Dana-Farber/Harvard Cancer Center Site Management Plan

This version of the Site Management Plan is effective for new DF/HCC protocols submitted to the IRB on or after January 31, 2020. Protocols submitted prior to that date will continue to follow the previous December 2018 version of the Site Management Plan.

1.0 Oversight Responsibilities of the Principal Investigator

Each participating institution has a designated PI, who is responsible for the coordination, conduct, and oversight of the trial at that participating institution. For each DF/HCC protocol, there will be a designated core site. The PI of the core site may have additional responsibilities related to regulatory documentation and IRB submissions, as defined in policy RCO-102.

There will be a separate Form FDA 1572 signed by each respective PI. Participating sub-investigators, as designated by the PI, are listed on the Form FDA 1572. Each PI maintains an investigator's file at their respective site, in accordance with policy RCO-204 and the DF/HCC Regulatory File – Required Document List.

Brigham and Women's Hospital and Boston Children's Hospital are considered clinical facilities of Dana-Farber Cancer Institute (DFCI) and therefore will be listed on a DFCI PI's 1572 when applicable.

DF/HCC requires submissions of new and continuing human subject research to OHRS for feasibility, ancillary and scientific review, regardless of the IRB of record. The PI is responsible for all regulatory reporting specific to their institution as required by the protocol, regulations, IRB and/or sponsor or funding agency. This includes the submission of adverse events and protocol deviations/violations that are generated at their sites. The PI at the core site is responsible for the submission of all amendments, administrative modifications, continuing reviews, protocol changes and consent changes. The PI at the core site will keep other participating DF/HCC sites informed of the status of such submissions.

2.0 Institutional Review Board

The DFCI IRB may act as the IRB of record for cancer-related human subject research at the clinical institutions that comprise Dana-Farber/Harvard Cancer Center. Cancer-related research conducted under the auspices of the DF/HCC may be reviewed by another external IRB under a Reliance Agreement. Reliance Agreements are maintained by the Office for Human Research Studies (OHRS).

Communication from the IRB of Record is sent to each PI. This includes official approval documents. If the DFCI IRB is the IRB of record, original stamped or signed copies of approval letters are not issued. This is not a requirement of the Food and Drug Administration (FDA), and is not the policy of the DFCI IRB. Other IRBs follow their own policies and procedures for issuing approval documents. The core site is responsible for communicating external IRB of Record determinations to the OHRS.

3.0 Study Oversight/Dissemination of Study Safety Information

The PI may designate a study coordinator or other research staff to aid in study logistics, including coordination of study visits (e.g. pre-qualification and site initiation visits). Each PI is also responsible for overseeing subject recruitment at their respective DF/HCC institution.

IND Safety Reports
Each PI reviews safety information received from external sponsors per RCO-204. When necessary, the core site is responsible for submission to the IRB. The core site notifies all participating sites of submissions made to the IRB.

SAE Reports
Each individual site generates its own SAE reports for the PI, IRB and sponsor, if applicable (in accordance with procedures described in the protocol).

Study Supplies
Sponsors must provide each DF/HCC participating site with its own investigational agent/device supply and other study supplies (e.g. Laboratory kits, ECG machines, Glucometers etc.).

4.0 Training of Site Study Staff

Per EDU-100, all research personnel listed on the delegation of authority log receive protocol-specific training as appropriate for their role and delegated responsibilities in research. Each PI is responsible for ensuring that initial training is completed prior to an individual performing any research activity, and ongoing training is completed as appropriate. Additionally, EDU-100 requires DF/HCC Policy training and ongoing Human Subject Protection and Good Clinical Practice Training for all applicable research personnel. Training documentation is required for all research staff and may be maintained individually or centrally.

Investigators Meeting and/or Site Initiation Visit (SIV), if required by sponsor
Research team members attend the Investigator's Meeting and/or Site Initiation Visit (SIV) where details of protocol eligibility, treatment schedule, toxicity management, etc. are discussed. Research team members who are unable to attend the Investigator's Meeting or SIV receive and review the materials and this is documented prior to performing their protocol specific tasks.

In-Service(s), if required
Infusion room nurses and pharmacists receive an in-service, where the specifics of the protocol such as drug administration are discussed, by the research nurse staff. Nurses and pharmacists who attend the in-service are required to sign an attendance sheet. Infusion nurses that are unable to attend the in-service will review the protocol and attest that they have reviewed the protocol per their institutional process, prior to caring for subjects enrolled on the protocol. Pharmacists not able to attend an in-service will also have the opportunity to learn about the protocol through staff communication and self-learning through the Online Protocol System (OncPro). Pharmacists must review key sections of the protocol each time prior to verifying a clinical trial patient's medication order.

5.0 Informed Consent Documents

The most recent approved version of the informed consent document is available on the Oncology Protocol System (OncPro), and thus all informed consent documents must be printed from OncPro to ensure the correct version is used. The date and time (of the local machine) that an informed consent document is printed is noted at the top of the

informed consent document. Each PI is informed by OHRS when a new or revised informed consent document is posted for use on OncPro.

DF/HCC requires that subjects in clinical trials be registered in the DF/HCC Clinical Trial Management System (CTMS). This registration is required in addition to any registration by the study sponsor. Documentation of informed consent and subject eligibility must be in place prior to registration. If a subject is not properly registered, s/he cannot receive protocol therapy. An investigator listed on the Form FDA 1572 will ensure that each subject is consented and is eligible to participate in the research.

6.0 Study Drug Storage/Transport/Dispensation

Maintenance of Drug Accountability Records
At MGH, DFCI and BIDMC a standardized drug accountability form is utilized for maintaining drug accountability records for all DF/HCC clinical trials, except those which are sponsored by the National Cancer Institute (NCI). In those cases, the MGH, DFCI and BIDMC can print the electronic drug accountability forms in either standard NCI Drug Accountability Record Format (DARF) or in the NCI oral DARF.

Handling of Used Vials and Unused Drug
The pharmacist or a pharmacy technician under the supervision of a pharmacist at each site will be responsible for handling the vials and drugs within the pharmacy.

As per INV-100, all empty and partially used containers of investigational drugs are to be treated as hazardous substances with disposal occurring immediately after use into the hazardous drugs waste stream containers. The research pharmacies under no circumstances will store used product containers (vials, bottles, empty boxes, etc), un-blinded/open label tear-off labels, or ancillary supplies for accountability purposes. Products will be prepared per standard pharmacy guidelines and used vials (or other products) will be destroyed as per institutional policy.

Storage
All DF/HCC research pharmacies store investigational agents in locked areas under temperature control with restricted access.

Drug Destruction Policy

BIDMC: All used or unused investigational drug products are placed in chemo/hazard waste barrel immediately after drug preparation and dispensation. Each container is sealed when it reaches its full capacity. Environmental Services removes the container upon request from pharmacy and transports it to a third party outside vendor hired by BIDMC. All materials are then incinerated at an off-site facility. Please refer to the BIDMC Standard Operating Procedure for further detail.

DFCI: The drug destruction DFCI Standard Operating Procedure is on file. A copy can be provided if required.

MGH: All used investigational products are placed in a Chemotherapy Waste Container immediately after drug preparation and dispensation. Each container is then sealed and stored with other containers of chemotherapy waste. At the end of each day, Environmental Services removes the containers from the pharmacy to the building's loading

dock for pickup by an outside vendor hired by MGH. All materials are then incinerated at an off-site facility. Please refer to the MGH Standard Operating Procedure for further details.

Management of Drug Expiration
Medications that expire will be held for 30 days from the date of expiration for sponsor disposition. At the end of the 30 days, any remaining expired drug will be destroyed per each research pharmacy's institutional policy.

Processes for Prevention of Errors in Drug Dispensation
All investigational drugs are marked with the DFCI IRB protocol number. Each subject is registered in the OnCore Clinical Trials Management System before they can receive study drug. This registration is verified prior to dispensing.

Study Drug/Supply Shipment for BIDMC, DFCI, MGH main institutions:
Drug and other pharmacy study supplies are shipped from the sponsor to the research pharmacy of each site.

Study Drug/Supply Shipment for Satellites and Network Affiliates sites (see definitions):
Satellites generally receive study drug and pharmacy supplies from the main institution's research pharmacy. However, a sponsor must ship study drug directly to each Satellite location in some instances. These include, but are not limited to, the following:

- Cooperative group studies and other studies where drug is supplied by the NCI Pharmaceutical Management Branch (PMB)
- Studies using an Interactive Web & Voice Response system (IWRS or IVRS system) to assign study drug to individual subjects.

DF/PCC Network Affiliates will receive all pharmacy study supplies directly from the sponsor and NCI.

7.0 Source Documents

Electronic medical records and/or paper charts are maintained by each site according to the respective institutional policy. Access to source documentation will be provided according to institutional policy.

8.0 Case Report Forms (CRFs)

The study coordinator responsible for the study at each site completes CRFs. Monitoring occurs at each individual site. Query resolution should be directed to the study coordinator at the site maintaining the CRF that generated the query. The PI has ultimate responsibility for all aspects of trial performance including CRF completion.

Data Submission and Entry Requirements

DF/HCC will follow the sponsor's timeline for electronic CRF data management provided that those timelines minimally allow 10 days from a subject visit for data entry and 5 days for query resolution. When requested by the sponsor, investigator sign off of the CRFs will occur for formal database locks and prior to study completion.

9.0 Maintenance/Record Retention of Regulatory Files

Each site maintains regulatory files according to DF/HCC policy RCO-203. Upon IRB completion of the research, the documents may be shipped to a long-term storage facility where they are kept for the period required by DF/HCC policy RCL-101. Documents can be retrieved from the long-term storage facility upon request.