

Section 35: Conducting PI-initiated Multi-center Trials at DF/HCC

An Overall Principal Investigator (PI) of a DF/HCC PI-initiated protocol may invite investigators from non-DF/HCC (non-DF/PCC network affiliate) institutions to participate in the clinical trial. In these cases, the PI is ultimately responsible for the conduct of the trials at all participating sites, and the institution of the Overall PI is designated as the overall coordinating center (Lead Site) for the study. The Lead Site is required to manage all trial related documents and data.

This section provides an overview of the processes and oversight an Overall PI and Lead Site should have in place to ensure proper study management. For more information, please refer to the DF/HCC clinical research policy governing multi-center trials, SOP [PM-402](#).

35.1 Purpose and Function of a Lead Site

The Lead Site provides administrative, data management, and organizational support in the conduct of the multi-center trial. It functions as the central location for trial documents and subject registration, and monitors the conduct and progress of the clinical trial at all participating sites.

35.2 Overall PI Responsibilities

The DF/HCC Overall PI has ultimate responsibility for the conduct of the study, and for monitoring its safety and progress, at all participating sites. The Overall PI is also responsible for the coordination, development, submission, and approval of the protocol, and its subsequent amendments. It is the responsibility of the Overall PI to ensure that all participating sites are using the correct version of the protocol. The model research consent document must include a statement that data will be shared with the overall Lead Site (DF/HCC) and Data Safety Monitoring Committee (DSMC).

Additional responsibilities of the Overall PI include:

- Study staff training
- All regulatory reporting requirements
- Timely review of all serious adverse event (SAE) reports from all sites
- Review of all study data submitted for analysis
- Regular communication with all participating sites
- May delegate authority within the study team for ongoing trial management

Note: An Overall PI who holds an IND is bound to the investigator and sponsor requirements written in [21 CFR Part 312](#) and DF/HCC SOP [PM-408](#).

35.3 Lead Site Responsibilities

The Lead Site manages the regulatory documents and central participant registration process with QACT for each participating site, establishes procedures for submitting adverse events and unexpected problems involving research to the Overall PI and appropriate oversight entities, coordinates staff training, and facilitates monitoring and auditing visits.

35.4 Participating Site PI Responsibilities

Site PIs are responsible for the conduct of the trial at their individual site. It is the responsibility of the Site PI to ensure that his or her study team has the current version of protocol and informed consent documents and that the study team is conducting the clinical trial within the guidelines of Good Clinical Practice. Additional responsibilities of the Participating Site PI include:

- Designating a study coordinator and/or research nurse as the study contact
- Timely submission of study data
- Prompt reporting of serious adverse events (SAEs) and unexpected problems involving research to their IRB and to the DF/HCC Overall PI

35.5 Regulatory Binder

Each site must compile a regulatory binder specific to its function. The documents should be maintained or updated, as appropriate, throughout the course of the trial. Refer to DF/HCC SOP [PM-409](#) for the contents of the Lead Site and Non-Lead Site regulatory binders.

35.6 Staff Training

The Overall PI must ensure that all participating Site PIs and study staff are trained on the conduct of the protocol, study procedures, SAE reporting, and data collection. This may be accomplished through on-site visits or via teleconference. The general areas to be discussed should include, but are not limited to:

- Study design and procedures
- Informed Consent and registration procedures
- Adverse event reporting procedures and requirements
- Data Collection and Submission
- Ongoing meeting procedures
- Monitoring and auditing arrangements
- Pharmacy and drug administration procedures
- Participating site responsibilities and documentation

35.7 Central Participant Registration

The DF/HCC Quality Assurance Office for Clinical Trials (QACT) serves as the central location for registering all participants enrolled in a DF/HCC trial. The QACT maintains a participant registration list and a copy of each eligibility checklist and signed consent form.

35.8 Adverse Event Reporting

The Overall PI is responsible for the timely review of all SAE reports to assure the safety of participants. The Lead Site is the central location for the collection and maintenance of adverse event documentation and promptly submits SAE reports to the Overall PI.

The Lead Site maintains documentation of all adverse events in a regulatory binder for each site. Each non-Lead Site maintains its own documentation as required.

All adverse events must be reported as outlined in the protocol. Participating sites may need to report adverse events to their own IRB as well as to the DF/HCC Lead Site.

Note: A physician who is the IND holder is responsible for reporting to FDA. Non-lead sites do not report directly to the FDA on a sponsor-investigator trial [[21 CFR Part 312](#) and DF/HCC SOP [PM-408](#)].

35.9 Data Collection

The participating sites should submit case report forms (CRFs) to the Lead Site in a timely manner. For paper case report forms, the Lead Site will forward the documents to the QACT. Sites should be aware that they might need to send source documentation to DF/HCC.

35.10 Quality Assurance

The Overall PI is responsible for the integrity and accuracy of data collected at each participating site. The monitoring and auditing plans* should be based on the complexity and risk level of the trial and should be consistent with the standards outlined in the DF/HCC Clinical Trials Audit Manual. Typical monitoring and auditing visits may include review of original consent forms, case report forms and source documentation, treatment administration records, protocol compliance, and drug accountability. Sites should be aware that they might be audited by the DF/HCC in addition to any oversight delegated to an external Contract Research Organization (CRO).

* Refer to the [DF/HCC Multi-center DSMP](#) on the QACT website.

35.11 Site Communication

The Overall PI and Lead Site should have regular and documented communications with the participating sites to update and inform them about the progress of the trial.

35.12 Drug Ordering

Each participating site is responsible for the ordering, storing and dispensing of investigational agent(s) from the sponsor or company that is supporting the trial.

35.13 Inter-institutional Agreement/Contract

A formal agreement/contract is generally required. The agreement must be reviewed and approved by the DF/HCC Research Administration Office.

35.14 Multi-center Coordinating Committee (MCC)

The MCC was created in November 2007 to provide assistance to the PI and study team in the development of a PI-initiated multi-center trial and to assure compliance with DF/HCC SOP [PM-402](#). The PI/study team must follow the DF/HCC multi-center procedures for submitting a new multi-center protocol to the OHRS or whenever a single center protocol is being amended to add an external site. Please refer to the QACT website for the procedures and templates.