

Relying on an External IRB: Step-By-Step Guidance

The following guidance is intended to give an overview of the process when DF/HCC sites rely on external IRBs. This guidance is intended to be used when a new study is being started, or DF/HCC sites are joining an existing IRB study. Some guidance is subject to the requirements of the relied upon IRB and the order may be modified as required.

Please note that when DF/HCC sites chose to rely on an external IRB, the IRB review is the only aspect of the protocol review being completed by an external group. All other reviews (e.g., feasibility, ancillary, and scientific reviews) still occur at DF/HCC and must be considered as part of the timeline of submission. This includes other reviews and signoffs like the Office of Research Integrity, the Clinical Trials Agreement offices, Clinical Trials offices, etc.

Study Start-Up Compliance Meeting

Study teams are encouraged to contact OHRSCentral_IRB@dfci.harvard.edu to set up an initial meeting if the investigative team is new to the reliance process. OHRs will provide research teams with an overview of the process as described below, as well as answer any other study-specific questions.

Submit the Request to Rely

The purpose of the Request to Rely submission is to allow OHRs to determine the feasibility of ceding IRB oversight to an external IRB. Submitted in iRIS, the Request to Rely provides OHRs with information on the research purpose, the DF/HCC participating sites and their role in the research, and the proposed IRB of record.

- OHRs may reach out to the point of contact on the request to rely with any additional questions regarding the request.
- OHRs will communicate with the IRB offices at each participating DF/HCC to seek their approval to rely on the external site
- OHRs will provide a confirmation email to the point of contact to provide the outcome of the Request to Rely, via letter.

Note: The Notification of Request to Rely Approval memo does not constitute IRB approval. OHRs requires that the research team submit a New Project Application in iRIS as outlined in the flowchart above.

Request to Rely submissions are **not required** for studies that rely on **NCI CIRB** or **NMDP IRB**. Those reliance agreements are already in place.

When submitting to independent IRBs (e.g., WCG and Advarra), the Request to Rely Approval memo is used as confirmation that DF/HCC sites are willing to rely on the IRB of record.

Please keep in mind that federal requirements mandate which studies must rely on a single IRB of record, protocols which do not fall under the sIRB requirement will be considered for reliance on a case-by-case basis. Please also note that DF/HCC sites will not rely on an external IRB for exempt research. Please contact OHRSCentral_IRB@dfci.harvard.edu should there be any questions about whether a study may qualify for an exemption, and how best to approach the exemption process.

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OHRS aims to process Request to Rely submissions within **10 business days**. However, this timeline may be prolonged if additional clarification or information is required to assess the request, and the length of time for each DF/HCC site to agree to the reliance.

If the study team has not yet contacted OHRS for an initial meeting, the Request to Rely Approval memo will prompt them to do so again.

Create and Execute the Reliance Agreement

When relying on an external IRB, each DF/HCC institution will enter into a reliance agreement with the IRB of record separately. OHRS will maintain the fully executed reliance agreements for each study.

The timing of creating the reliance agreement may depend on the IRB of record, and the relying sites. While the DF/HCC sites maintain some master reliance agreements (e.g., an agreement that is in place to cover all prospective agreements), many times a reliance agreement will need to be set up for an individual study. OHRS can advise on this for the specific requests. Master reliance agreements are in place with the NCI CIRB, NMDP, and WCG.

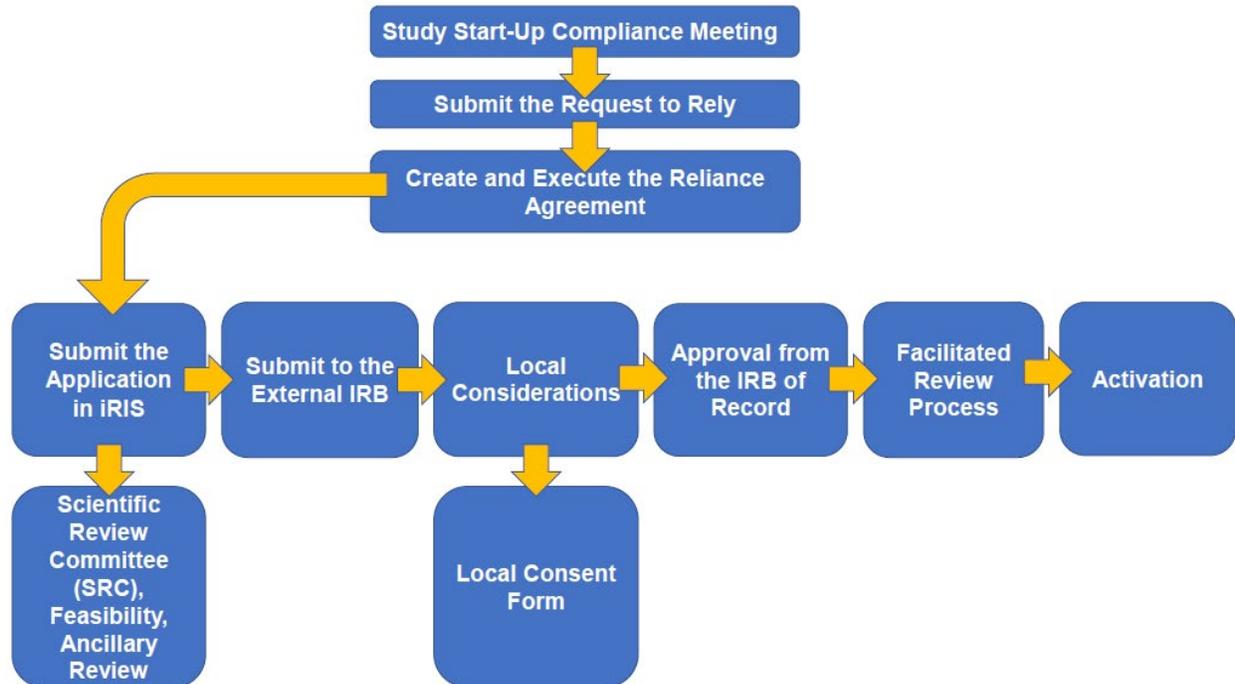
Whenever possible, the DF/HCC sites will utilize the [SMART IRB](#) system, an online reliance system that can facilitate the creation of reliance agreements for single protocols. Over 1000 institutions have signed on to the SMART IRB reliance platform. It will be up to each site to determine the appropriate platform to create the reliance agreement. If using the SMART platform, research teams will need to create a [user ID](#) and create a new reliance within the system; each participating IRB's point of contact will coordinate the sign off on the submission established by the research teams. The SMART system has several documents and work instructions to create the request in the system.

Protocols which are utilizing the [iREX](#) system (a web-based portal supporting single IRB review documentation for sIRB studies) will follow a different workflow and instructions will be provided by the iREX contact person.

When relying on an external IRB, the IRB of record typically requests a local context survey, which provides further information regarding DF/HCC requirements. The local context questionnaire helps the reviewing IRB collect information about requirements including any state or local laws, regulations, institutional policies, standards or other local factors relevant to the research being conducted at DF/HCC. Those IRBs with whom DF/HCC has an established relationship (e.g., NCI, WCG, Advarra, and NMDP) have already reviewed and approved the DF/HCC local context information. Other IRBs may request a local context form, or other document be filled out by the DF/HCC research teams to facilitate their review.

Timing of Submission

The below flowchart depicts the required steps when a research team or sponsor decides to cede IRB oversight to an external IRB. Each step is described in further detail below.



Submit the Application in iRIS

After the request to rely has been approved, the DF/HCC research team will submit a New Protocol Application in iRIS for review. This will create a DF/HCC study number for the project. The New Protocol Application should be filled out fully, and all supporting study documents should be submitted. A draft version of the protocol and consent may be submitted, however all other documents required for ancillary reviews should be provided at this point, this includes may not be limited to:

- Investigator Brochure
- Laboratory Manual
- Pharmacy Manual
- Imaging Manual
- Instructions for Use

Scientific Review Committee (SRC), Feasibility, Ancillary Review

iRIS will automatically route to the required feasibility and ancillary reviews, based on the information provided in the New Protocol Application. The committees may request changes to the form which will need to be communicated to the IRB of record. The types of reviews required will depend on the type of submission. OHRS will also route the New Protocol Application for either expedited or full Scientific Review

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Committee (SRC) review as required by the type of protocol submission, and requirements of the cancer consortium grant.

Submitting to an External IRB

Depending on the type of external IRB (i.e., academic, commercial, NCI CIRB), DF/HCC research teams may have to create an account in the external IRB's system before submitting to the IRB of record. For further information on creating an account for Advarra, WCG IRB, or NCI CIRB, see the document for [Creating a Single IRB Platform Account](#).

DF/HCC research teams are responsible for following the IRB of record's process for submission and approval. Once the IRB of record has approved DF/HCC's participation in the study, the approval documents (e.g., approval letter/memo or certificate of action, and locally approved consent documents and other patient facing documents) may be submitted in iRIS.

Local Considerations

If requested by the IRB of record, OHRS and the DF/HCC study teams may receive a local context survey. This survey will provide the IRB of record with any important considerations for their review. OHRS has negotiated approved local context information with Advarra, WCG, NMDP and the NCI CIRB. For other external IRBs, the IRB of record may request that the research team and OHRS provide study specific consent information to be included in the local consent form. The responsibility of updating the local consent forms will fall on either the research team and OHRS, or the external IRB, depending on the IRB of record.

Creation of Local Consent Form

If consent will be obtained DF/HCC sites, the consent form must be updated to include language that is required by the DF/HCC (e.g., injury language, local contact information, and DF/HCC HIPAA language).

When relying on NMDP, WCG, and Advarra, the IRB analysts at the respective IRB of record will update the consent forms that have been approved at the protocol level for each site with the local context information on file at that site. This information is available on the OHRS website.

The NCI CIRB will provide a model consent form and the research teams are responsible for adding in the local context information.

When working with all other IRBs of record, the Core site study team should receive IRB of Record approved consent template(s) for insertion of local language. The core site team will insert the local language (including any required language requested by the DF/HCC ancillary reviews) using tracked changes and confirm with OHRS that the updates are correctly included. This can be done by emailing OHRSCentral_IRB@dfci.harvard.edu. OHRS can advise on the appropriate language to be included into the template.

The IRB of Record Approves DF/HCC sites

As part of their review, the IRB of record will review the local consent forms and approve the DF/HCC sites. The IRB of record will provide an approval letter/memo. This may be the initial study approval, site approval, or an amendment adding DF/HCC sites to the study protocol.

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The research team is responsible for providing OHRS with the approved study documents, and the corresponding approval letter/memo to be uploaded into iRIS. This may be accomplished one of two ways:

- The study team may email the approved documents to OHRSCentral_IRB@dfci.harvard.edu and OHRS will upload the documents on the study team's behalf.
- Alternatively, if the ancillary and SRC reviews are completed prior to the receipt by OHRS of the IRB approval, OHRS will issue a condition in iRIS to request these documents for the study team to upload.

DFCI IRB Facilitated Review Process

Once the New Protocol Application has completed all necessary local reviews, it will advance to the IRB queue in iRIS. At this point, OHRS staff will conduct a facilitated review to confirm the submission contains all the necessary documentation from the IRB of record. Depending on the IRB of record and the submission, during the facilitated IRB review, OHRS will:

- Review the external IRB approval letter/memo for the following elements:
 - Expiration date
 - Approval Date
 - List of IRB reviewed and approved documents
 - Protocol version date
- Review the consent form(s) to ensure the local context language and signature lines/blocks are appropriately included
- Check Good Clinical Practice and Human Subject Protections training expiration dates of all listed study team members
- Cross-reference the protocol version date with the consent form(s) and protocol document
- In many cases, DFCI will act as the privacy board for the study; this responsibility will be outlined in the reliance agreement. If DFCI is to act as the privacy board, OHRS will confirm all appropriate HIPAA determinations, per the information included in the New Protocol Application. The research team will be prompted to provide the standard HIPAA information in the New Protocol Application.

OHRS will issue a condition in iRIS if additional information is required. The conditions presented in iRIS are study specific. Therefore, the requirements may be different depending on the IRB of record. However, once the research team has adequately responded to the conditions, OHRS will issue the **Notification of IRB Outcome – Single IRB Approved Study** memo. This memo indicates that the DFCI IRB has acknowledged the approval of the external IRB for all DF/HCC sites. However, it is essential to note that no research interventions may begin until the study is activated.

High Priority Submissions

Please contact [OHRS](#) with the DF/HCC protocol number, iRIS reference number, and deadline requirement for high-priority submissions to prioritize its review. Depending on the complexity of the submission, there is no guarantee that the deadline will be met. However, OHRS will do its best to facilitate any necessary communication between the various departments.