Fred Hutch Cancer Center

Institutional Review Board

Policy/Procedure

Title:	IRB Reliance Agreements
Version:	1.00
Effective Date:	February 3, 2025
Responsible Office:	Institutional Review Office (IRO)
Responsible Official / Approved By:	Meghan Scott, IRO Director

POLICY STATEMENT

The Fred Hutchinson Cancer Center (Fred Hutch) will serve as the Institutional Review Board (IRB) of record for Fred Hutch investigators and investigators at other sites with which Fred Hutch has reliance agreements. When single IRB (sIRB) review is called for, Fred Hutch will serve as the single IRB of record for multi-site studies in which a Fred Hutch investigator is involved. Fred Hutch will also rely on review by other sIRBs of multi-site studies involving Fred Hutch investigators. In each situation, the reliance arrangement for IRB review will be agreed upon and documented by the Fred Hutch Institutional Review Office (IRO) and the corresponding organization's IRB office prior to IRB review of the participating site.[1]

Fred Hutch will comply with the requirements set forth in 45 CFR 46, Section 114 and 21 CFR 56, Section 114 regarding cooperative research projects, and with the *NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research*.

This policy only applies to research conducted in the United States.

DEFINITIONS

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

Delayed Onset Research

Engaged in Research

Federalwide Assurance (FWA)

Institutional Official* / *Organizational Official

IRB of Record

IRB Reliance Agreement

An IRB reliance agreement may be one of the following:

a. *Individual Investigator Agreement* – Used for investigators collaborating on research overseen by the Fred Hutch IRB and who are not performing the research under a participating site that has an Federalwide Assurance. An individual investigator can agree to abide by the Fred Hutch IRB review requirements and terms of the Fred Hutch Federalwide Assurance using *HRP-278 - FORM - Individual Investigator Agreement*. See *HRP-115 - POLICY - Federalwide Assurance.*

b. *IRB Authorization Agreement* – Used when the Fred Hutch IRB serves at the IRB of record for participating sites with a Federalwide Assurance engaged in the research, or when a Fred Hutch investigator relies on another institution's IRB as the IRB of record.

[1] HHS: 45 CFR 46.103(e)

c. *Cooperative Review Agreement* – Used for certain institutions in the state of Washington who are engaged in frequent research collaborations with Fred Hutch investigators and wish to avoid duplicate IRB review.

d. *IRB Services Contract* – Used to establish the reliance arrangement between Fred Hutch and an independent IRB where the independent IRB will serve as the IRB of record for certain established research projects. May also be called a master services agreement.

e. *SMART IRB* - A platform that offers a master IRB reliance agreement (the SMART IRB Agreement) and a web-based system (SMART IRB's Online Reliance System) that provides a central process for participating institutions and their investigators to request, track, and document study-specific reliance arrangements.

Local Research Context

Multi-Site Study

Participating Site

Single IRB (sIRB)

PRINCIPLES/OVERVIEW

When a Fred Hutch investigator is engaged in a multi-site research study, Fred Hutch IRB will either:[2]

1) serve as the IRB of record for the Fred Hutch investigator and any other investigators from institutions with which Fred Hutch IRB has a reliance agreement, including in cases where Fred Hutch IRB will serve as the sIRB and perform the IRB review for all participating sites, or

2) rely on another IRB as the IRB of record, including in cases where that IRB will serve as the sIRB, when the Fred Hutch investigator is engaged as a participating site. The Fred Hutch investigator agrees to comply with the determinations and requirements of the reviewing IRB.

IRB reliance requests and agreements must be pre-approved by the IRO Director, or designee.

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to 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. Grant Application Requirements for Multi-site Studies (NIH Funding Only)

a. Effective January 25, 2018, new or competing continuation grant or contract applications/proposals submitted to the NIH are subject to the NIH Single IRB policy if involving multi-site non-exempt human subjects research using the same research protocol. NIH applicants do not need to submit a plan describing the use of a single IRB at the time of application submission. However, applicants required to use a single IRB must provide the name of the single IRB of record during Just-in-time submission before an award is issued. Providing the name of the sIRB of record satisfies the sIRB policy requirement for an sIRB plan for NIH grant applicants.

b. While a formal plan is not required to be submitted to the NIH, the reliance arrangement should be known at the time of funding application. If Fred Hutch is requested to be the sIRB, the PI must discuss these plans with the IRO prior to submitting the funding application to ensure Fred Hutch has the capacity to fulfill this role. Signed reliance agreement(s) do not have to be in place at the time funds are requested, but do need to be completed prior to sIRB review of the research.

2. General Fred Hutch Institutional Requirements for Multi-site Studies

a. The participating site must have an approved FWA with OHRP. In addition, when Fred Hutch relies on an sIRB, the sIRB's registration must be current with OHRP.

[2] Single IRB review required by National Institutes of Health (NIH) for all NIH-funded research effective January 25, 2018. See https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html for guidance.

b. A Fred Hutch PI who coordinates 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 sIRB, each site PI will provide sufficient information about the participating site(s), including the local research context, so the Fred Hutch IRB can evaluate if the site's investigator is qualified, and the site adequate, to conduct the research activities. Refer to *HRP-120 - POLICY - Multi-Center Study Coordination – IRB Review and Oversight* for site submission requirements.

c. The Fred Hutch PI or study team informs the IRO Director (or designee) of a multi-site study(ies) in which the PI plans to participate. The PI identifies the sIRB for the multi-site study in consultation with the IRO Director (or designee) and the participating sites' investigators and IRB offices.

d. The IRO Director (or designee) contacts the IRB office(s) at the other site(s), or at the independent IRB (if applicable), to discuss the following:
    - Accreditation status
    - Type of reliance agreement to be used and scope of reliance (e.g., project-specific or for multiple projects)
    - Who will serve as the IRB of record

e. If there are any questions about the proposed reliance agreement, the IRO Director will consult the Office of General Counsel.

f. A reliance agreement must be in place before a participating site submits their site application to the Fred Hutch IRB.

g. A reliance agreement must be in place before a Fred Hutch investigator may submit research for review to another IRB.

3. Fred Hutch Serves as the sIRB

If it is agreed that the Fred Hutch IRB will be the IRB of record and that the participating site(s) will rely on Fred Hutch, the IRB Reliance Coordinator will determine the type of reliance agreement that will be required for each participating site:

SMART IRB

a. *When possible, Fred Hutch generally prefers to utilize the SMART IRB agreement to enable IRB reliance.* The IRB Reliance Coordinator will determine if the participating site has joined SMART IRB and may use the SMART IRB agreement to enable IRB reliance. Reliance using the SMART IRB agreement may be documented through the SMART IRB online reliance system or outside the reliance system using a letter of acknowledgment.

    SMART IRB online reliance system:

    i. To utilize the online reliance system, the Fred Hutch study team must first submit a request for reliance through the SMART IRB online reliance system.

    ii. The IRB Reliance Coordinator will review the request and determine if Fred Hutch will serve as the reviewing IRB for some or all sites.

    iii. Once reliance has been confirmed in the online reliance system by both Fred Hutch and the participating site, the IRB Reliance Coordinator will prepare the implementation checklist using *HRP-282b - FORM - SMART IRB Letter of Acknowledgement and Agreement Implementation Checklist (Online Request Implementation)* to document the flexible terms to be utilized during the study.

    Documentation outside the online reliance system:

    i. For participating sites that will rely on the SMART IRB agreement, but will not utilize the online system, the IRB Reliance Coordinator will prepare and send a letter of acknowledgement to the participating site utilizing the *HRP-282a - FORM - SMART IRB Letter of Acknowledgement and Agreement Implementation Checklist*.

    ii. The IRB Reliance Coordinator and IRO Director will work with the participating site to confirm all flexible terms to be utilized during the study.

iii. The letter of acknowledgment is signed by the participating site's institutional official and the IRO Director (or designee) to confirm reliance outside the online system.

Institutional Authorization Agreement (IAA)

a. If the participating site has not joined SMART IRB, or the preference is not to utilize SMART IRB to document reliance for a specific study, the IRB Reliance Coordinator will prepare the appropriate reliance agreement outlining responsibilities of the Fred Hutch IRB and the participating site. Refer to *HRP-277a - FORM - IRB Authorization Agreement A*. The IRB Reliance Coordinator will send drafts to the participating site(s) relying on the Fred Hutch IRB.

b. If the participating site proposes edits to the template agreement, the IRB Reliance Coordinator will route the proposed edits to the Office of General Counsel (OGC) for review.

c. Reliance is confirmed once the IAA is signed by both the participating site's institutional official and the IRO Director (or designee).

Individual Investigator Agreement (IIA)

a. For investigators collaborating on research overseen by the Fred Hutch IRB, who are not performing the research under a participating site that has an Federalwide Assurance, reliance will be documented using an Individual Investigator Agreement.

b. The IRB Reliance Coordinator will prepare the IIA utilizing *HRP-278 - FORM - Individual Investigator Agreement*. The IRB Reliance Coordinator will send the draft agreement to the collaborating investigator for review.

c. If the collaborating investigator proposes edits to the template agreement, the IRB Reliance Coordinator will route the proposed edits to the Office of General Counsel (OGC) for review.

d. Reliance is confirmed once the IIA is signed by both the individual investigator and the IRO Director (or designee).

Once reliance is confirmed, and the study protocol and model consent form have been reviewed and approved by the Fred Hutch IRB, the relying site must submit a new Participating Site submission in Hutch IRB for review. The relying site must obtain approval from the Fred Hutch IRB prior to starting research activities at the site. Refer to *HRP-120 - POLICY - Multi-Center Study Coordination – IRB Review and Oversight* for documents required to be submitted in the application.

The PI will provide the IRB with an appropriate level of information regarding the site and the local investigator so the IRB can evaluate the qualifications of the investigator and the adequacy of the site before approving research to be conducted at the site. Information about the site is provided on in the Participating Site SmartForm in Hutch IRB and in *HRP-893 - FORM - Participating Site Supplement* and associated attachments. The IRB, or the IRO Director (or designee), can request additional information about the site, as necessary.

4. Fred Hutch Relies on Another Institution or Organization's sIRB

Institutional IRBs

When a Fred Hutch PI wants to rely on another institution's IRB:

a. The IRO Director (or designee) ensures the institution's IRB is either AAHRPP accredited or has a robust HRPP with policies and procedures that show the IRB can provide sufficient review.

b. For non-AAHRPP accredited organizations, the IRB Reliance Coordinator will consult with the IRO Director to ensure the organization has the appropriate expertise to review a particular study. Factors such as the risk-level of the study, familiarity with the study population, location of research procedures, etc. will be taken into consideration when assessing the external IRB. If the IRB does not appear to have the appropriate expertise, the IRO Director (or designee) will discuss with the site whether a plan to use a different IRB (including Fred Hutch IRB, if applicable) is appropriate.

c. If needed, the IRB Reliance Coordinator will assist with drafting a reliance agreement outlining responsibilities of the Fred Hutch IRB and the institution's IRB. Refer to *HRP-277b - FORM - IRB Authorization Agreement B*.

d. Once the reliance agreement is signed by both the IRO Director (or designee) and the site's institutional official, the Fred Hutch PI will prepare a draft version of the sIRB application. Before

submitting the external IRB, the Fred Hutch PI must submit a New Study submission in Hutch IRB, indicating a request for an external IRB to review the study instead of the Fred Hutch IRB. The PI will complete and attach *HRP-892 - FORM - External IRB Supplement* to the submission. The IRO uses the information in the SmartForm and *HRP-892 - FORM - External IRB Supplement* to maintain a record of the external IRB application and to ensure any other Fred Hutch institutional requirements are met. Refer to *HRP-120 - POLICY - Multi-Center Study Coordination – IRB Review and Oversight* for documents required to be submitted in the application. Once the IRO has confirmed all institutional requirements are met, the IRO will issue *HRP-272 - FORM - IRO Endorsement of External IRB Application*. After receiving endorsement from the IRO, the Fred Hutch PI may submit their application to the external IRB.

e. The Fred Hutch investigator is responsible for submitting IRB-approved documents to the Fred Hutch IRO throughout the life of the study.

Independent IRBs

When a Fred Hutch PI wants to rely on an independent IRB:

a. The IRO Director (or designee) will determine whether a reliance agreement exists and whether it is appropriate for the Fred Hutch PI to use the independent IRB in lieu of the Fred Hutch IRB.

    i. Generally, it is appropriate to rely on an independent IRB for multi-site, industry-sponsored studies where the Sponsor has selected the independent IRB as the central IRB for the study.

    ii. If no reliance agreement exists and it is appropriate to rely on the independent IRB, the IRO Director (or designee) works with OGC to establish a reliance agreement with the independent IRB. OGC must approve the final IRB reliance agreement, as well as the final consent form for each project, if the research is industry sponsored.

b. The IRO Director (or designee) provides written confirmation to the PI and study team when it is appropriate to use an independent IRB.

c. Once the reliance agreement is signed by both the IRO Director (or designee) and the independent IRB's organizational official, the Fred Hutch PI will prepare a draft version of the independent IRB application. Before submitting the independent IRB, the Fred Hutch PI must submit a New Study submission in Hutch IRB, indicating a request for an external IRB to review the study instead of the Fred Hutch IRB. The PI will complete and attach *HRP-892 - FORM - External IRB Supplement* to the submission. The IRO uses the information in the SmartForm and *HRP-892 - FORM - External IRB Supplement* to maintain a record of the external IRB application and to ensure any other Fred Hutch institutional requirements are met. Once the IRO has confirmed all institutional requirements are met, the IRO will issue *HRP-272 - FORM - IRO Endorsement of External IRB Application*. After receiving endorsement from the IRO, the Fred Hutch PI may submit their application to the external IRB.

d. The Fred Hutch investigator is responsible for submitting IRB-approved documents to the Fred Hutch IRO throughout the life of the study.

5. Cooperative Review Agreements

Fred Hutch has grandfathered Cooperative Review Agreements with organizations within the state of Washington that were initially signed prior to June 15, 2015. The following organizations are involved in these agreements and copies are maintained in the IRO:

- University of Washington (UW)
- Seattle Children's Hospital (SCH)
- Kaiser Permanente (formerly Group Health Cooperative)
- Benaroya Research Institute at Virginia Mason (BRI at VM)
- Washington State Department of Health (WSDH)

These institutions may accept, for the purpose of meeting the IRB review requirements, the review of an IRB established under another assurance of compliance with the Department of Health and Human Services. Such acceptance will be in writing, approved and signed by this institutions' directors, approved and signed by correlative officials of each of the other cooperating institutions. Cooperative Review Agreements between Fred Hutch and the institutions described above cover a broad scope of

research projects and sIRB reliance, but generally serve the same function as IRB authorization agreements for individual research projects.

6. Transferring a Study from Another IRB to Make Fred Hutch the IRB of Record

As applicable, the Fred Hutch PI will follow the instructions in *HRP-261 - FORM - Transfer Agreement* and *HRP-260 - FORM - Transfer Supplement* documents when arranging to transfer the IRB review to Fred Hutch IRB from another institution or organization's IRB.

7. Terminating Reliance Agreements

For study-specific reliance agreements, the agreement is valid through the date of study closure or through the date of site closure for participating sites.

To terminate an agreement prior to study closure or to terminate a broad agreement, the Fred Hutch PI, or the participating site when Fred Hutch is the sIRB, submits a letter or email to the IRO that includes the effective end date and reason for the agreement termination. The Fred Hutch IRO or IRB, or the external IRB when Fred Hutch relies on one, may also terminate an agreement as arranged by those offices, as applicable.

Refer to *HRP-111 - POLICY - Closure and Re-Open* for instructions on closing studies and sites.

SUPPORTING DOCUMENTS

HRP-001 - Glossary of Terms and Acronyms

HRP-111 - POLICY - Closure and Re-Open

HRP-115 - POLICY - Federalwide Assurance

HRP-120 - POLICY - Multi-Center Study Coordination – IRB Review and Oversight

HRP-260 - FORM - Transfer Supplement

HRP-261 - FORM - Transfer Agreement

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

HRP-277a - FORM - IRB Authorization Agreement A

HRP-277b - FORM - IRB Authorization Agreement B

HRP-278 - FORM - Individual Investigator Agreement

HRP-282a - FORM - SMART IRB Letter of Acknowledgement and Agreement Implementation Checklist

HRP-282b - FORM - SMART IRB Letter of Acknowledgement and Agreement Implementation Checklist (Online Request Implementation)

HRP-892 - FORM - External IRB Supplement

HRP-893 - FORM - Participating Site Supplement

REFERENCES

45 CFR 46.103

45 CFR 46.114

21 CFR 56.114

FDA Information Sheets: Non-Local IRB Review

OHRP Guidance on Engagement in Research

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

NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

VERSION HISTORY

Version	Effective Date
-	-