DF/HCC CCSG Protocol Review and Monitoring Requirements

As required by the Dana-Farber/Harvard Cancer Center (DF/HCC) National Cancer Institute (NCI) Cancer Center Support Grant (CCSG), DF/HCC conducts centralized protocol review and monitoring for all cancer-related hypothesis-driven clinical research studies undertaken by investigators at DF/HCC institutions. For the purposes of the CCSG, NCI defines clinical research as interventional and non-interventional patient-oriented research, epidemiological and behavioral research, health services research, and pragmatic clinical trials in which participants are randomized at the group level in real world settings. Patient-oriented research includes treatment, supportive care, prevention, diagnostic, and screening, as well as research with human specimens collected by investigators through direct interaction with research subjects. NCI also expects that any human subjects research taking place at DF/HCC institutions that is funded by NCI, even if not directly cancer-related (e.g., tobacco use studies) be centrally monitored. DF/HCC convenes Scientific Review Committees (SRC) to oversee protocol review and monitoring of all cancer related clinical research as required under the CCSG.

Scientific review is separate from and in addition to Institutional Review Board (IRB) review, which focuses on the protection of human subjects. DF/HCC institutions have agreed to rely on the Dana-Farber Cancer Institute (DFCI) IRB for ethical review of most cancer-related clinical research. Some multi-institutional or externally sponsored studies rely on commercial or external single IRBs. DFCI has, in turn, agreed to rely on DF/HCC institutions for review of certain research as well. The DF/HCC institutions include:

- Beth Israel Deaconess Medical Center (BIDMC)
- Boston Children's Hospital (BCH)
- Brigham and Women's Hospital (BWH)
- Dana-Farber Cancer Institute (DFCI)
    - The Dana-Farber Cancer Institute at Londonderry (Dana-Farber/New Hampshire Oncology-Hematology)
    - Dana-Farber Cancer Institute at St. Elizabeth's Medical Center
    - Dana-Farber/Brigham and Women's Cancer Center At Milford Regional Medical Center
    - Dana-Farber/Brigham and Women's Cancer Center In clinical affiliation with South Shore Hospital
    - Dana Farber-Merrimack Valley
    - Dana-Farber Cancer Institute at Foxborough
- Massachusetts General Hospital (MGH)
    - Massachusetts General/North Shore Cancer Center
    - Mass General Cancer Center at Newton-Wellesley
- Harvard Medical School (HMS)
- Harvard School of Public Health (HSPH)

The DF/HCC Office for Human Research Studies (OHRS) is the office at DFCI that manages DF/HCC SRC review and DFCI IRB review, including reliance on external IRBs. All submissions to OHRS and DF/HCC are accomplished in the iRIS system.

Centralized data-safety monitoring (DSMC/DSMB) and auditing are part of the DF/HCC protocol review and monitoring system. The DF/HCC Office for Data Quality (ODQ) is the office at DFCI that manages the DF/HCC data safety monitoring and auditing.

Under the conditions of the CCSG, the NCI requires regular reporting of all DF/HCC research activities. For all research reviewed under the DF/HCC protocol review and monitoring system, reporting is managed by DF/HCC Research Informatics Office and ODQ. For research that is CCSG relevant but not reviewed under the DF/HCC protocol review and monitoring system, individual investigators may be responsible for providing protocol data to DF/HCC for inclusion in reports to the NCI.

To help determine what research requires submission to DF/HCC, the following decision tree is provided as a guidance:

1a. Is the research cancer relevant (e.g., specifically recruiting patients with cancer or asking cancer-relevant scientific questions including cancer screening, cancer prevention, cancer-related outcomes, or assessments of cancer risk)?
This may include interventional research, observational research involving cancer patients and/or healthy populations, as well as specimen-based research. See the following section for specific examples.

AND

1b. Is the protocol hypothesis-driven and statistically powered to answer a scientific question?

Yes (CCSG relevant and requires submission to DF/HCC)

or

No (next question)

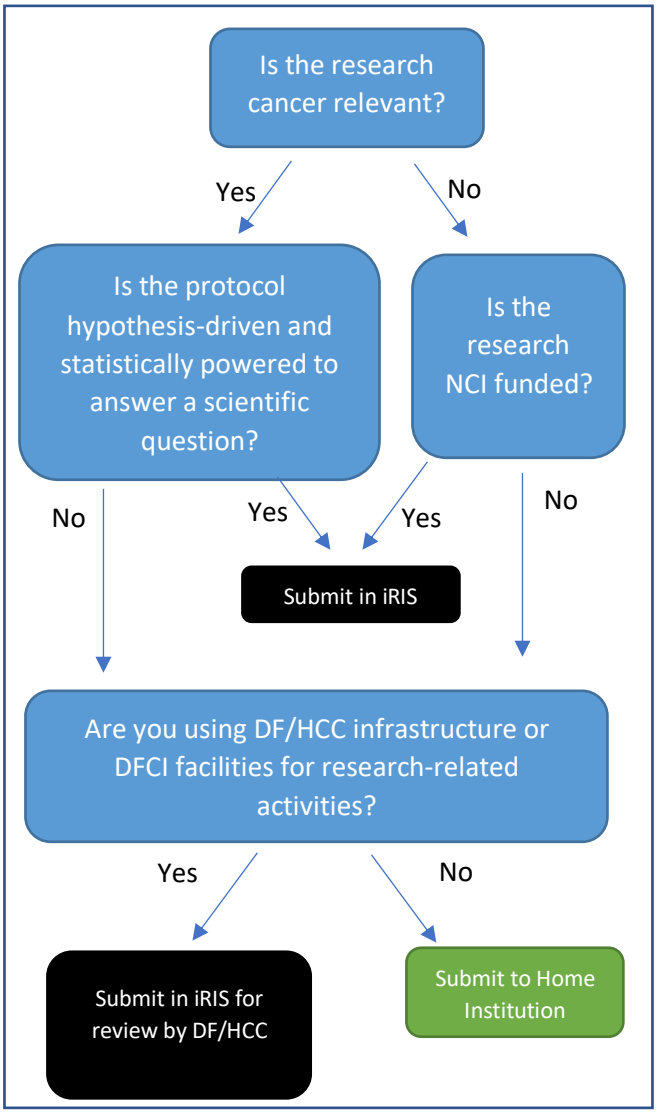
2. Is the research funded by the NCI?

Yes (CCSG relevant and requires submission to DF/HCC)

or

No (next question)

3. Does the research use DF/HCC infrastructure or DFCI facilities for research-related activities, causing Dana-Farber Cancer Institute to be engaged in human subject research?



For non-cancer relevant research in which DFCI is engaged or DF/HCC infrastructure is used, submission to OHRS in iRIS for feasibility reviews may be required; review by the DFCI IRB is optional. Examples of DF/HCC infrastructure or DFCI facilities are listed below:

- DFCI Research Pharmacy Services
- DFCI Cell Manipulation Core Facilities (CMCF)*
- Electronic Forms Capture
- Data Safety and Monitoring
- Data Management
- Registration in OnCore or OncPro

Yes (Submit to DF/HCC for operational and/or IRB review)

or

No (submission to DF/HCC is not required)

**Non-cancer research that utilizes the CMCF needs to be evaluated by OHRS on a case-by-case basis.*

IRB Offices and Contacts for Questions:

Beth Israel Deaconess Medical Center - Committee on Clinical Investigation (IRB)
Contacts: Andrea Collins / Wendy Moy
Boston Children's Hospital Institutional Review Board
Contacts: Susan Kornetsky
Dana-Farber Cancer Institute - Office for Human Research Studies (OHRS)
Contacts: OHRS@dfci.harvard.edu Lara Sloboda / Caroline Kokulis / Jeffrey Meyerhardt, M.D.
Mass General Brigham IRB
Contacts: Martha Jones

What Research is Considered CCSG-Relevant?

The following table is intended to help clarify certain types of cancer related research studies that may be CCSG relevant and require submission to DF/HCC. Research that is submitted to DF/HCC may rely on an external IRB for ethical review in some cases, but a full submission of the research to OHRS is still required for scientific review and CCSG reporting.

Investigators should seek guidance from their institutional IRB office before completing application forms if there is any uncertainty about the most appropriate review process for a specific study.

Research Involving	Required to Submit To
Chemotherapeutic drugs or immunotherapy to treat malignant tumors or used to treat the following nonmalignant tumors: Meningiomas, Schwannomas, Neurofibromas, Pancreatic cysts or Neuroendocrine pancreatic tumors.	Submit to DF/HCC through the iRIS system – For review by DFCI IRB or reliance on external IRB *For DFCI engaged non-cancer research, submission is required for the relevant feasibility review, but IRB review may be at home institution
Cryotherapy or radioablation of malignant tumors	
Novel surgical approaches to cancer therapy	
Pain management OR alternative medicine approaches to cancer therapy	
Radiological diagnostic techniques directed at patients with cancer or follow-up of cancer therapy	
Cancer risk, screening or prevention	
Questionnaires / surveys directed at patients with cancer	
Health services research / cost effectiveness analysis	
Mixed Patient Populations including a subset of cancer patients where cancer-relevant populations are specifically recruited and/or cancer-relevant scientific questions are researched	
*Greater than Minimal Risk, Non-Malignant Hematology when Dana-Farber Cancer Institute is engaged in research	

Research Involving	May be submitted to
Treatment of the following **nonmalignant tumors without chemotherapy or immunotherapy**: Meningiomas, Schwannomas, Neurofibromas, Pancreatic cysts or Neuroendocrine pancreatic tumors.	Principal Investigator's Institution
Treatment of osteomas	
Treatment of warts / localized papilloma	
Mixed Patient Populations where the inclusion of cancer-related populations is incidental	
Nursing practice and/or quality improvement projects related to cancer care	
Collection of blood/tissue for genetic testing directed at patients with cancer when Dana-Farber Cancer Institute is not engaged in research	
Health / medical records of patients with cancer when Dana-Farber Cancer Institute is not engaged in research	
Tissue banks and/or sample/data repositories without scientific objectives	
Infectious Disease Research	
Humanitarian Use Device / Humanitarian Device Exemptions for clinical treatment of patients	

What are the reporting requirements for CCSG-relevant research?

DF/HCC institutions must satisfy NCI reporting obligations for research that is CCSG-relevant (steps 1 and 2 in the above decision tree). The table below summarizes key NCI CCSG reporting requirements and CTRP registration requirements for cancer relevant research studies conducted at any institution that is part of an NCI-designated cancer center.

REQUIRED REPORTING:

	DF/HCC Investigator-Sponsored	Externally Sponsored (Industry)	Externally Sponsored (non-industry)
Site Information	Required for all participating institutions, including sites outside of DF/HCC.	Required for DF/HCC institutions and affiliates only.	Required for DF/HCC institutions and affiliates only.
Interventional Trial Accrual	Subject Level Accrual Reporting is required for all participating institutions, including sites outside of DF/HCC.	Subject Level Accrual or Summary Accrual Reporting is required for DF/HCC institutions and affiliates only.	Subject Level Accrual Reporting is required for DF/HCC institutions and affiliates only.
Observational, Ancillary and Correlative Trial	Subject Level Accrual Reporting is requested.	Subject Level Accrual or Summary Accrual	Subject Level Accrual Reporting is requested.

Accrual	Summary Accrual may be allowed upon request. Accrual must be reported for all participating institutions, including sites outside of DF/HCC.	Reporting is required for DF/HCC institutions and affiliates only.	Summary Accrual may be allowed upon request. Accrual must be reported for DF/HCC institutions and affiliates only.
Study Documentation	All reportable study types. Approval memos for DF/HCC lead site only.	Not required.	Not required.

DEFINITIONS:

- **Interventional:** Individuals are assigned prospectively by an investigator based on a protocol to receive specific interventions. The participants may receive diagnostic, treatment, behavioral, or other types of interventions. The assignment of the intervention may or may not be random. The participants are followed and biomedical and/or health outcomes are assessed.

- **Observational:** Studies that focus on cancer patients and healthy populations and involve no prospective intervention or alteration in the status of the participants. Biomedical and/or health outcome(s) are assessed in pre-defined groups of participants. The participants in the study may receive diagnostic, therapeutic, or other interventions, but the investigator of the observational study is not responsible for assigning specific interventions to the participants of the study.

- **Ancillary:** Studies that are stimulated by, but are not a required part of, a main clinical trial/study, and that utilize patient or other resources of the main trial/study to generate information relevant to it. Ancillary studies must be linked to an active clinical research study and should include only patients accrued to that clinical research study. Only studies that can be linked to individual patient or participant data should be reported.

- **Correlative:** Laboratory-based studies collecting specimens to assess cancer risk, clinical outcomes, response to therapies, etc. This includes research with human specimens collected by study investigators through direct interaction with research subjects. Only studies that can be linked to individual patient or participant data should be reported.

- **DF/HCC Investigator-Sponsored:** Investigator-initiated research where an investigator at one of the DF/HCC member institutions takes responsibility for the initiation, management, and /or financing. For example, when research is conducted under an IND/IDE, the IND/IDE holder is the Sponsor.

- **Externally Sponsored:** Research where an individual, company, institution, or organization outside the DF/HCC consortium designs and initiates the study and has regulatory responsibility for management and oversight.

- **Site Information:** The name and contact information for the PI of each site, and the status dates (i.e., Date of SRC Review, Date of IRB approval, date of activation (open to accrual), date closed to accrual, date of IRB completion) for each site.

- **Subject Level Accrual Reporting:** CTRP requires data on each subject enrollment including: Enrollment Date, Subject Identifier, Enrolling Site, Zip Code, Date of Birth, Gender, Ethnicity, Race, and Disease Code. Accruals must be reported separately for each site and by calendar year.

- **Summary Accrual Reporting:** Reporting the number of subjects enrolled at each site by calendar year. Demographic information, if available, can be summarized and reported.

- **Study Documentation:** CTRP requires submission of all approved protocol documents (clean and tracked) and consent forms (clean and tracked) and IRB approval memos for the **initial submission** and **any amendments**. In addition, IRB approval of continuing review must be provided.

What if I have a CCSG-relevant research project that was not initially submitted to DF/HCC?

DF/HCC is still obligated to report on National Cancer Institute (NCI) Cancer Center Support Grant (CCSG) relevant studies conducted at any DF/HCC member institution. Please contact the DF/HCC Office of Data Quality (ODQ) to determine the best way to ensure this reporting occurs.

DF/HCC may request data from the investigator to support the reporting of these trials.