1. BACKGROUND:

DF/HCC Investigator-Sponsored Multi-Center Trials are defined as research where a DF/HCC investigator is the regulatory sponsor of the trial, and participation will be extended to one or more external (non-DF/HCC or DF/PCC) institutions.

All DF/HCC Investigator-Sponsored Multi-Center Trials must obtain institutional approval and sign off prior to ~~Office of Human Research Subjects (OHRS)~~~~iRIS~~IRB submission. ~~Overall~~ Principal Investigators acting as the sponsor of multi-center research for the first time will be required to complete a New Multi-Center Sponsor Training prior to ~~receiving IRB approval~~study activation. Additionally, certain required elements must be present in the protocol language prior to the addition of external sites. The process for how these requirements are met and verified is outlined below.

2. ASSOCIATED DF/HCC POLICIES:

2.1. MULTI-100

3. PROCEDURE:

3.1. Obtaining Institutional Approval

3.1.1. Follow the institutional multi-center review process as required by the Sponsor-Investigator's home institution to obtain a DF/HCC Institutional Approval Form for Investigator-Sponsored Multi-Center Trials.

3.1.2. Per institutional requirements, approval may be obtained prior to new protocol submission ~~to OHRSiRIS~~, or for active trials, prior to an ~~add-site~~ amendment submission to ~~OHRSiRIS~~convert the study to a multi-center trial. The completed DF/HCC Institutional Approval Form must be included in the new protocol or ~~add-site~~amendment submission to OHRS.

3.1.2.1. Once a study is approved and activated as a multi-center trial, external sites are added to the study via a separate Add Site submission to OHRS. The coordinating center makes this submission, and must include documentation of IRB approval from the IRB of record for the site being added. Please review the OHRS Request to Add Site: Required Documentation Checklist for additional required documents that must be included in your submission to add a site to a DF/HCC led study~~, including an Add Site Amendment Form~~.

3.1.3. Additional contact information and resources for the institution-specific review processes can be found on the Multi-Center Trials page on the DF/HCC website: http://www.dfhcc.harvard.edu/research/clinical-research-support/office-of-data-quality/services-support/dfhcc-multi-center-trials/

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3.2. **Completion of the New Multi-Center Sponsor Training Requirement**

3.2.1. DF/HCC Investigators who are acting as the Sponsor-Investigator for multi-center research for the first time are required to complete the DF/HCC New Multi-Center Sponsor Training prior to initiating research at external sites, per MULTI-100.

3.2.2. The New Multi-Center Sponsor Training is offered as an e-learning module, managed by the Office of Data Quality (ODQ).

3.2.3. Sponsor-Investigators are encouraged to complete the New Multi-Center Sponsor Training proactively if they know they will be conducting multi-center research. To request the training, investigators may contact ODQeducation@dfci.harvard.edu.

3.2.4. Sponsor-Investigators required to complete training will be identified during the ODQ's departmental review of protocol submissions, or during the activation review for add-site amendments.

3.2.5. To complete the training:

3.2.5.1. ODQ will send the Sponsor-Investigator the training module.

3.2.5.2. The Sponsor-Investigator must complete the training and return the signed and dated training completion form to ODQ prior to activation of research at the external site.

3.2.5.3. ODQ will update the New Multi-Center Sponsor Training credential in OnCore for tracking purposes.

3.1. **Verification of DF/HCC Required Multi-Center Protocol and Data Safety Monitoring Plan (DSMP) Language**

3.1.1. Protocol language should account for the inclusion of all participating sites when explaining operational specifics and other applicable elements (e.g. distribution of investigational agent)

3.1.2. Clinical trials that are required to include a Data Safety Monitoring Plan (DSMP) with their protocol must ~~should~~ use the DF/HCC Multi-Center DSMP Template to ensure the required elements are included. This requirement persists regardless of the IRB of record, although adjustments to the template language may be required when using a single IRB.

3.1.2.1. The DF/HCC Multi-Center DSMP Template contains DF/HCC required and recommended language for ~~DSMP development~~sponsor oversight of DF/HCC trials. ~~All s~~Many sections may be modified as necessary to meet the aims of the study and management plan of the protocol.

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3.1.3. During the departmental review and/or activation process, the ODQ will review Multi-Center trials for certain required elements in the protocol and DSMP (if applicable) including, but not limited to:

~~3.1.3.1.~~Outline of roles and responsibilities of the DF/HCC Sponsor, coordinating center and participating institutions throughout the conduct of the research protocol.

~~3.1.3.2.~~

~~3.1.3.3.~~3.1.3.1.

~~3.1.3.4.~~3.1.3.2. Plan for distribution of the ~~DFCI~~ IRB approved protocol and any subsequent amended protocols to all participating institutions, as well as appropriate plan for notification of protocol revisions and closures to the participating institutions.

~~3.1.3.5.~~3.1.3.3. Applicable DF/HCC informed consent requirements, as defined in CON-100 and outlined in the DF/HCC Guidance Document on Model Consent Language for Investigator-Sponsored Multi-Center Trials.

~~3.1.3.6.~~3.1.3.4. Participant registration and randomization, for all participating sites, must be completed through the DF/HCC coordinating center.

~~3.1.3.7.~~3.1.3.5. Language related to the continued reporting requirements to the DF/HCC Sponsor and ~~DFCI~~ IRB for all protocol deviations, exceptions and violations per DF/HCC and ~~DFCI~~ IRB policy.

~~3.1.3.8.~~3.1.3.6. Explanation of data management procedures, including specific language for trials where data will be managed by the DF/HCC.

~~3.1.3.9.~~3.1.3.7. A plan for requisitioning and distributing the investigational agent to all participating institutions, when applicable.

~~3.1.3.10.~~3.1.3.8. A plan for ongoing monitoring of protocol compliance and data accuracy at all participating institutions, including remote and/or on-site monitoring. Monitoring reports will be reviewed by the DF/HCC Sponsor-Investigator to ensure protocol compliance.

~~3.1.3.11.~~3.1.3.9. A plan for ongoing communication (e.g. teleconferences) between the coordinating center and participating institutions.

~~3.1.3.12.~~3.1.3.10. The establishment and monitoring of accrual expectations for each participating institution. Sites that are not meeting their accrual expectations may be subject to termination.

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~~3.1.3.13.~~ —Language outlining an auditing plan and stating that all participating institutions are subject to an internal audit by the DF/HCC Office of Data Quality (ODQ).

~~3.1.3.14.~~3.1.3.11.

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