Fred Hutch Cancer Center

Institutional Review Board

Policy/Procedure

Title:	Multi-Center Study Coordination – IRB Review and Oversight
Version:	1.00
Effective Date:	February 3, 2025
Responsible Office:	Institutional Review Office (IRO)
Responsible Official / Approved By:	Meghan Scott, IRO Director

POLICY STATEMENT

It is the policy of Fred Hutchinson Cancer Center (Fred Hutch) Institutional Review Board (IRB) that a Fred Hutch principal investigator (PI) coordinating a multi-site study is responsible for the oversight and management of IRB approval for each participating site and individual investigator engaged in research they oversee. When Fred Hutch IRB is the IRB of record for participating sites, the Fred Hutch IRB will evaluate the site investigator's qualifications and the adequacy of the site to conduct the research activities.

DEFINITIONS

See *HRP-001 - Glossary of Terms and Acronyms* for full definitions of the following:

Coordinating Center ***(also known as Operations Center)***

Engaged in Research

Federalwide Assurance (FWA)

IRB of Record *(**also known as Reviewing IRB**)*

IRB Reliance Agreement ***(including Individual Investigator Agreement, IRB Authorization Agreement, Cooperative Review Agreement, and IRB Services Contract)***

Local Research Context

Multi-Site Study

Participating Site

sIRB

PRINCIPLES/OVERVIEW

When the Fred Hutch IRB reviews a multi-site study where the PI is responsible for the operations center or coordinating center (which generally includes managing all protocol updates and controlling the template consents), the Fred Hutch IRB reviews the entire research proposal described in the protocol and consents to ensure it satisfies the criteria for IRB approval. In addition, the Fred Hutch IRB determines whether the oversight responsibilities of the coordinating center are managed properly to safeguard the rights and welfare of research participants.

When the Fred Hutch IRB serves as the IRB of record for participating sites outside the Cancer Consortium (which may or may not include managing all protocol updates and controlling the template consents), the Fred Hutch IRB reviews the entire research proposal described in the protocol and consents to ensure the research satisfies the criteria for IRB approval. In addition, for each institution that is engaged in human subjects research (according to the *OHRP Guidance on Engagement in Research*), a separate Participating Site submission will be created and submitted in Hutch IRB. The site investigator

will complete *HRP-893 - FORM - Participating Site Supplement* (and any required attachments) and provide the information to the Fred Hutch study team to submit on the site's behalf in Hutch IRB for IRB review. Sites outside the cancer consortium do not have access to Hutch IRB. The Fred Hutch IRB will evaluate the qualifications of the site investigator and the adequacy of the site to conduct the research. The IRB, or the Institutional Review Office (IRO) Director (or designee), can request additional information about the site as necessary.

When Fred Hutch is also serving as the single IRB (sIRB), the IRO Director or designee will work closely with the appropriate Fred Hutch research team to ensure adequate mechanisms are in place to facilitate communications between the sIRB and the participating sites relying on Fred Hutch IRB for review.

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to Institutional Review Office (IRO) staff, IRB members, employees of Fred Hutch, and investigators from other institutions who submit research studies to the Fred Hutch IRB for review and approval.

PROCEDURES

1. Study Review (Lead File) When Fred Hutch is the IRB of Record

The Study submission in Hutch IRB includes the appropriate IRB Application and study-wide documents. The Study in Hutch IRB is also called the "Lead" IRB file. The Study must be approved prior to the review of a participating site.

The PI creates and submits a New Study in Hutch IRB, attaching the appropriate *IRB Application* form for review outlining the research to be conducted (see *HRP-121 - POLICY - New Application*). The Study submission SmartForm and IRB Application provide the IRB information about the operations, responsibilities, and procedures used by the coordinating center or single IRB project to oversee the multi-center research. The submission provides information about the entire research proposal under review, regardless of whether all activities are happening locally. Because the coordinating center or single IRB is generally managing all protocol updates and controlling the template consents, the Fred Hutch IRB reviews all the documents to ensure the research as a whole satisfies the criteria for IRB approval.

The IRB's review of the Study submission generally includes the review of the local Cancer Consortium sites. The list of current Cancer Consortium sites is included in the Local Research Locations SmartForm page in Hutch IRB.

The PI also submits *HRP-254 - FORM - Multi-Center Supplement*:

- For operations or coordinating centers: The Multi-Center Supplement helps the Fred Hutch IRB to determine that the operations or coordinating center has sufficient mechanisms in place to ensure that (i) management, data analysis, and Data Safety and Monitoring (DSM) systems are adequate, given the nature of the research involved; (ii) sample protocols and informed consent documents are developed and distributed to each collaborating institution; (iii) each collaborating institution holds an applicable OHRP-approved Assurance; (iv) each site will be reviewed and approved by an IRB prior to the enrollment of research participants; (v) any substantive modification by the collaborating institution of sample consent information related to risks or alternative procedures is appropriately justified; and (vi) informed consent is obtained from each subject in compliance with HHS regulations.
- When Fred Hutch IRB will be serving as the single IRB: The Multi-Center Supplement helps the Fred Hutch IRB determine that the proposal satisfies the Common Rule's cooperative research requirements and/or the NIH's Policy on the Use of a Single IRB for Multi-Site Research.

Note: Certain programs such as the HIV Vaccine Trials Network (HVTN) have coordinating center files that are purely administrative/regulatory and only house overall operations documents and do not house any research activities, even data analysis. These types of files may be submitted on *HRP-251 - FORM - IRB Application (No Contact)*. All other programs serving as a coordinating center should consult with IRO staff before submitting a coordinating center file on this type of application.

2. Review of Participating Sites (outside the Cancer Consortium) When Fred Hutch is the IRB of Record

In order for Fred Hutch to be the IRB of record for a participating site outside the Cancer Consortium, the following items are necessary:

- IRB reliance agreement between Fred Hutch and the site relying on Fred Hutch IRB (unless a broad agreement already exists).
- Local context information about the participating site.
- *HRP-893 - FORM - Participating Site Supplement* and attachments as indicated in the application.
- Participating Site submission in Hutch IRB

The protocol and other study-wide documents included with the Study submission do not need to be attached to the Participating Site submission. The coordinating center or lead study team is responsible for distributing study-wide documents to each participating site.

Note: The participating site's institution may require additional documentation, and the Fred Hutch PI should consult with them to provide such information, as applicable.

a. IRB Reliance Agreement:

When a participating site relies on Fred Hutch as the IRB of record, an IRB reliance agreement must be finalized before the IRB may review the site. For more information on reliance agreements, refer to *HRP-130 - POLICY - IRB Reliance Agreements.*

i. Individual Investigator Agreement*:*

When an individual investigator will be relying on Fred Hutch IRB through an Individual Investigator Agreement, the following documentation must be provided:

- *HRP-278 - FORM - Individual Investigator Agreement* signed by the Individual Investigator and the Fred Hutch IRO Director or designee.
- Signed letter of support from appropriate official at institution where the Individual Investigator will be conducting research.

ii. IRB Authorization Agreement:

For participating sites that will be relying on Fred Hutch IRB through an IRB Authorization Agreement, the following documentation must be provided:

- *HRP-277a - FORM - IRB Authorization Agreement A* signed by an official of the participating site and the Fred Hutch IRO Director or designee.

b. Local Context Information:

In order to conduct the review of research taking place at a participating site outside the Cancer Consortium, the Fred Hutch IRB will take into account the local laws and cultural context of the participating site. A local context consultant from the participating site's community is contacted to provide the necessary contextual information. The IRO Director or designee may communicate with the IRB office at the participating site to assess local context or obtain additional information.

For participating sites Fred Hutch interacts with frequently (e.g., Fred Hutch Network sites), there may be no additional requirements beyond the completed *HRP-893 - FORM - Participating Site Supplement* and associated attachments. For sites Fred Hutch interacts with infrequently, or who are geographically distant from Fred Hutch, a separate *HRP-270 - FORM - Local Context Review* questionnaire will normally be required from a local context reviewer at the participating site. During its review, the IRB may also request or require additional information.

c. Participating Site Supplement:

If the Fred Hutch IRB will be the IRB for participating sites **outside** the Cancer Consortium, the Fred Hutch lead study team works with the site investigator to complete *HRP-893 - FORM - Participating Site Supplement*. This form must be signed by the site PI.

HRP-893 - FORM - Participating Site Supplement provides sufficiently detailed information about the participating site so the Fred Hutch IRB can determine the adequacy of the site and the qualifications of the local investigator and research team.

HRP-893 - FORM - Participating Site Supplement should include confirmation that the local participating site investigator has mechanisms to ensure research personnel are appropriately trained and qualified, and information about the site's adequacy to conduct clinical research such as emergency room access and regulatory support structure.

d. Participating Site submission in Hutch IRB:

The Fred Hutch lead study team will work with the participating site to obtain all required documents. Once the site documents are obtained, the lead study team will create and submit a new Participating Site submission in Hutch IRB on behalf of the site. Sites outside the Cancer Consortium do not have access to the Hutch IRB electronic system.

The lead study team will complete the participating site SmartForm, which include basic information about the site, including any site-specific funding. The following information must be attached to the Participating Site submission in Hutch IRB on the Local Site Document page.

- Site-specific consent form(s) (include track changes version with site-specific changes tracked into the model consent form AND clean version)
- Site-specific materials intended to be seen or heard by subjects
- *HRP-893 - FORM - Participating Site Supplement* and any other IRB supplements prompted by this form.
- Current Curriculum Vitae (CV) or biosketch for the site investigator.
- Human Subjects Protection training completion certificate for the site investigator.
- Good Clinical Practice (GCP) training certificate for the site investigator, if applicable (see *HRP-062 - POLICY - Training*).
- Current medical license for the site investigator if the research involves clinical procedures and/or is subject to FDA regulation 21 CFR 50 and 56.

The PI and PI Proxies of the Study record have permission to submit site materials on behalf of the participating site in Hutch IRB.

IMPORTANT: Research activities at the Participating Site may <u>not</u> begin until the Fred Hutch IRB has issued approval for the site. Approval of the overall study does not cover the activities of the participating site.

The IRB Analyst follows the *HRP-896 - WORKSHEET - Participating Site* for pre-review and post-review steps for the site submission.

After IRB approval of the participating site, IRB correspondence is sent to the PI, Primary Contact, and PI Proxies of the Study record. 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. The IRB Analyst will also send a copy of the IRB result letter to the site PI using the Correspond with Site activity and attaching a copy of the letter. The lead Fred Hutch study team is responsible for providing any IRB approved documents to the participating site for their records. The site investigator can begin research activities once the site is approved.

Refer to *HRP-113 - POLICY - Continuing Review* for information about continuing review of participating sites.

3. Level of Review for Participating Site Applications for non-Cancer Consortium Sites:

Generally, participating sites may be reviewed by an IRB Chair (or designee) via expedited review as a minor change to previously approved research.

However, some sites will be automatically scheduled to a convened IRB meeting for review, for example:

- The PI or other site personnel has a conflict of interest.
- The site is outside the U.S.
- The site anticipates enrolling prisoners.

The assigned designated reviewer reviewing a participating site submission may refer the file to the fully convened IRB meeting if there are concerns about the site's ability to conduct the research, for example:

- The site does not appear to have the necessary facilities to conduct the research activities.
- The PI or study staff does not appear to have the relevant education or training necessary to oversee the local research activities.
- Regulatory or disciplinary actions have been taken against the site investigator in the past, and there are concerns about whether the corrective action taken was sufficient.
- The recruitment or consenting practices of this site do not appear appropriate.
- The site does not describe adequate protections for enrollment of special populations.
- Site-specific compensation to participants appears coercive.
- Privacy protections do not appear adequate.

For Modifications: Generally, the incorporation of IRB-approved model consent form language into the site-specific consent form is considered a minor modification and would therefore also qualify for expedited review.

4. Fred Hutch Investigators Relying on an External IRB as the IRB of Record:

The Fred Hutch Institutional Review Office maintains administrative records on research where Fred Hutch is engaged, regardless of whether Fred Hutch is the IRB of record or not. The IRO pre-review of applications going to an external IRB ensures institutional policies are met and allows the IRO to address research participant questions and concerns.

After a reliance arrangement has been finalized with the external IRB, the PI must first obtain authorization from the Fred Hutch Institutional Review Office (IRO) before submitting to the external IRB. To obtain authorization from the IRO, the PI (or designated PI Proxy) creates and submits a New Study application in Hutch IRB. In the study SmartForm, the PI answers "Yes" to the question "Are you requesting authorization for an external IRB to review the study instead of the Fred Hutch IRB?." The PI will complete the study SmartForm questions and attach the following required materials to the record in Hutch IRB:

- *HRP-892 - FORM - External IRB Supplement* (and any attachments prompted by the form)
- Draft copy of the IRB application form required by the external IRB
- Protocol
- Consent(s)

Once received in the IRO, the IRB Reliance Coordinator follows the *HRP-895 - WORKSHEET - External IRB* to confirm all Fred Hutch institutional requirements have been met. Once the Fred Hutch institutional requirements have been confirmed, the IRO Director or designee will issue *HRP-272 - FORM - IRO Endorsement of External IRB Application* to authorize the study team to submit to the external IRB. The PI, Primary Contact, and PI Proxies will receive an automated email notification from Hutch IRB about this action.

Copies of any initial approval documents issued to the PI by the external IRB must be uploaded in Hutch IRB promptly. The PI (or designed) will run the Add Comment activity to notify the assigned IRB Coordinator. The external IRB approval documentation, including final IRB approved documents should be attached to the activity in Hutch IRB.

Modifications to the study after initial approval do not need to be submitted to the IRO, with the exception of a change in PI.

The PI must provide the IRO with continuing review approvals and current study documents, at least annually. Refer to *HRP-113 - POLICY - Continuing Review* for more information. In the case of minimal risk studies that qualify to forgo annual Continuing Review, the PI must still comply with the Fred Hutch annual Status Report requirements. Refer to *HRP-133 - POLICY - Status Reports for IRB Files* for more information.

SUPPORTING DOCUMENTS

HRP-001 - Glossary of Terms and Acronyms

HRP-062 - POLICY - Training

HRP-113 - POLICY - Continuing Review

HRP-121 - POLICY - New Application

HRP-130 - POLICY - IRB Reliance Agreements

HRP-133 - POLICY - Status Reports for IRB Files

HRP-251 - FORM - IRB Application (No Contact)

HRP-254 - FORM - Multi-Center Supplement

HRP-270 - FORM - Local Context Review

HRP-272 - FORM - IRO Endorsement of External IRB Application

HRP-277a - FORM - IRB Authorization Agreement A

HRP-278 - FORM - Individual Investigator Agreement

HRP-892 - FORM - External IRB Supplement

HRP-893 - FORM - Participating Site Supplement

HRP-895 - WORKSHEET - External IRB

HRP-896 - WORKSHEET - Participating Site

REFERENCES

45 CFR 46.114

21 CFR 56.114

FDA Information Sheets: Non-Local IRB Review

OHRP Guidance on Engagement in Research

OHRP Memorandum – IRB Knowledge of Local Research Context (retired)

FDA Guidance: IRB Responsibility for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether and IND/IDE is Needed

NOT-OD-16-094: Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

VERSION HISTORY

Version	Effective Date
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