FRED HUTCH
Institutional Review Board

Policy/Procedure

Title:	Multi-Center Study Coordination – IRB Review and Oversight
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Responsible Office:	Institutional Review Office (IRO)
Responsible Official:	Meghan Scott, IRO Director  2/20/2020 *Signature/date*

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POLICY STATEMENT

It is the policy of Fred Hutchinson Cancer Research Center (Fred Hutch) 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 *IRB Glossary of Terms and Acronyms* (050) for full definitions of the following:

Engaged in Research

Federalwide Assurance

IRB of Record

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

Local Research Context

Multi-Site Study

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

Participating Site

sIRB

PRINCIPLES/OVERVIEW

When the Fred Hutch IRB reviews a multi-site study where the Principal Investigator (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*), the site investigator will submit a *Participating Site Application* (0395) to the IRB. The Fred Hutch IRB will evaluate the qualifications of the investigator and the adequacy of the site to conduct the research. The IRB, or the 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. Lead File Review When Fred Hutch is the IRB of Record

The main study application and study-wide documents must be approved prior to review of a participating site. This is called the “Lead” or “Master” IRB file.

The PI submits the appropriate *Application for Review* form outlining the research to be conducted (see *IRB Policy 2.1 New Application* [028]). This submission provides 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 lead file *Application for Review* generally includes review of the local Cancer Consortium sites. The list of current Cancer Consortium sites is included on the *Application for Review.*

The PI also submits a *Multi-Center Supplement* (0323):

- 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 the *Application for Review: Human Specimen or Data Research* (0326). 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.
- *Participating Site Application (0395)* and attachments as indicated in the application.

The protocol and other study-wide documents approved under the lead file do not need to be submitted with the Participating Site application. 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 *IRB Policy 2.24 IRB Reliance Agreements* (0178).

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:

- *Individual Investigator Agreement* (052) 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.

The IRB Reliance Coordinator follows the *Screener: New Individual Investigator Agreement* (0136) to process the Individual Investigator Agreement.

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:

- *IRB Authorization Agreement* (043) signed by an official of the participating site and the Fred Hutch IRO Director or designee.

The IRB Reliance Coordinator follows the *Screener: New or Updated IRB Reliance Agreement When Fred Hutch is the IRB of Record* (0293) to process the IRB Authorization Agreement.

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., SCCA Network sites), there may be no additional requirements beyond the completed *Participating Site Application* (0395) and associated attachments. For sites Fred Hutch interacts with infrequently, or who are geographically distant from Fred Hutch, a separate *Local Context Review* (0301) 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 Application:

If the Fred Hutch IRB will be the IRB for participating sites **outside** the Cancer Consortium, once the lead study file is approved, the site investigator completes a *Participating Site Application* (0395) for IRB review. Adding non-Cancer Consortium sites does not require a modification to the Lead study file (the Multi-Center Supplement should be updated at the time of the Lead file's next Continuing Review).

The *Participating Site Application* (0395) 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. Required information includes:

- 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 *IRB Policy 2.20 Training* [038]).
- 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 *Participating Site Application* (0395) 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.

The participating site submission also includes information about any site-specific funding, site-specific waivers, and site-specific consent form/HIPAA language. The IRB, or the IRO Director (or designee), may request additional information or documentation from the site as necessary to ensure risks to subjects are minimized at the participating site.

The IRB Analyst follows the *Screener: Participating Site Application* (0397) to screen and final process the site application.

After IRB approval of the *Participating Site Application* (0395) outlining the site investigator's role in the research, IRO staff notifies the site investigator and the Lead file IRO Contact of the approval. The site investigator can begin research activities.

Refer to *IRB Policy 2.2 Continuing Review* (010) for information about continuing review of participating sites.

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

Generally, participating site files 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 Chair or designee reviewing a participating site 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 performed at Fred Hutch 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, when the Fred Hutch PI is ready to submit to an external IRB for review, the PI must first submit the prepared IRB application to the Fred Hutch IRO using the *External IRB Cover Sheet: New Application* (0327).

Once received in the IRO, the IRB Reliance Coordinator follows the *Screener: External IRB Cover Sheet - New Application* (0292) to screen the external IRB application and create an IRO administrative file to record the research activities. If the Fred Hutch institutional requirements are met, the IRO Director or designee will use the *IRO Endorsement of External IRB Application* (0338) form to authorize the study team to submit to the external IRB.

Copies of any initial approval documents issued to the PI by the external IRB must be sent to the IRO promptly. Modifications to the study after initial approval do not need to be submitted to the IRO. However, as applicable, the PI must provide the IRO with continuing review approvals and current study documents, at least annually. 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 *IRB Policy 2.28 Status Reports for IRB Files* (0403) for more information.

SUPPORTING DOCUMENTS

IRB Policy 2.1 New Application (028)
IRB Policy 2.2 Continuing Review (010)
IRB Policy 2.20 Training (038)
IRB Policy 2.24 IRB Reliance Agreements (0178)
Application for Review Human Specimen or Data Research (0326)
Application for Review Interventional Research (0324)
Application for Review Observational Research (0325)
External IRB Cover Sheet - New Application (0327)
Individual Investigator Agreement (052)
IRB Authorization Agreement – Fred Hutch as Institution A (043)
IRB Authorization Agreement – Fred Hutch as Institution B (043)
IRB Glossary of Terms and Acronyms (050)
IRO Endorsement of External IRB Application (0338)
Local Context Review (0301)
Multi-Center Supplement (0323)
Participating Site Application (0395)
Screener: External IRB Cover Sheet – New Application (0292)
Screener: New or Updated IRB Reliance Agreement When Fred Hutch is the IRB of Record (0293)
Screener: New Individual Investigator Agreement (0136)
Screener: Participating Site Application (0397)

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