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 multi-site 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 multi-site 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 multi-site non-exempt research studies.

Definitions

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

2. **Single IRB (sIRB):** an IRB that has been selected to conduct the IRB review of research studies for all sites participating in a multi-site study. The IRB of Record for the study.

3. **Relying IRB**: the IRB that has ceded IRB review to another IRB to provide ethical oversight for a multi-site study or set of studies.

4. **Reliance Agreement** (*also referred to as the IRB Authorization Agreement*): a formal written agreement between 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 all future multi-site studies involving two or more sites.

General Description

The Dana-Farber Cancer Institute IRB (DFCI IRB) functions as the single IRB (sIRB) of record for institutions that comprise the Dana-Farber Harvard Cancer Center (DF/HCC) Consortium. All oncology related research conducted by the following five Harvard clinical 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 DFCI IRB has reliance agreements in place with Partners 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 a sIRB, each site's respective IRBs will also need to engage in a reliance agreement along with the DFCI IRB.

The DFCI IRB also reviews oncology related research for DF/HCC satellite sites and affiliated sites and in limited circumstances independent institutions such as the Broad Institute. 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 reliance agreement with the National Cancer Institute Central IRB (NCI CIRB) to review oncology research conducted at DF/HCC sites. **A request to rely is not required for studies under the NCI CIRB.**

The DFCI IRB has existing reliance agreements available for the following IRBs for review of DF/HCC conducted research:

- National Marrow Donor Program IRB (NMDP IRB)
- Western IRB (WIRB)

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's for multi-site studies.

Establishing a New Reliance Agreement on a sIRB

The criteria provided below will be considered by OHRS when deciding whether reliance on an external IRB is applicable:

- 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 external parties or complete site activation for any DF/HCC participating site(s) without consulting with OHRS.

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

- For institutions located outside of the United States
- In most cases, 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 proposed study 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, etc.

Due to the NIH's mandate for the use of a sIRB, if a decision is made to decline reliance on an NIH-funded study that requires sIRB, the study will be unable to be implemented 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

The Request to Rely form must be submitted to OHRS by the research team 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 to determine if a cede review is appropriate for approval.

Once the reliance agreement is in place, a Notification Request to Rely Approval memo will be sent to the research team. **This memo does not constitute IRB approval**. A sIRB New Protocol Application submission is required to initiate ancillary, feasibility and DF/HCC SRC review, if applicable.

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.

A study must receive all ancillary, feasibility and SRC approvals prior to a DF/HCC site being added or approved by the sIRB.

Note: 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

1. When submitting a new application for review, include:
   - sIRB New Protocol Application (sIRB NPA)
   - Alert Page (if applicable)
   - Outside Interest Log Sheet (if applicable)
   - Participant Drug Diary (if applicable)
   - Pharmacy Manual, Laboratory Manual, Imaging Manual (if applicable)
   - Investigators Brochure / Instructions for Use (if applicable)
   - Protocol Document

2. Ancillary, Feasibility, and Scientific Reviews
   Once the sIRB NPA has been submitted, the protocol will be routed for the following required Cancer Center Ancillary, Feasibility, and Scientific reviews, as applicable:
   - Biosafety Committee

- Radiation Safety Committee
- Scientific Review Committee
- All applicable feasibility review committees (e.g. COI, Pathology, Nursing, Data Security)

OHRS will provide the SRC Outcome Letter to the research team when all the reviews have been completed**. Please note that NCI CIRB new protocol submissions do not receive full SRC review.** At this time, the lead research team will notify the sIRB of participation by following the steps outlined by the sIRB.

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 COI management plan. The sIRB may also have to review site specific patient information sheets and consent forms that incorporate the FCOI and ICOI language.

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

- 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 (if applicable)
- sIRB approved Data Collection Materials Given to participants: questionnaires, surveys, etc. (if applicable)
- Alert page (if applicable)
- Investigator Brochure (IB) (if applicable)
- Laboratory Manual (if applicable)
- Pharmacy Manual (if applicable)
- Imaging Manual (if applicable)
- Instructions for Use (if applicable)

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 final activation steps including research team Operational Readiness.

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 modification(s)/amendment(s), 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 rely 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 (*Training requirements are outlined in EDU-100.)*
- Ensure all engaged DF/HCC affiliates have disclosed any Conflicts of Interest (COI) and any COI 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. CTA execution, MTA, DUA, 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.

Note: For more information on the responsibilities of an Overall Principal Investigator and designated Lead Research Team member, please review the **SMART IRB** checklist.

DFCI OHRS Responsibilities

- Ensure that the reliance agreement is appropriately executed
- Manage Requests to Rely submissions and collaborate with the DF/HCC participating site(s) to determine if ceding IRB review is appropriate
- Communicate decision on reliance and initiate communications with relying site regarding reliance agreement / reliance platform software options
- Provide local context information when requested by the IRB of Record with assistance from DF/HCC research team(s)
- Ensure the sIRB application is submitted and all required ancillary, feasibility, and scientific committee reviews are captured and documented (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 provided and submitted to OHRS at time of notification of the sIRB approval of such documents.

- The research team is responsible for submitting the sIRB approval documents as well as the sIRB Amendment Application
- All amendments may be subject to, if applicable, site 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 local (or DF/HCC) approval will expire, and subjects will not be able to start and/or continue the research at DF/HCC 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 IRB 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 IRB of Record policies and procedures. In addition to adhering to the IRB of Record's policies and procedures, the principal investigators and research teams are expected to report to the OHRS any reports of unanticipated problems and/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

The DFCI IRB may act as the sIRB for oncology related studies (as defined by the NCI Cancer Center Support Grant) with a limited number of non-DF/HCC external sites that have an existing relationship with the DF/HCC, such as Harvard Catalyst members. DF/HCC may also act as the sIRB for oncology related research at Harvard Medical School and Harvard School of Public Health. The DFCI IRB is not able to serve as a sIRB for interventional or greater than minimal risk studies for sites external to DF/HCC.

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 the OHRS. If an exception is granted, OHRS may limit the total number of non-DF/HCC sites that may rely on the DFCI IRB.

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