all applicable additional elements of consent. See *HRP-090 - POLICY - Informed Consent*.

If your research study meets the requirements for an Exempt determination 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.
- Description of what measures will be followed to protect the privacy of participants and the confidentiality of their information and/or biospecimens

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 in order for the IRB to be able to determine whether informed consent for these activities is required.

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, defer research or disapprove research:

- Approval: Made when all criteria for approval are met.
- 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 available meeting.
- Deferred: Made when the IRB determines that the board is unable to approve research and the IRB suggests modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB in writing.
- 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 writing.

How does the IRB decide whether to approve Human Research?

The criteria for IRB approval can be found at 45 CFR 46.111.

You are encouraged to write your 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 research, requires modifications to secure approval, or has deferred or disapproved the research.

- If the IRB has approved the research: The research may commence once all other institutional approvals have been met. IRB approval is usually good for a limited period of time which is noted in the approval letter.
- If the IRB requires modifications to secure approval: Make the requested modifications and submit them to the IRB. If all requested modifications are made, the IRB may grant 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 defers the research: The IRB will provide a statement of the reasons for deferral and suggestions to make the study approvable and give you an opportunity to respond in writing. Your response will be scheduled for review at the next regularly scheduled meeting of the same Committee that made the deferral determination.
- If the IRB disapproves the research: The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in writing. If you choose to respond, your

response will be scheduled for review at the next regularly scheduled meeting of the same Committee that made the disapproval determination.

All IRB correspondence is sent to the PI, Primary Contact, and PI Proxies. These individuals will receive an automated email notification from Hutch IRB that provides a link to the submission, where the formal result letter is available for download.

In all cases, you have the right to address your concerns to the IRB directly in writing.

What are my obligations after IRB approval?

1) Do not start research activities until you have the final IRB approval letter.
2) Do not start 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. See *HRP-309 - WORKSHEET - Ancillary Review Matrix*.
3) The PI is responsible to be familiar with the *Human Research Protections Policy* (HRPP).
4) To consent participants, use the IRB approved-stamped versions of the consent or ensure the IRB approval date appears on all documents that will be used in obtaining consent.
5) 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.
6) 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.
7) Update the IRB office with any proposed changes to the Principal Investigator.
8) Personally conduct or supervise the research. Recognize that the investigator is accountable for the failures of any study team member or anyone who is delegated to conduct research activities.
    a) Conduct the 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 is obtained in accordance with the relevant current protocol and consent plan as approved by the IRB.
    c) Do not modify the research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects. Review *HRP-119 - POLICY - Modifications to Ongoing Activities*.
    d) Protect the rights, safety, and welfare of subjects involved in the research.
9) Submit to the IRB:
    a) Proposed modifications as described in this manual. (See How do I submit a modification?)
    b) A continuing review application as requested in the approval letter. (See How do I submit continuing review?)
    c) A continuing review submission when the research is closed. (See How Do I Close Out a Study?)
10) Submit within ten calendar days for any event that meets the IRB reporting criteria described in *HRP-124 - POLICY - Reporting Obligations for Principal Investigators*, *HRP-024 – POLICY – Noncompliance*, and *HRP-131 – POLICY – Unanticipated Problems Involving Risks to Subjects or Others*.
11) Submit a Modification if you or a study team member has a new or revised Conflict Management Plan for a financial interest.
12) Do not accept or provide payments to professionals in exchange for referrals of potential subjects (“finder’s fees”).
13) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment (“bonus payments”).

14) Follow the institution's policy regarding enrollment of non-English speakers in research, including translating the full consent form after any use of the short form consent process. Review *HRP-129 - POLICY - Use of Interpreter Services and Translated Documents*.

15) See additional requirements of various federal agencies in Appendix A. These represent additional requirements and do no override the baseline requirements of this section.

16) 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. Clinical Research Support assists this process for investigator-initiated trials; contact CTgov@fredhutch.org.

    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 the overall study PI for an sIRB study when Fred Hutch is the IRB?

1) Coordinate with IRO to determine whether the Fred Hutch IRB can act as the single IRB for all or some institutions participating in the study or if an external IRB will assume oversight.

2) Identify all sites that will be engaged in the human research and requiring oversight by the IRB.

3) Work with IRO on the reliance agreement with relying sites, as applicable.

4) Document roles and responsibilities for communicating and coordinating key information between all sites being reviewed by the Fred Hutch IRB. Generally, the Fred Hutch study team must assume responsibility for coordinating communications between the IRB and the relying sites.

5) Respond to questions or information requests from the sites or the IRB.

6) Provide relying site investigators with the policies of the Fred Hutch IRB.

7) Provide relying site investigators with the IRB-approved versions of all study documents.

8) Help prepare and submit to the Fred Hutch IRB on behalf of all sites that are relying on Fred Hutch. This includes initial review, modifications, changes in PI, reportable new information and continuing review information for all sites, if applicable.

9) Establish a process for obtaining and collating information from all sites and submitting this information to the reviewing IRB. This includes site-specific variations in study conduct, such as the local consent process and language, subject identification and recruitment processes and local variations in study conduct. See *HRP-893 - FORM - Participating Site Supplement*.

10) Ensure that consent forms used by relying sites follow the consent template approved by the reviewing IRB and include required language as specified by the relying sites and undergo IRB review.

11) Provide site investigators with all determinations and communications from the reviewing IRB.

12) Submit reportable new information from relying sites to the reviewing IRB in accordance with the terms outlined in the authorization agreement or communication plan.

13) Report the absence of continuing review information from relying sites if they do not provide the required information prior to submission of the continuing review materials to the reviewing IRB. Notifying the relying site of their lapse in approval and applicable corrective actions.

14) Provide study records to the relying institution, reviewing IRB or regulatory agencies upon request.

15) Follow the institution's policy regarding enrollment of non-English speakers in research, including translating the full consent form after any use of the short form consent process. Review *HRP-129 -*

POLICY - Use of Interpreter Services and Translated Documents. Note: If a participating site under our review has differing policies regarding translations, the most stringent policy should be followed.

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

1) Obtain authorization from the Fred Hutch IRO prior to seeking review by another IRB.
2) Comply with determinations and requirements of the reviewing IRB.
3) In collaboration with the IRO, 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) Obtain IRB approval from the reviewing IRB and satisfy all ancillary reviews required by the protocol or Fred Hutch institutional requirements (e.g., scientific review, biosafety, radiation safety, etc.) prior to enrolling participants in research.
5) In collaboration with the IRO, notify the reviewing IRB when local policies that impact IRB review are updated.
6) 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.
7) Disclose conflicts of interest as required by the reviewing IRB and complying with any additional management plans that may result.
8) 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.
9) When enrolling participants, obtain, document and maintain records of consent for each participant or each participant's legally authorized representative, unless the IRB has granted a waiver of consent.
10) Promptly report to the reviewing IRB any unanticipated problems involving risks to participants or others according to the policies of the reviewing IRB.
11) Provide the reviewing IRB with data safety monitoring reports in accordance with the reviewing IRB's reporting policy.
12) Report non-compliance, participant complaints, protocol deviations or other events according to the policies of the reviewing IRB.

How do I document consent?

Refer to *HRP-090 - POLICY - Informed Consent* and *HRP-129 - POLICY - Use of Interpreter Services and Translated Documents*.

How do I submit a modification?

Complete the Modification SmartForm in the electronic IRB system and attach all requested supplements. *HRP-362 - FORM - Modification Supplement* is required if you are changing "Other parts of the study," but *not* required if you are only changing "Study team members." Have the Modification submitted by the PI or PI Proxy by clicking the "Submit" activity.

To update existing IRB approved documents, you must click **Update** to replace the existing document with the new version.

All documents must be submitted as Word documents because this allows the system to enable the Compare feature for future document revisions. If updating a Word document that already has IRB approval, you only need to replace the existing document (using the **Update** function) with a clean copy. The system automatically creates a tracked changes version.

The only exception is if you do not have a PDF copy such as for an industry-sponsored protocol or Investigator Brochure. If updating a PDF, you need to replace the existing document (using the **Update** function) and also attach a tracked changes PDF version.

Maintain electronic copies of all information submitted to the IRB in case revisions are required. The modification cannot be implemented until IRB approval is received, unless it is a modification to eliminate an apparent immediate hazard to an enrolled participant. Refer to *HRP-119 - POLICY - Modifications to Ongoing Activities* for more information.

How do I submit continuing review?

Complete the Continuing Review SmartForm in the electronic IRB system and attach all requested supplements. *HRP-253 - FORM - Continuing Review Supplement* is required. Have the SmartForm submitted by the PI or PI Proxy by clicking the "Submit" activity. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

If the continuing review involves modifications to previously approved research, submit those modifications either as a combined Modification and Continuing Review or as a separate request for modification using the Modification SmartForm in the electronic system. Note that if submitting a combined MODCR, issues with approving the modification could impact the ability to renew IRB approval on the study, so if the modification is complex it is recommended to submit a modification separately.

If the approval of research expires, all 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. Advertisements currently running in the media must be pulled. Continuing research procedures is a violation of federal regulations. If current subjects will be harmed by stopping research procedures that are available outside the research context, provide these on a clinical basis as needed to protect current subjects. If you believe that current subjects will be harmed by stopping research procedures that are not available outside the research context, identify the research procedures that need to continue and the number of participants affected, describe the reasons that these procedures need to continue, and immediately provide the IRB office with this information.

How do I close out a study?

For studies that have annual continuing review requirements: Complete the Continuing Review SmartForm in the electronic IRB system to request closure and attach all requested supplements. *HRP-253 - FORM - Continuing Review Supplement* is required. Have the SmartForm submitted by the PI or PI Proxy by clicking the "Submit" activity.

For studies that do not have annual continuing review requirements: Complete the Continuing Review SmartForm in the electronic IRB system to request closure. *HRP-253 - FORM - Continuing Review Supplement* is **not** required. Have the SmartForm submitted by the PI or PI Proxy by clicking the "Submit" activity.

Maintain electronic copies of all information submitted to the IRB in case revisions are required.

Important: **All closing criteria must be met for the study to close and no longer have IRB oversight**. A study is closed when:

- Accrual of research participants is complete and all research activities have ceased. This means no interaction/intervention is planned for the purpose of research with research participants and no long-term follow-up.
- Data collection and analysis are complete.
- Identifiable data has been destroyed or archived according to institutional policy; and all remaining biospecimens have been either destroyed or transferred to another IRB file, to the sponsor, or to a designated third-party as required by protocol or contract.

How long do I keep records?

Maintain your research records according to the policies of your institution. If Fred Hutch, refer to the Record Retention Guides on CenterNet.

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

What if I need to use an unapproved drug, biologic, or device and there is not sufficient time for IRB review?

"Not sufficient time" for IRB review and approval is defined by Fred Hutch as seven (7) business days or less. Refer to *HRP-023 - POLICY - Emergency Use or Compassionate Use of an Investigational Drug or Device*.

What if I need to use an unapproved drug, biologic, or device for compassionate use or under expanded access?

If there is sufficient time for IRB review (more than 7 business days), the activity is submitted as a new study in Hutch IRB. Refer to *HRP-023 - POLICY - Emergency Use or Compassionate Use of an Investigational Drug or Device*.

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 Policies and Procedures page of the IRB web site.

For general questions, contact the Institutional Review Office (IRO) at (206) 667-5900 or IRO@fredhutch.org.

For questions related to a specific IRB submission, contact the IRB Coordinator listed on the submission workspace in Hutch IRB.

If you have questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, contact:

Meghan Scott
Director, Institutional Review Office
Institutional Review Office
1100 Fairview Ave. N., J2-100
Seattle, WA 98109
206-667-4372
mscott@fredhutch.org

If you have questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance *that cannot be resolved through the IRO*, or if you have input regarding the Human Research Protection Program, you may contact the Institutional Official (Fred Appelbaum, MD) and/or the Vice President & Chief Compliance Officer (Marcia Gonzales).

Appendix 1: Single IRB Studies

1. That National Institutes of Health expects that all sites participating in multi-site studies involving non-exempt human subjects research funded by the NIH will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46.

    a. This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.

    b. This policy applies to domestic awardees and participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies will not be expected to follow this policy.

    c. Exceptions to the NIH policy will be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.

2. The Office for Human Research Protections expects that all sites located in the United States participating in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

    The following research is not subject to this provision:

    a. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or

    b. Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.

    c. For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.

Appendix 2: 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).

Resource for Developing Study-Specific Emergency/Disaster Risk Mitigation Plans for Ongoing Research

Review *HRP-108 - FLOWCHART - Study-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 10 calendar 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 Modification 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."*** This requirement to report is not relevant if the research subject's action or inaction caused the event. 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 or others. Such changes may be implemented without IRB approval, but are required to be reported to the IRB within 10 calendar days afterward in accordance with *HRP-131 – POLICY – Unanticipated Problems Involving Risks to Subjects or Others*.