Dana-Farber/Harvard Cancer Center Consortium, the Dana-Farber Cancer Institute IRB and the NIH sIRB Rule

I. NIH Policy on the Use of a Single Institutional Review Board (sIRB) for Multi-Site Research effective January 25, 2018.

The NIH Policy on the use of a single IRB for Multi-site research sets the expectation that multi-site studies conducting the same protocol will use a single IRB to carry out the ethical review of the proposed research. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html

NIH will support applicant and awardee institutions as they implement the new policy with guidance and resources located here: https://osp.od.nih.gov/clinical-research/irb-review/

Detailed instructions about completing the forms-e and are available here:

https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/multi-project-forms-e.pdf.

- *M.500 – PHS Human Subjects and Clinical Trials Information.* Page 143 of the PDF.
- 3.2 *Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?* Page 165 of the PDF.
    - *If yes, describe the single IRB plan.* Page 166 of the PDF.

IMPORTANT:

The DFCI IRB has no plans to act as a Single IRB under the NIH policy, with limited exceptions as described within this document.

Investigators are advised not to state that the DFCI IRB will be the IRB of record for the proposed research without documentation from the Office for Human Research Studies (OHRS) confirming that the DFCI IRB will act as the sIRB for external (non-DF/HCC) institutions.

Questions about relying on a sIRB should be directed to OHRS by emailing: OHRSCentral_IRB@dfci.harvard.edu or calling (617) 632-3029.

II. DF/HCC Consortium, the DFCI IRB and the NIH sIRB Rule.

The DFCI IRB functions as the sIRB of record for the institutions that comprise the Dana-Farber/Harvard Cancer Center (DF/HCC) Consortium. All cancer related research conducted by the following five Harvard clinical institutions falls under the jurisdiction of the DFCI IRB acting on behalf of the DF/HCC:

- Beth Israel Deaconess Medical Center
- Boston Children's Hospital
- Brigham and Women's Hospital
- Dana-Farber Cancer Institute
- Massachusetts General Hospital

The DFCI IRB also reviews cancer 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.

For cancer related research conducted within the DF/HCC and under existing reliance agreements, OHRS suggests using the following language in your grant application:

The Dana-Farber/Harvard Cancer Center (DF/HCC) consortium sites included in this grant proposal comply with the NIH policy on the use of a single IRB for multi-site research. The Dana-Farber Cancer Institute (DFCI) IRB is the designated single IRB for all cancer related research within the DF/HCC consortium and affiliated sites. All DF/HCC consortium and affiliated sites associated with this application have agreed to rely on the DFCI IRB for cancer related research.

The DF/HCC Office for Human Research Studies (OHRS) is the office that manages the DFCI IRB. OHRS maintains records of the DF/HCC reliance agreements and communicates DFCI IRB determinations to all participating sites. OHRS also posts IRB approved / activated research documents (protocol, consent forms, etc.) to the Oncology Protocol System (OncPro) for study sites to access.

DF/HCC Consortium Only Research - Costs:
The cost of sIRB review under the DFCI IRB (and within the DF/HCC consortium) should not be included in the NIH grant budget and an IRB liaison does not need to be identified.

III. The DFCI IRB as the sIRB for NIH funded multi-center studies:

The DFCI IRB may act as the sIRB of record for cancer 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 or National Comprehensive Cancer Network (NCCN) member institutions.

OHRS must grant this exception in writing before the DFCI IRB can be listed in the NIH grant as the sIRB of record for any research.

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

Note: If at any time in the future the research will require adding more sites than permitted by the DFCI IRB, please plan to work with an Independent sIRB at the outset.

The following information and tables will help determine what may be reviewed under the DFCI IRB and when review by an Independent (external) sIRB will be required.

Table 1. NIH Funded Multi-Center Clinical Trials:

DF/HCC Sites plus:

Total non-DF/HCC Sites:	Harvard Catalyst Member Sites **Only**	Harvard Catalyst Member Sites **and/or** NCCN Member Institution Sites	Harvard Catalyst Member Sites **and/or** NCCN Member Institution Sites **and/or** Other Institutions
0 – 3 Sites	DFCI IRB – Submit a Request to Rely*	Consult with OHRS via Email.**	Consult with OHRS via Email.**
3 – 5 Sites	DFCI IRB – Submit a Request to Rely*	Consult with OHRS via Email.**	Independent sIRB
5 - 10 Sites	DFCI IRB – Submit a Request to Rely*	Independent sIRB	Independent sIRB
10 + Sites	Independent sIRB	Independent sIRB	Independent sIRB

*A Request to Rely on the DFCI IRB must be submitted for OHRS consideration at least 20 business days before the NIH grant is due for Grants and Contracts Review and/or funding agency submission.

**A consult with OHRS must be initiated at least 30 days before the NIH grant is due for Grants and Contracts review and/or due to the funding agency submission.

Table 2. NIH Funded Multi-Center Non-Clinical Research:

DF/HCC Sites plus:

Total non-DF/HCC Sites:	Harvard Catalyst Members **ONLY**	Harvard Catalyst Member Sites **and/or** NCCN Member Institution Sites	Harvard Catalyst Member Sites **and/or** NCCN Member Institution Sites **and/or** Other Institutions
0 – 3 Sites	DFCI IRB – Submit a Request to Rely*	DFCI IRB – Submit a Request to Rely*	Consult with OHRS via Email.**
3 – 5 Sites	DFCI IRB – Submit a Request to Rely*	Consult with OHRS via Email.**	Independent sIRB
5 + Sites	DFCI IRB – Submit a Request to Rely*	Independent sIRB	Independent sIRB

*A Request to Rely on the DFCI IRB must be submitted for OHRS consideration at least 20 business days before the NIH grant is due for Grants and Contracts Review and/or funding agency submission.

**A consult with OHRS must be initiated at least 30 days before the NIH grant is due for Grants and Contracts review and/or funding agency submission.

Minimum Requirements for External Sites to rely on the DFCI IRB as a sIRB:

1) The Study Investigator must confirm in writing that all External Sites agree to rely on the DFCI IRB as the sIRB.

2) All non-DF/HCC participating sites must agree to rely on the DFCI IRB using the SMART Reliance Agreement: https://smartirb.org/. Note: The DFCI Office for Human Research Studies (OHRS) will maintain copies of the reliance agreements for all participating sites.

3) Participating external institutions must agree to follow DF/HCC Policies and Procedures where they apply to Multi-Center Research: http://www.dfhcc.harvard.edu/research/clinical-research-support/document-library-forms-sops-etc/dfhcc-sop-library/

4) The grant must include the following suggested language:

   The Dana-Farber Cancer Institute (DFCI) IRB is the designated single IRB for the research described in this grant. All Dana-Farber/Harvard Cancer Center (DF/HCC) consortium, DF/HCC affiliated sites, and non-DF/HCC sites associated with this application have agreed to rely on the DFCI IRB as the sIRB for this research.

   The DF/HCC Office for Human Research Studies (OHRS) is the office that manages the DFCI IRB. OHRS maintains records of all IRB reliance agreements. OHRS communicates DFCI IRB determinations to participating DF/HCC sites and posts IRB approved / activated research documents (protocol, consent forms, etc.) to the Oncology Protocol System (OncPro) for DF/HCC participating sites to access. Non-DF/HCC participating sites are required to follow DF/HCC Policies and Procedures applicable to Multi-Center Research (i.e. required DF/HCC audits).

   An IRB liaison on the project will be responsible for facilitating communications among External Sites, OHRS and the DFCI sIRB. The IRB liaison will be responsible for establishing reliance agreements, facilitating timely local reviews, and maintain communication among all stakeholders to ensure compliance with DFCI IRB-approved documents, determinations and DF/HCC policies and procedures.

5) A member of the Lead Site's study team must be identified as being responsible for managing communications with the external sites. Including but not limited to:

- Understand and communicate the policies and processes of the reviewing IRB, and be familiar with the research and the sites
- Work with the sites and their research compliance or IRB offices to establish reliance agreements with the reviewing IRB
- Coordinate the timing of initial review and modifications across all sites
- Assist the participating sites with completing and submitting materials to the reviewing IRB, which may include preparing and submitting all materials on their behalf
- Facilitate the continuing IRB review for the entire study by collecting information from all sites and submitting it to the reviewing IRB
- Serve as an intermediary between the reviewing IRB and the participating sites
- Obtain local context considerations (e.g., a state's age of majority) for each site and ensure that the information is provided to the reviewing IRB
- Assist the participating sites with responding to IRB requests
- Plan IRB and other regulatory approval timelines and troubleshoot challenging situations
- Coordinate the payment of IRB fees by the lead site
- May require travel to accomplish job duties, e.g., when assisting a participating site in responding to an inspection request from the reviewing IRB.

Note: SMART IRB describes the responsibilities of an Overall PI and designated Lead Study team member here: https://smartirb.org/sites/default/files/PI_checklist.pdf

The individual, typically a Regulatory Coordinator, must be included in the NIH grant's budget for all multi-center studies, regardless of the IRB of record.

OHRS suggests this sample language for the Key Personnel or Budget Justification sections of the grant application.

TBN, Research Study Coordinator/DFCI sIRB Liaison
Effort = 12.0 months calendar (100% FTE) in Years 1-5 [adjust FTE & years to match the study]

A Regulatory Coordinator will be hired to serve as the DFCI sIRB Liaison for all participating sites to facilitate the complex and time-sensitive communications among sites, and between the participating sites and the DFCI sIRB. Under the direction of the Overall DF/HCC Lead Principal Investigator, the DFCI sIRB Liaison will facilitate and coordinate IRB approval and related regulatory compliance activities for all participating sites. This includes serving as an

intermediary between the DFCI sIRB and the External Sites to: (1) establish reliance agreements; (2) facilitate timely initial review, modifications, and continuing review; and (3) establish and maintain communication plans among all stakeholders to ensure consistency among DFCI sIRB-approved consent forms, other materials, and procedures among all sites.

6) DF/HCC – Lead Institution Multi-Center Approval is required: http://www.dfhcc.harvard.edu/research/clinical-research-support/office-of-data-quality/services-support/dfhcc-multi-center-trials/

DFCI sIRB Costs:
Researchers must plan in their NIH budget that the DFCI IRB will charge to review multi-center site research for institutions outside of the DF/HCC Consortium. The costs will largely depend on the length and complexity of the study.

After the DFCI IRB agrees to be the IRB of record for the research, a sIRB cost analysis of the project must be conducted. Please plan ahead as this analysis may take up to 15 business days. If this analysis delays the submission of your grant please consider using an Independent sIRB. OHRS will provide a cost estimate by email that must then be added to the grant budget.

Note: In the NIH grant, the cost of sIRB review outside of the DF/HCC consortium sites must be included as a Direct Cost.

External Site Costs:
Relying (non-DF/HCC) institutions may also charge a fee for overseeing the conduct of the research locally and ancillary reviews (as required per study) (e.g. Radiation Safety, Biosafety Review, operational assessments). Please contact the outside sites for information about institution specific fees to be included in your grant budget.

IV. Reliance on an External sIRB

If the DFCI IRB will not be the sIRB of record for the research, an external sIRB must be identified and minimum criteria must be met before DFCI and DF/HCC consortium sites will agree to rely on an external sIRB.

More information about minimum criteria to rely on an external sIRB is available here: http://www.dfhcc.harvard.edu/crs-resources/OHRS_Documents/02_-_Investigator_Resources/IS_-_Operations_-_Guidance_for_Single_IRB_Review_Process.pdf

Independent (External) Single IRBs that DF/HCC Sites may rely upon include:

ADVARRA IRB: https://www.advarra.com/

QUORUM REVIEW IRB: http://www.quorumreview.com/

WIRB-COPERNICUS GROUP: http://www.wcgclinical.com/

Minimum Requirements to rely on an External sIRB:

1) The Study Investigator must confirm in writing that all External Sites agree to rely on the selected External sIRB as the sIRB for the research.

2) If an Academic External sIRB is selected, the SMART Reliance Agreement must be utilized: https://smartirb.org/ The study team is responsible for maintaining copies of all reliance agreements. The OHRS will maintain copies of reliance agreements for DF/HCC Institutions.

3) If an Independent sIRB is selected, OHRS will help determine what reliance agreements are appropriate to use for the DF/HCC consortium sites.

4) All participating institutions must agree to follow DF/HCC Policies and Procedures where they apply to Multi-Center Research: http://www.dfhcc.harvard.edu/research/clinical-research-support/document-library-forms-sops-etc/dfhcc-sop-library/
5) A member of the Lead Site's study team must be identified as being responsible for managing communications with the external sites. Including but not limited to:

- Understand and communicate the policies and processes of the reviewing IRB, and be familiar with the research and the sites
- Work with the sites and their research compliance or IRB offices to establish reliance agreements with the reviewing IRB
- Coordinate the timing of initial review and modifications across all sites
- Assist the participating sites with completing and submitting materials to the reviewing IRB, which may include preparing and submitting all materials on their behalf
- Facilitate the continuing IRB review for the entire study by collecting information from all sites and submitting it to the reviewing IRB
- Serve as an intermediary between the reviewing IRB and the participating sites
- Obtain local context considerations (e.g., a state's age of majority) for each site and ensure that the information is provided to the reviewing IRB
- Assist the participating sites with responding to IRB requests
- Plan IRB and other regulatory approval timelines and troubleshoot challenging situations
- Coordinate the payment of IRB fees by the lead site
- May require travel to accomplish job duties, e.g., when assisting a participating site in responding to an inspection request from the reviewing IRB.

Note: SMART IRB describes the responsibilities of an Overall PI and designated Lead Study team member here: https://smartirb.org/sites/default/files/PI_checklist.pdf

6) The individual described above, typically a Regulatory Coordinator, must be included in the NIH grant's budget for all multi-center studies, regardless of the IRB of record. OHRS suggests this sample language for the Key Personnel or Budget Justification sections of the grant application.

TBN, Research Study Coordinator/External sIRB Liaison
Effort = 12.0 months calendar (100% FTE) in Years 1-5 [adjust FTE & years to match the study]

A Regulatory Coordinator will be hired to serve as the External sIRB Liaison for all participating sites to facilitate the complex and time-sensitive communications among sites, and between the participating sites and the single IRB (sIRB). Under the direction of the Overall DF/HCC Lead Principal Investigator, the External sIRB Liaison will facilitate and coordinate External sIRB approval and related regulatory compliance activities for all participating sites. This includes serving as an intermediary between the External sIRB and the sites

to: (1) establish reliance agreements; (2) facilitate timely initial review, modifications, and continuing review; and (3) establish and maintain communication plans among all stakeholders to ensure consistency among External sIRB-approved consent forms, other materials, and procedures among all sites.

7) DF/HCC – Lead Institution Multi-Center Approval is required: http://www.dfhcc.harvard.edu/research/clinical-research-support/office-of-data-quality/services-support/dfhcc-multi-center-trials/

External sIRB Costs:
The cost to rely on an external sIRB will largely depend on the number of sites, length and complexity of the study. Please contact the sIRB directly for fee structures and help with budget development.

In the NIH grant, the cost of sIRB review by an external IRB must be included as a Direct Cost.

The DF/HCC Office for Human Research Studies also charges a fee of $1500.00 for overseeing the conduct of multi-center research under an external sIRB. This fee covers the cost of ensuring that local and ancillary reviews (as required per study) (e.g. Radiation Safety, Biosafety Review, operational assessments) are completed before the research begins.

Relying institutions may also charge a fee for overseeing the conduct of the research locally and ancillary reviews (as required per study) including Radiation Safety, Biosafety Review, operational assessments, etc. Please contact each external site for information about institution specific fees.

V. Links and References:

DFCI Office for Human Research Studies: Single IRB
http://www.dfhcc.harvard.edu/research/clinical-research-support/office-for-human-research-studies/single-irb/

Harvard Catalyst https://catalyst.harvard.edu/

National Comprehensive Cancer Network https://www.nccn.org/

SMART IRB – National IRB Reliance Initiative https://smartirb.org/

NIH's Definition of a Clinical Trial:
https://grants.nih.gov/policy/clinical-trials/definition.htm

Single IRB Policy for Multi-Site Research / grants.nih.gov
https://grants.nih.gov/policy/clinical-trials/single-irb-policy-multi-site-research.htm

Final Common Rule: Cooperative Research Requirement effective January 19, 2020
https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects

Clinical Trials Transformation Initiative: Central IRB Project
https://www.ctti-clinicaltrials.org/projects/central-irb

Office for Human Research Protections
https://www.hhs.gov/ohrp/about-ohrp/index.html

SACHRP Recommendations
https://www.hhs.gov/ohrp/sachrp-committee/recommendations/index.html