| **TITLE:** Regulatory Documentation | | |
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| **POLICY #:** RCO-203 | **Page:** 1 of 7 | **Effective Date:** ~~9/30/22~~1/3/2023 |

## 1. POLICY STATEMENT:

Essential regulatory documents will be maintained for research sponsored by or conducted at Dana-Farber/Harvard Cancer Center (DF/HCC) to assure compliance with regulatory requirements.

**Commented [SC1]:** 5.1.2.1. Language added to clarify that data/records in iRIS, OnCore or other DF/HCC systems must still be captured and saved in the regulatory file as necessary. Teams cannot simply point to the systems to satisfy a regulatory binder requirement.

## 2. BACKGROUND:

Regulatory documents individually and collectively permit evaluation of the conduct of the research and the quality of data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of good clinical practice (GCP) and with all applicable regulatory requirements. Upon request of the monitor, auditor, Institutional Review Board (IRB), or regulatory authority, regulatory documents must be made available for review.

## 3. RESPONSIBLE PERSONNEL:

3.1. Investigator acting as a Sponsor
3.2. Principal Investigator (PI)
3.3. Subinvestigator
3.4. Research Nurse
3.5. Study Coordinator

## 4. DEFINITIONS:

4.1. **Core Site:** The designated DF/HCC site that coordinates common regulatory submissions for DF/HCC sites.

4.2. **Subsite:** Participating DF/HCC sites that are not the Core Site. Satellite or Network Affiliate sites that have their own PI are considered subsites.

4.3. **Satellite Site:** A site licensed and accredited under one of the DF/HCC institutions that functions under the wider umbrella of the parent institution.

4.4. **Network Affiliate:** Select community hospitals that have a contractual agreement with a DF/HCC member institution.

4.5. **Trial Master File:** Regulatory documents maintained by the Sponsor.

4.6. **Investigator Regulatory File:** Regulatory documents maintained by the investigator at the investigative site.

4.7. **Sponsor**: The entity (i.e., individual, company, institution, or organization) that initiates a research project and bears direct responsibility for the overall conduct of the study.

4.8. **Principal Investigator (PI):** An individual who actually conducts and provides oversight for the research at their site. In the event the research is conducted by a team of individuals, the principal investigator is the responsible leader of the team.

4.9. **Subinvestigator**: A subinvestigator is any other member (i.e., other than the PI) of the study team who will make clinical decisions during the study or make a direct and significant contribution to the data. The ICH GCP guideline defines sub-investigator as "any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions".

4.10. **Form FDA 1572:** An agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic.

4.11. **Curriculum Vitae (CV):** A special type of resume traditionally used within the academic and research community. Earned degrees, teaching and research experience, publications, presentations, and related activities are featured to demonstrate training and experience to conduct research trials

4.12. **Delegation of Authority Log:** A list of the appropriately qualified persons to whom significant trial-related duties have been delegated.

## 5. POLICY:

### 5.1. Regulatory Document Requirements

5.1.1. This policy applies to all protocols activated on or after September 17, 2012. National Cancer Institute (NCI) National Clinical Trials Network (NCTN) trials must follow Clinical Trials Monitoring Branch (CTMB)

requirements and are not required to adhere to this policy where it differs from CTMB requirements.

5.1.2. The Trial Master File, and Investigator Regulatory File must contain the required regulatory documents as per the DF/HCC Regulatory File: Required Document List and are subject to regulatory review.

5.1.2.1. Data stored in central DF/HCC systems (e.g., OnCore, iRIS, OncPro) are not considered part of the Trial Master File or Investigator Regulatory File. Regulatory documents must be separately filed in a distinct Trial Master File/Investigator Regulatory File.

5.1.3. There is one Investigator Regulatory File for each protocol at each participating DF/HCC core site and subsite.

5.1.3.1. The Investigator File maintained at the core site may have additional requirements, as outlined in the DF/HCC Regulatory File: Required Document List. The Investigator Regulatory File may be merged with the Trial Master File when appropriate.

5.1.3.2. Financial information (e.g. budget, contracts, billing records, funding notifications, grant applications, etc.) and internal audit information are not subject to regulatory review and must be kept in a separate file.

5.1.4. Regulatory documents need not be stored together in one location. However, the location of files stored separately (including centrally or electronically) must be documented in a Note to File per DOC-100.

5.1.5. During the course of the research, regulatory documents will be stored in a secure location, accessible only to research team members, and updated contemporaneously. After site close out or study completion, regulatory documents will be maintained as per RCL-101.

5.1.6. All versions of essential regulatory documents must be maintained in the regulatory file. Old versions of essential regulatory documents must not be destroyed or discarded.

5.2. **Delegation of Authority Requirements**

5.2.1. Each PI must maintain a delegation of authority log for all non-exempt human subject research. Unless otherwise required by an external sponsor

(e.g., when NCI requires the use of the CTSU delegation of tasks log), the DF/HCC Delegation of Authority Log Template must be used.

5.2.1.1. Banking, tissue collection, and IRB-determined, minimal risk research are exempted from this requirement.

5.2.2. The delegation of authority log must include all individuals who will be delegated to perform any significant research activity, including (when applicable) all activities regulated by the Food and Drug Administration (FDA).

5.2.2.1. Staff members performing routine procedures (i.e. commercial services or standard of care assessments) will not be listed. Therefore, infusion unit or inpatient nurses, radiologists, pathologists, pharmacy technicians, phlebotomists, Tumor Imaging Metrics Core (TIMC) staff, residents, fellows, ophthalmologists, dermatologists and office staff are not included unless it is determined by the PI that they make a direct and significant contribution to the research.

5.2.2.2. Individuals performing only sponsor responsibilities (e.g., 21 CFR 312 parts 50 through 59) on investigator-sponsored trials do not need to be listed.

5.2.2.3. While authority to perform specified tasks may be delegated, the overall responsibility for those tasks always remains with the PI. Therefore, it is not necessary to list the PI.

5.2.3. Individuals on the delegation of authority log must be qualified to perform their delegated tasks by means of education, training and experience.

5.2.3.1. The DF/HCC Key: Delegation of Tasks for Clinical Research defines which activities an individual may perform based on their research role. Any additional qualifications or restrictions detailed in the protocol document, to the extent that they are more restrictive, take precedence over DF/HCC policy and state law. For example, if state law permits nurse practitioners to perform physical examinations under physician supervision, but the protocol specifies that a physician must do the physical examination, the protocol's requirements take precedence to the extent that they do not contravene state law.

5.2.3.2. All individuals on the delegation of authority log must be trained on DF/HCC Policies as required by EDU-100, and personally sign and

initial the Policy Training and Signature record. This training record also serves as a central signature record for the individual to ensure handwritten entries in the research documentation can be attributed to the person responsible for the information. This is filed at the individual's home institution.

5.2.4. The PI must approve the delegation log prior to initiating research on the protocol. The PI, or designee, will assure that the delegation of authority log is kept up-to-date. The addition of individuals to the delegation log and/or any changes to roles or start dates must be approved by the PI before the additional individual can perform the newly delegated tasks.

5.3. **Form FDA 1572 Requirements**

5.3.1. All Food and Drug Administration (FDA) regulated research conducted under an Investigational New Drug Application (IND) requires a protocol specific Form FDA 1572. For research where multiple DF/HCC sites are participating, there must be a separate 1572 signed by each respective PI. Each participating institution will maintain copies of the Form FDA 1572 for their site, including the initial form and any subsequent revisions.

5.3.2. The PI must list in section 6 of the FDA 1572 all subinvestigators at that site who will make a direct and significant contribution to the reporting of research data (e.g. recruiting subjects, administering the informed consent document, determining subject eligibility, generating study data, assessing primary endpoints, evaluating efficacy data, etc.). At DF/HCC, this includes physicians, physician assistants, nurse practitioners, and research nurses.

5.3.2.1. Research nurses may be listed the Form FDA 1572 if the PI believes they will be making a direct and significant contribution to the data for a particular study.

5.3.2.2. Research pharmacists, pharmacy technicians, study coordinators, infusion or inpatient nurses, radiologists, surgeons, pathologists, radiation oncologists, phlebotomists, ophthalmologists, dermatologists, radiation nurses, residents, fellows and office staff are not generally included when they provide ancillary or intermittent care but do not make a direct and significant contribution to the data. However, they may be included on the Form FDA 1572 if the PI believes they are involved in protocol mandated research or activities which go beyond routine clinical care and which significantly contribute to the research.

5.3.3. The Form FDA 1572 must be double-sided or, if the form has multiple pages and/or attachments, stapled together.

5.3.4. The PI must personally sign and date the Form FDA 1572 (either by hand or using an acceptable electronic method per institutional policy). Stamped signatures and pre-filled dates are not acceptable.

5.3.5. Revisions to the Form FDA 1572 may be batched for periodic updates. New subinvestigators are not required to be listed on the FDA 1572 prior to participating in the research but must be added at the next update.

5.3.6. The Form FDA 1572 does not need to be revised for a laboratory or testing facility that is used infrequently and only to obtain standard of care results. However, any laboratory or testing facility that performs protocol-specific procedures or is responsible for generating significant endpoint, safety, or efficacy data must be added to the 1572.

5.4. **Curriculum Vitae (CV) Requirements**

5.4.1. The PI, or a designated research team member, must obtain and file a current CV for each individual listed on the protocol specific Form FDA 1572. Current CVs are defined as documents that have been updated within the last 2 years. CVs must be signed and dated via ink or electronic means on the first or last page.

5.4.2. An individual's current CV only needs to be filed once at study start up or at the time they join the study team. Upon request, a copy of the CVs on file will be provided to external sponsors. CVs will not be provided for individuals who are not listed on the protocol specific Form FDA 1572. CVs will be provided to sponsors in the format in which they are received from investigators and will not be altered to accommodate sponsor-specific formats.

5.5. **Licensure Requirements**

5.5.1. The PI, or designee, must verify at the time of study start-up the presence of a valid professional license from the applicable state medical board for physician investigators, nurse practitioners, physician assistants, and research nurses who are listed on the protocol specific Form FDA 1572.

5.5.2. Sponsors seeking to validate licensure will be directed to the relevant state licensing websites, which will allow them to download medical and professional licenses of DF/HCC research personnel. For Massachusetts:
MA state licensing website for physicians:
http://profiles.ehs.state.ma.us/Profiles/Pages/FindAPhysician.aspx
MA state licensing website for Nursing:
https://checkalicense.hhs.state.ma.us/MyLicenseVerification/

5.5.3. All professional licenses will be renewed per state regulations. The Overall PI or designated research team member is responsible for ensuring continued licensure for the duration of each investigator's participation in the clinical trial.

## 6. APPLICABLE REGULATIONS & GUIDELINES:

21 CFR 50 – Protection of Human Research Subjects
21 CFR 54 – Financial Disclosure by Clinical Investigators
21 CFR 56 – Institutional Review Boards
21 CFR 312 - Investigational New Drugs – Drugs for Human Use
21 CFR 812 – Investigational Device Exemption
45 CFR 46 – Protection of Human Subjects
FDA Industry Guidelines and Information Sheets
FDA Compliance Policy Guidance Programs: 7348.809, 7348.810, and 7348.811
Form FDA 1572 located at CDER forms
U.S.C. Title 18, Sec.1001

## 7. RELATED REFERENCES:

International Conference on Harmonisation – E6
DF/HCC Site Management Plan

## 8. RELATED FORMS & TOOLS:

DF/HCC Regulatory File: Required Document List
DF/HCC Delegation of Tasks for Clinical Research Key
DF/HCC Delegation of Authority Log Template
DF/HCC Policy Training and Signature Record