

**DANA-FARBER / HARVARD CANCER CENTER
STANDARD OPERATING PROCEDURES FOR CLINICAL RESEARCH**

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| TITLE: Conducting PI-Initiated Multi-center Trials | |
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Applicable Regulations

& Guidelines:

21 CFR 312.60 General responsibilities of investigators;
21 CFR 312.62 Investigator record keeping and record retention;
21 CFR 312.64 Investigator Reporting Requirements;
21 CFR 312.68 Inspection of investigator's records and reports
ICH E6 GCP Consolidated Guidelines

Other References:

Policies and Procedures for Dana-Farber/Partner's CancerCare (DF/PCC) Affiliate Network Clinical Trials
QA-717 Data Management of DF/HCC PI-Initiated Therapeutic Protocols
QA-706 Notifying DF/HCC of External Audits
PM-407 Reporting Unexpected Events (Violations/Deviations/Exceptions) to the IRB for Approved Protocols
AE-601 Procedures for Identifying, Documenting, and Reporting Adverse Events
PM-409 Regulatory Binder Management
PM-408 Responsibilities of the Sponsor-investigator
DF/HCC Multi-center Data and Safety Monitoring Plan
SM-501 Obtaining Informed Consent in Human Research Studies
Forms and Templates posted on the DF/HCC Clinical Research Unit website

Responsible Personnel:

Members of the study team, the Dana-Farber Quality Assurance Office for Clinical Trials, Multi-center Coordinating Committee, and the DFCI IRB office.

Policy Statement:

All DF/HCC Principal Investigators conducting multi-center trials must follow the process outlined below to ensure compliance.

Definitions:

Multi-center: Refers to inclusion of at least one site external to DF/HCC and the DF/PCC Affiliate Network.

Overall PI: The Overall Principal Investigator has the ultimate responsibility for the conduct of the clinical trial to ensure subject safety and data integrity. This individual is the Principal Investigator named on the single DF/HCC 1572 form.

Site PI: The Site Principal Investigators will be listed as a sub-investigator on the protocol specific FDA 1572 form. There is one Site PI for each participating site of a multi-center trial.

Lead Site: This is the site of the Overall PI, which serves as the coordinating center for the trial.

Procedure:

NOTE: The Overall PI must have the necessary resources to adhere to these procedures. This may include but is not limited to a project manager, additional study coordinator(s) and/or a CRO. Additionally, if the proposed multi-center trial may include international site(s), you must contact the OPRS office for guidance.

ROLES AND RESPONSIBILITIES

1. Overall Principal Investigator (Overall PI)

- Act as single liaison with outside regulatory agencies, with DF/HCC internal review and oversight committees, and with participating sites, although this may be delegated as appropriate and necessary (e.g. when she/he is out of town).
- Coordination of the approval of the initial protocol as well as its subsequent amendments. It is the responsibility of the Overall PI to ensure that the sites are using the correct version of the protocol.
- Identify a Study Coordinator (CRC/CRA) or Research Nurse as a study contact.
- Select qualified sites for participation. The Overall PI must obtain the DFCI IRB approval and inform the study sponsor, if applicable, which non-DF/HCC institutions will be involved in the study.
- Ensure all participating site investigators and study staff are trained on the DF/HCC SOPs, the conduct of the protocol, study procedures, SAE reporting, and data collection.
- Monitor progress and oversee the overall conduct of the trial at all participating sites.
- Responsible for the analysis, reporting, integrity and accuracy of data.
- Sponsor-Investigator IND Holders have additional responsibilities as written in the Code of Federal Regulations. Refer to SOP PM-408, Responsibilities of the Sponsor-investigator.
- Inter-institutional agreement / contract, if applicable: This may be required in situations, (1) where patient information, patient samples, or both are sent by or between study teams and coordinating center(s), (2) where financial arrangements are made, or (3) where no other agreements, such as network affiliate agreements, exist between the institutions. The agreement must be reviewed and approved by the DF/HCC Research Administration Office.

2. Site Principal Investigators (Site PI)

- Responsible for the conduct of the trial at their individual site. The Site PI may delegate authority within the site for conduct of trial.
- Identify the physician members of the study team who will be obtaining consent and signing the consent form for therapeutic protocols. It is DF/HCC policy that Nurses and Fellows cannot obtain consent to greater than minimal risk trials. The Site PI may designate non-physician members of the study team to obtain consent and sign the consent form for participation in a study that has been deemed minimal risk.
- Identify a Study Coordinator (CRC/CRA) or Research Nurse as a study contact.

- Submit data in a timely fashion to the Overall PI.
- Timely reporting of all SAEs and unexpected problems involving research (violations/deviations/exceptions) to the IRB of record and to the Overall PI.
- Ensure that their study team members have the current version of protocol and informed consent documents.
- Ordering, storage and dispensing of the study drugs. Investigational agents should be supplied free of charge to each participating site by the sponsor or company that is supporting the trial.

3. Quality Assurance Office for Clinical Trials (QACT)

- QACT Central Patient Registration is required for all participating sites.
- The DF/HCC Data Safety Monitoring Committee/Board (DSMC/DSMB) reviews all PI-initiated multi-center trials at least twice a year.
- All external audit reports must be submitted to the QACT per SOP QA-706 referenced above.
- Coordination of data collection, QA and computerization

4. Multi-Center Coordinating Committee (MCC)

- Assist in Protocol review
- Assure Multi-center criteria defined in this SOP are met

COORDINATION

Protocol

There will be one protocol document and each participating site will utilize that document. The site of the Overall PI is designated as the overall coordinating center (Lead Site) for the study.

Protocol must include:

- 1) DFCI Protocol Front Sheet, and Title page, if applicable (e.g., NCI, CTEP sponsored trials), with name of each participating institution and the site PI.
- 2) *Outline of procedure for central registration
- 3) *Outline of data submission schedule and process
- 4) *Section describing how SAEs and Deviations/Violations/Exceptions will be reported from each participating site to the overall Lead Site and to regulatory agencies, if applicable
- 5) *Section describing on-site auditing/monitoring plan for each participating site. This plan must be consistent with DF/HCC standards (refer to Multi-center Auditing and Monitoring SOP).
*Refer to the DF/HCC Multi-center Data and Safety Monitoring Plan.

Informed Consent

The Lead Site study team develops the model research consent document that must include a statement that data will be shared with the sponsor or its agents (which may include an outside CRO, medical monitor, Lead Site (DF/HCC), DSMB/DSMC and Lead Site's study team. The consent form must state that data shared with the Lead Site may include subject identifiers (name, date of birth, medical record

number). The Overall PI or designee is responsible for obtaining copies of each site's IRB approved consent forms. Each consent form must be reviewed for compliance with the DF/HCC multi-center consent template.

Central Specimen Collection, if applicable

A detailed process for this must be clearly outlined in the protocol and a method for tracking the information. Signed informed consent must occur before specimens are collected and the consent form may include a separate area for the research subject to opt out of optional research samples. If the subject chooses not to participate in the collection of optional specimens there must be a well-defined process for tracking this to prevent the collection of specimens without informed consent.

Regulatory paperwork

Study initiation: The Overall PI must obtain documentation of IRB approval from each participating site prior to the first subject registration at that site. The Overall PI must obtain and review the FDA 1572 form/ CV. This applies to both IND and non-IND trials.

The Regulatory Binder for the study is kept at the Lead Site. It should be noted that the non-lead sites maintain a non-lead regulatory binder for their reference in managing the trial; however we do not keep duplicate regulatory binders at the sites.

The Overall PI or designee at the Lead Site will manage all regulatory documents. The Overall PI is responsible for obtaining the regulatory documents from each participating site during the conduct of the study.

Site Communication

There must be documentation of regular communication with all participating sites. Participation includes all appropriate research staff, including investigators, research nurses and study coordinators. Communication may be by convened meetings, teleconferences or email distributions with the participating sites to update and inform about progress of the trial in a manner that is consistent with safe conduct of the trial. Documentation of the study communication regarding protocol/research subject related issues must be filed in the Lead Site regulatory binder.

SAE Reporting

All participating sites report SAEs directly to the IRB of record and to the Overall PI. The Overall PI or designee will submit SAEs to the DFCI IRB if they meet the DFCI IRB SAE reporting requirements. SAEs from non-DF/HCC participating sites are reported to the DFCI IRB using the DFCI IRB IND Safety Reporting Form.

Reporting unexpected problems involving research (violations/deviations/exceptions)

All participating sites report violations/deviations/exceptions directly to the IRB of record and to the Overall PI. The Overall PI or designee will submit violations/deviations/exceptions to the DFCI IRB per the DFCI OPRS Policy & Procedure for Deviation/Violation/Exception reporting requirements.

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