DANA-FARBER
CANCER INSTITUTE
DANA-FARBER / HARVARD CANCER CENTER

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Letter to Sponsors/Collaborators Regarding DF/HCC Protocol Review and Approval

All cancer research involving human subjects conducted by the clinical institutions that comprise the Dana-Farber/Harvard Cancer Center (DF/HCC) are subject to the following requirements outlined below. This letter is intended to communicate to sponsors frequently requested regulatory information and highlight some of the important review related requirements for research to be approved and conducted at DF/HCC.

Regulatory Information:

The **Dana-Farber Cancer Institute (DFCI)** has an approved Federal Wide Assurance (FWA - **FWA00001121**) on file with the U.S. Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP). This FWA expires **August 19, 2029**.

The following DFCI Institutional Review Boards (IRBs) are registered with OHRP and are designated in the DFCI FWA to conduct reviews of research involving human subjects for the Dana-Farber Cancer Institute:

IRB00000052 (#1 / Panel A)
IRB00000753 (#2 / Panel B)
IRB00001186 (#3 / Panel C)
IRB00003340 (#4 / Panel D)
IRB00005504 (#5 / Panel E)
IRB00006224 (#6 / Panel F)
IRB00007493 (#7 / Panel G)

The DFCI IRB Organization number is **IORG0000035** and expires on **May 5, 2028.**

The DFCI IRBs are also registered in compliance with the Food and Drug Administration (FDA) regulations at 21 CFR Part 56.

The DFCI IRBs are the designated IRBs of record for oncology protocols conducted by the five clinical institutions that comprise the DF/HCC consortium, including:

- 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)

Additionally, the DFCI IRBs serve as the IRBs of record for several affiliated institutions pursuant to inter-institutional agreements.

The DF/HCC human research protection program has received full Association for the Accreditation of Human Research Protection Programs (AAHRPP) accreditation. For more information please go to the AAHRPP website at: http://www.aahrpp.org/learn/find-an-accredited-organization

All research involving human subjects reviewed by the DFCI IRBs is guided by the ethical principles in *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* prepared by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The DFCI IRBs are duly constituted, fulfilling Federal requirements for membership; have written procedures for initial and continuing review for human subjects research; prepare written minutes of convened meetings; and retain records pertaining to the review and approval process all in compliance with the requirements for IRBs defined in DHHS 45 Code of Federal Regulations (CFR) Parts 46 and 164, Food and Drug Administration (FDA) 21 CFR Parts 50 and 56, and Guidelines of the International Conference on Harmonization relating to Good Clinical Practices (GCPs) to the extent that those guidelines reflect the regulations and guidance set forth by the FDA regulations.

The DFCI IRBs do not post membership rosters or release names of IRB members. Any IRB member who is an investigator, co-investigator or has any other conflict of interest with a protocol under review by the DFCI IRBs will not participate in the deliberation or vote of that protocol although he or she may be called upon to answer questions during the review.

The DFCI IRBs do not require the IRB Chairs or any other member of the IRB to sign approval memoranda. There is no regulatory requirement for such signatures. Final IRB approval occurs when the IRB votes to approve a research protocol and that approval is reflected in the minutes. With respect to a conditional approval, an IRB member reviews and confirms on a verification form that the investigator has met all of the IRB conditions for approval.

Office for Human Research Studies:

New oncology research is submitted by DF/HCC investigators to the Office for Human Research Studies (OHRS) for review and approval by the scientific review committee (SRC) and IRB. OHRS is the office charged with managing scientific and IRB review of human subject research for DF/HCC. OHRS is also responsible for obtaining departmental sign offs confirming that the study is ready to be started at each of the participating sites.

Process Overview:

- **All research should be offered to all DF/HCC sites** that have programs that could conduct the research.
- **All research is reviewed by a DF/HCC Scientific Review Committee (SRC)** for scientific merit, feasibility and prioritization.
- **The DFCI IRBs conduct ethical and regulatory review following Approval by the SRC**.
- **Activation sign off is required before the study can begin to accrue subjects.** Activation is a process by which each of the participating DF/HCC sites confirms that the study is ready to be conducted at their site. Activation sign offs are provided by a variety of different departments and will depend on the requirements of each study. Sign offs may include one or more of the

following departments: Research Nursing, Research Pharmacy, Pathology, Clinical Research Lab, Biomedical Engineering, etc.

Submission Forms and Consent Documents:

For submissions to be accepted by OHRS, DF/HCC investigators are required to use current OHRS forms and templates. If outdated forms or templates are used, the submission will be returned.

Current forms and templates are publicly available on the OHRS website:
http://www.dfhcc.harvard.edu/clinical-research-support/office-for-human-research-studies-ohrs

DF/HCC Investigators are required to use the appropriate DF/HCC model consent form template (biomedical or social/behavioral) provided on the OHRS website:
http://www.dfhcc.harvard.edu/clinical-research-support/office-for-human-research-studies-ohrs/consent-documents

Investigators may incorporate sponsor provided consent language into the DF/HCC model consent document where prompted if it meets the following minimum requirements:

1. **Sponsors must describe the risks of the study in lay language to subjects**. Sponsors are asked to utilize the NCCN Informed Consent Language (ICL) Database to describe these risks. The database is publicly available on the NCCN website:
   http://www.nccn.org/clinical_trials/informed_consent.asp
2. **Exculpatory and potentially exculpatory language is not permitted** (45 CFR 46.116). Examples of prohibited language includes any statement that a subject's injuries will be covered only if:
   a. The subject has followed all the instructions set out in the protocol
   b. The subject has not been negligent
   c. The investigator has not been negligent
   d. The investigator has complied with all protocol requirements
   e. Or other similar exculpatory language that attempts to impose standards of behavior or performance
3. **No statements are made that the subject will not share the consent or tell others about the research.** The consent must not include any statements to the effect that the protocol is confidential and that the subject may not share the consent or tell anyone about the research. The consent form is not a contract.
4. **HIPAA Authorization section is not altered** except to add the name of any individuals or groups with whom data may/will be shared.

OHRS staff conducts a pre-review of the submitted informed consent document(s) to provide study teams with information regarding issues that the IRB will/may raise at the IRB meeting. The requirements noted above will be reviewed and any other recommended revisions will be communicated to the study team prior to IRB review. If required/proposed OHRS changes are not made, the IRB will identify the required changes to be made for the submission to be IRB approved.

Documentation of Approval and Activation:

Once a study has been SRC and IRB approved, approval memoranda are generated by OHRS staff. The DFCI IRB approval memoranda serve to document IRB approval of the entire submission including, but not limited to, the protocol, the informed consent document, and, if applicable, the Investigator Brochure.

Subjects may not be registered to a trial until it is "Activated." Activated means that all operational requirements have been met ensuring that once a subject is enrolled, research procedures may commence immediately. Once activated, the Protocol and IRB approved consent forms are posted to the Oncology Protocol System (OncPro) as PDF documents for Investigators to use. Once posting is completed, an activation notification is sent to the study team and investigators may begin to consent and enroll subjects to the study.

Consent Form Versions:

OHRS does not use version numbers on informed consent documents, but the consent footer will capture the IRB approval date of the consent and the date is was "activated" and posted for use. DFCI IRB approved consent documents are also provided to Investigators as a Word document with the statement "not for subject use" in the header and can be used with future submissions to the IRB. This document is not to be used to consent subjects. Subjects must only be consented using consent documents posted to OncPro.

Although the consent form is reviewed at the time of IRB continuing review, consent forms are not automatically sent out with the Continuing Review Approval memos unless the text of the consent form has changed resulting in a new consent form version. Anytime a new consent form version is generated, the revised Word document will be provided to the study team with "not for subject use" added to the header and the version date will be updated on the PDF version posted to OncPro.

Short Form Consent Forms for Non-English Speaking Subjects:

The DFCI IRB has reviewed and approved the English 'short form' and 'short form addendum' consent documents posted on the OHRS website. The posted non-English 'short form' and 'short form addendum' informed consent documents are translations of the IRB approved English short form, and are to be used with an interpreter in the language understandable to the research participant. Certification of translation of the non-English short forms can be provided on request. Study teams must use the corresponding IRB approved Non-English Short Form and Non-English Short Form Addendum posted to the OHRS website when obtaining consent from Non-English speaking participants. If, however, the selection of posted Short Forms does not include the language needed, then the Investigator must obtain a translation of the posted English version of the 'short form' and 'short form addendum' and submit it to OHRS for IRB approval prior to use.

It is best practice to provide a fully translated long-version of consent form once the short form has been used once in a particular language. Sponsors may be expected to provide the translated form or provide resources to obtain a certified translation.

Informing Subjects of New Information:

After a study is IRB approved, the DFCI IRBs will review events arising during the research that may require informing and/or re-consenting research subjects. The DFCI IRB will consider an investigator or sponsor determination to inform or re-consent subjects but the DFCI IRB will make the final determination about how to notify subjects of new information based upon each specific context or situation.

Re-consenting of subjects is required when there is a new risk or event that impacts the risk/benefit ratio involved in participation in the research. Re-consenting is not required to inform of editorial or administrative changes, or, at the time of continuing review unless this is because of newly-discovered risks or other critical information which may affect the decision about continuing participation.

While there may be situations in which re-consent occurs because of a sponsor requirement, the re-consent will not be viewed as an IRB requirement unless the IRB specifically so determines. The DFCI IRB will also determine whether a new signed consent document is required, verbal re-consent with accompanying documentation in the medical or study record will be satisfactory, or if a letter to subjects is appropriate given the circumstances.

Investigator Brochures:

Upon receipt of Investigator Brochures, OHRS will issue a confirmation email to the study team to attest that the brochure was correctly submitted. After review, should OHRS require any additional information, a letter requesting that further action will be issued. Otherwise, no additional outcome letter will be provided to the study team. The email will act as proof of submission and receipt by the IRB.

IND / IDE Safety Reports:

The DFCI IRBs do not accept submissions from investigators of IND/IDE safety reports from outside sponsors detailing adverse events that have occurred at sites other than the DF/HCC unless the report is of an incident on a Phase I or Phase I/II trial that the DF/HCC PI has determined to be:

(1) serious or life-threatening;
(2) unexpected;
(3) related to the research intervention; and,
(4) has implications for the conduct of the study.

DF/HCC expects external study sponsors to directly notify DF/HCC Investigators of unanticipated problems and important safety information that has implications for the conduct of the research. (21 CFR 312.32, 21 CFR 312.55, 21 CFR 812.46, 21 CFR 812.150)

If the incident falls within the guidelines above, and the sponsor has notified the DF/HCC Investigator that the event has been determined to be an unanticipated problem, the IRB requires the submission of the report including an amendment and a plan for notifying subjects of the new information. If the study is actively enrolling/treating subjects, the consent form must be revised to include the new information and subjects must be re-consented. The DFCI IRBs require that new risks identified via an IND/IDE safety report will be added to the consent form document within 30 days of identification. If for any reason a sponsor does not agree with the addition of a risk to the consent that meets the

requirements outlined above, the investigator and IRB must consider whether the research can continue at DF/HCC. For further information, please refer to DF/HCC Policy RCO-204.
This letter does not include all the requirements for initial and continuing approval of research at DF/HCC. **Additional resources are publicly available on the OHRS website, including information sheets and policies.** If you require help with specific information not covered in this letter or available on our website, please contact our office at the number listed above for assistance.

Sincerely,
Sarah Kiskaddon

Sarah H. Kiskaddon, JD, MA
Senior Director, OHRS

Appendix: Sponsor Requirements for Submissions

This document lists the minimum requirements for external sponsors prior to initiating a new protocol submission or amendment at the Dana-Farber / Harvard Cancer Center (DF/HCC). Delays in responding to reviewer conditions and comments may result in a submission being put on hold or withdrawn.

The following documents must be provided prior to submission of a new study:

- ☐ Final and approved versions of the following study documents:
  - Protocol
  - Pharmacy and/or Investigational Product Manual (when applicable)
  - All patient-facing materials (diaries, questionnaires, advertisements, etc.)

- ☐ Draft or final versions of the following study documents:
  - Sponsor consent form template language
  - Laboratory manual, Pathology manual, Imaging manual, etc.

- ☐ Confirmation of FDA Approval / Clear to Proceed (for studies under an IND / IDE)

- ☐ Confirmation of which study agents are provided from investigational supply vs commercial supply, including which are provided free-of-charge vs billed to patient insurance

- ☐ Draft / template Clinical Trial Agreement

- ☐ Draft / template study budget

For **amendments**, the final version of all documents must be provided prior to submission.

To ensure timely activation, sponsors are expected to provide a 10 business day turnaround for responses to reviewer comments that require sponsor input or approval (including contract and budget revisions, consent form review, and all conditions from SRC or IRB).