Guidance on Single IRB Review Process

This document outlines how the DFCI IRB may rely on an external IRB to serve as the IRB of Record for a Dana-Farber Harvard Cancer Center (DF/HCC) site or Investigator. Additionally, this information sheet outlines the DFCI IRB policy on serving as the single IRB (sIRB) for sites external to the DF/HCC Consortium.

As of January 25, 2018, the single IRB mandate requires that NIH funded multisite studies, where all sites will conduct the same protocol for non-exempt research, undergo IRB review at a single IRB. The NIH mandated the use of single IRBs as a contingency for funding of domestic multisite studies submitted after that date. The NIH issued this policy to reduce burden and streamline the IRB process.

As of January 20, 2020, the U.S. Department of Health & Human Services (DHHS) extended this mandate to all domestic multisite non-exempt research studies.

Definitions

1. **Engaged**: an institution is engaged in human subjects research when its employees or agents either intervene or interact with living individuals, or obtain individually identifiable private information, for research purposes.

2. **Single IRB:** the IRB that has been selected to conduct the IRB review of research studies for all sites participating in a multisite study. This may also be referred to as the IRB of Record.

3. **Relying IRB**: the IRB that has ceded IRB review to the IRB of record.

4. **Reliance Agreement/IRB Authorization Agreement**: a formal written agreement between two or more organizations collaborating in non-exempt human subjects research that outlines each organization's responsibilities in the oversight of research and identifies which IRB will serve as the IRB of Record for the proposed study.

5. **Master Reliance Agreement**: An IRB Authorization Agreement designed to cover more than one future multisite study involving two or more sites.

General Description

The Dana-Farber Cancer Institute IRB (DFCI IRB) functions as the IRB of record for institutions that comprise the DF/HCC Consortium. All oncology related research conducted by the following institutions fall under the jurisdiction of the DFCI IRB:

- Beth Israel Deaconess Medical Center (BIDMC)

- Boston Children's Hospital (BCH)
- Brigham and Women's Hospital (BWH)
- Dana-Farber Cancer Institute (DFCI)
- Massachusetts General Hospital (MGH)
- The Broad Institute

The DFCI IRB has a master reliance agreement in place with MGB IRB, BCH IRB and BIDMC IRB to allow the DFCI IRB to oversee the oncology research conducted at DF/HCC. When there is a request by a DF/HCC investigator for DFCI IRB to rely on an IRB outside of the DF/HCC, each site's respective IRBs will also need to enter into a reliance agreement along with the DFCI IRB.

The DFCI IRB also reviews oncology related research for DF/HCC satellite sites and affiliated sites. When requested, the DFCI IRB will serve as the IRB of record for other research sites collaborating with a DF/HCC investigator. The DF/HCC Office for Human Research Studies (OHRS) is the office that oversees the DFCI IRB and communicates IRB determinations to participating DF/HCC sites

Reliance Agreements

The DFCI IRB has entered into a master reliance agreement with the National Cancer Institute Central IRB (NCI CIRB) to review oncology research conducted at DF/HCC sites.

The DFCI IRB has additional master reliance agreements with the following IRBs for review of DF/HCC conducted research:

- National Marrow Donor Program IRB (NMDP IRB)
- Western Copernicus Group IRB (WCG IRB)

When possible, OHRS will enter into reliance agreements using the SMART IRB common reliance agreement platform. SMART IRB is a platform that outlines the responsibilities, policies and procedures that will be adhered to by the investigator(s) and IRB(s) involved and enables reliance agreements for multisite studies.

Establishing a New Reliance Agreement with a sIRB

The criteria provided below will be considered by OHRS when deciding whether to rely on an external IRB:

- Current approved FWA, IORG, and IRB numbers with OHRP
- Current AAHRP Accreditation
- Qualification and experience in the review of oncology research, such as a designated NCI Comprehensive Cancer Center
- Requirement by funding source to use a sIRB
- No FDA warning letters within the past 5 years.

After evaluation of the above criteria, if OHRS determines that the external IRB may serve as the IRB of Record, a reliance agreement will be negotiated. It may take up to several weeks to finalize the new reliance agreement.

DF/HCC investigators should not commit to relying on an external IRB, or complete site activation for any DF/HCC participating sites without consulting with OHRS.

OHRS **will not** enter into a reliance agreement for the following scenarios:

- Institutions located outside of the United States
- Exempt research studies and/or non-NIH funded research limited to chart reviews / secondary research

OHRS reserves the right to decline entering into a reliance agreement or terminating an existing agreement for any reason including, but not limited to, the type of research, the risk of the research, the qualifications of the study staff, the resources required to conduct the research.

Due to the NIH's mandate for the use of a sIRB, if a decision is made to decline reliance on a NIH-funded study that requires a single IRB, the study will be unable to be conducted at the DF/HCC site. If a decision is made to decline a reliance agreement on a study that does not have NIH funding, OHRS will not execute the reliance agreement, and the DF/HCC investigator should submit the study directly to the DFCI IRB for oversight.

Operational Steps to Request to Rely

Please Note: A request to rely is not required for studies under the NCI CIRB or NMDP IRB.

Research teams must submit the Request to Rely form when a DF/HCC site would like to cede IRB review to an external IRB. OHRS will review the request and route to the appropriate participating DF/HCC consortium site IRBs for individual approval.

Once the Request to Rely is in place, a Notification Request to Rely Approval memo will be sent to the research team. **This memo does not constitute IRB approval**. OHRS will work in conjunction with the research team to finalize the IAA as necessary. After the Request to Rely is completed, the research team will submit a sIRB New Protocol Application submission to initiate any required ancillary, feasibility, and DF/HCC SRC review.

If the DF/HCC participating site's IRB determines that the study **may not** cede IRB review, a Notification Request to Rely Denial memo will be sent to the research team. This memo will provide information on why the request was denied and any next steps that are required by the research team.

To add a new DF/HCC site to a sIRB study, the research team must submit a Request to Rely form.

sIRB New Protocol Application to OHRS

Research teams may submit to the appropriate IRB of record after the Request to Rely is approved (as necessary). Please note that if the SRC or other ancillary reviews require any changes to the submitted documents, these changes will need to be communicated to the IRB of record. Therefore, OHRS recommends for some studies (e.g., investigator sponsored trials) to wait until the SRC approval is granted to submit to the IRB of record. For other studies (e.g.,

sponsor-initiated trials), submitting to the IRB of record and iRIS concurrently will decrease the time to activation.

Please note that NCI CIRB new protocol submissions do not receive full SRC review.

The research team should expect to submit to OHRS the protocol, consent documents including local context information, site specific worksheets, site specific documents created during review (alert pages, patient information documents), etc. Documents will vary by study type and the IRB of record.

1. Ancillary, Feasibility, and Scientific Reviews
   Once the sIRB NPA has been submitted, the protocol will be routed for the following required DF/HCC Ancillary, Feasibility, and Scientific reviews, as applicable
   - Biosafety Committee
   - Radiation Safety Committee
   - Scientific Review Committee
   - All applicable feasibility review committees (e.g., Conflict of Interest, Pathology, Nursing, Data Security)

Research team members' financial conflict of interest (FCOI) disclosures and/or institutional conflict of interest (ICOI) management plans may also need to be submitted to the sIRB who will review and determine the appropriateness of the Conflict of Interest management plan. The sIRB may also have to review site specific patient information sheets and consent forms that incorporate the FCOI and ICOI language.

2. Once the sIRB has approved your site for participation, the following documents are required to be submitted to OHRS, as applicable:

   - sIRB approval document for both the overall study and the local site(s)
   - sIRB approved consent document
   - sIRB approved protocol document
   - sIRB approved Study Recruitment Materials
   - sIRB approved Data Collection Materials Given to participants: questionnaires, surveys, etc.
   - Alert page
   - Investigator Brochure
   - Laboratory Manual
   - Pharmacy Manual
   - Imaging Manual
   - Instructions for Use

OHRS will perform an administrative review of the sIRB approved documents to ensure compliance with local institutional requirements and route to the Office of Data Quality for activation.

When the DFCI IRB acts as the Privacy Board for sIRB studies, OHRS will ensure compliance with HIPAA regulations 45 CFR Parts 160 and 164 via the expedited review procedure.

DFC/HCC Research Team Responsibilities

- Submit applicable amendments, progress report materials, and pertinent new reportable information to the sIRB and DFCI OHRS
- Ensure that any reports of unanticipated problems and/or protocol violations that may place a participant at greater risk than previously known or recognized as well as any instances of non-compliance including any incidents that have adversely impacted data integrity are reported to OHRS and/or the external IRB in a timely manner
- Disseminate IRB approved materials to relying sites
- Act as the liaison with the sIRB for the relying site research teams and OHRS
- Ensure all engaged DF/HCC affiliates have completed the required research training as defined by institutional policies (*as outlined in EDU-100)*
- Ensure all engaged DF/HCC research team members have disclosed any Conflicts of Interest COI and any management plans required by the Office of Research Integrity to the sIRB and that they have been implemented
- Ensure all institutional requirements, beyond those of OHRS, have been met (e.g., Clinical Trial Agreements, Material Transfer Agreements, Data Use Agreements, Activation)

The cost to rely on an external sIRB will largely depend on the fee schedule of the external IRB, whether it is an independent or academic IRB. It is the responsibility of the principal investigator to ensure costs are covered through the grant as a direct cost or in the clinical trial agreement with the sponsor. The principal investigator and research team are responsible for ensuring appropriate payment is made to the IRB of Record as stipulated in the clinical trial agreement or grant.

DFCI OHRS Responsibilities

- Ensure that the reliance agreement is appropriately executed
- Manage Requests to Rely submissions and collaborate with the DF/HCC participating sites to determine if ceding IRB review is appropriate
- Communicate decision on reliance and initiate communications with relying sites regarding reliance agreement / reliance platform software options
- Provide local context information when requested by the IRB of Record with assistance from DF/HCC research teams
- Ensure the sIRB application is submitted and all required ancillary, feasibility, and scientific committee reviews are completed (e.g., Radiation Safety, Biosafety, Nursing, Pharmacy, SRC, ORI/COI, Pathology, Data Security Review)
- Ensure that external IRB determinations are uploaded and maintained, as appropriate

Reporting Requirements to the DFCI IRB

Amendments

The research team maintains responsibility for providing OHRS with all revised protocol documents approved by the sIRB. Revised documents must be submitted to OHRS at time of notification of the sIRB approval of the amendment.

- The research team is responsible for submitting the sIRB approval documents as well as the sIRB Amendment Application
- All amendments may be subject to, feasibility, ancillary, and SRC review. An outcome letter for such reviews will be provided.
- The expectation is that all sIRB approved amendments will activated within 30 days of OHRS receipt

Progress Reports

The research team maintains responsibility for providing OHRS documentation of continuing review approval from the sIRB. If continuing review approval is not provided to OHRS before the approval lapses, the DF/HCC approval will expire, and subjects will not be able to continue the research at any DF/HCC site until current continuing review approval is provided.

- The research team is responsible for submitting the sIRB approval documents as well as the Progress Report Application to OHRS
- The minor deviation/violation log will be reviewed, if applicable.
- The study will also be routed for a Scientific Progress Review, if applicable.

Adverse Events, Unanticipated Problems, Deviation, Violation, Other Events

DF/HCC principal investigators must adhere to the policies and procedures of the IRB of Record for reporting purposes. It is expected that the principal investigator and research team read and familiarize themselves with the sIRB requirements prior to initiation of research at DF/HCC. In addition to adhering to the IRB of Record's policies and procedures, the principal investigators and research teams are expected to report to OHRS any unanticipated problems or protocol violations which may place subjects at greater risk than was previously known or recognized as well as any instances of non-compliance including any incidents that have adversely impacted data integrity. In the unlikely event that the study is suspended or terminated for any reason, it is expected that the DF/HCC principal investigator report this event to the OHRS.

DFCI as the IRB of RECORD

DFCI is willing to act as the IRB of record for sites outside of the DF/HCC. OHRS will make a determination as to the appropriateness of acting as the IRB of record on a case-by-case basis. The following may be taken into account when determining whether the DFCI IRB can act as the IRB of record:

- Whether participating sites use the SMART Reliance Agreement.
- Whether relying sites are AAHRPP accredited.
- Whether external sites can act as privacy boards, as necessary, for their respective institutions.
- The number of relying sites
- The level of risk associated with the research.

Investigators are advised not to state that the DFCI IRB will be the IRB of Record for the proposed National Institutes of Health (NIH) research without documentation from OHRS. Research teams may reach out to OHRS@dfci.harvard.edu or OHRSCentral_IRB@dfci.harvard.edu should they require confirmation of OHRS' willingness to act as the IRB of record for preliminary grant applications, or at the time of Just In Time.

Questions about sIRB should be directed to OHRS by emailing OHRS@dfci.harvard.edu or OHRSCentral_IRB@dfci.harvard.edu.