TITLE: Responsibilities of Investigators		
POLICY #: RCO-102	**Page:** 1 of 8	**Effective Date:** 9/1/21

1. POLICY STATEMENT:

DF/HCC research is conducted under a system where a single core site functions as a regulatory coordinating center, but a principal investigator is designated at each participating DF/HCC institution. The principal investigator takes responsibility for the conduct and oversight of research at their site(s). The principal investigator at the core site has some additional responsibilities.

2. BACKGROUND:

The Principal Investigator for the site is fully responsible for protocols conducted under his or her name as set out for example on the Food and Drug Administration (FDA) Form 1572, in Investigator Agreements, and on Institutional Review Board (IRB) approved protocols. This responsibility includes the protection of human subjects; ensuring the research is conducted in accordance with federal, state, and local laws and regulations, institutional policies, protocol requirements and IRB determinations; and delegation of research responsibilities and personal supervision of the research team.

3. RESPONSIBLE PERSONNEL:

3.1. Principal Investigator (PI)
3.2. Sub-investigator

4. DEFINITIONS:

4.1. **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.

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

4.3. **Sub-investigator**: Any member of the research team, other than the PI, who will make clinical decisions during the research or make a direct and significant contribution to the data, as determined by the PI. The International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines define sub-investigator as “any individual member of the clinical trial team designated and supervised by the investigator to perform critical trial-related procedures and/or to make important trial-related decisions”.

4.4. **Sponsor:** The individual, pharmaceutical company, government agency, academic institution, private organization, or any other organization who takes responsibility for the initiation, management, and/or financing of a trial and holds the IND/IDE when applicable.

4.5. **Sponsor-Investigator:** An individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug is administered or dispensed is referred to as a Sponsor-Investigator by the FDA.

5. POLICY:

5.1. This policy applies to both clinical and non-clinical research. Where indicated, some requirements are specific to certain types of research.

5.2. All PIs and sub-investigators involved in the conduct of National Cancer Institute (NCI) sponsored or funded research must register with the NCI and renew their registration annually.

5.3. All active protocols must have a designated core site and, when applicable, a separate PI for each other participating DF/HCC site. The following individuals may serve as a PI:

5.3.1. Active faculty members with privileges at a DF/HCC institution

5.3.2. For research deemed minimal risk by the IRB only, DF/HCC institution employees that are either faculty members without a medical license or privileges at a DF/HCC institution, nurse researchers with the endorsement of the respective institutional nursing department, or trainees and other non-faculty research personnel with the inclusion of a faculty mentor.

5.3.3. For satellites of main DF/HCC institutions, a separate PI for each satellite location may be designated or the PI at the main institution may serve as the PI for the satellite location.

5.4. **The following individuals may serve as sub-investigator:**

5.4.1. Active faculty members with privileges at a DF/HCC institution

5.4.2. Trainees or non-faculty staff affiliated with a DF/HCC institution who will be directly involved in the performance of procedures required by the protocol or the collection of data

5.4.3. Other individuals if they will make a significant intellectual or scientific contribution to the development and/or conduct of the research.

5.5. **Responsibilities of the PI:**

5.5.1. The PI assumes the responsibility for the conduct of the research at their site and must personally oversee the conduct of the research ensuring that it complies with applicable regulations and institutional policies. These responsibilities include:

5.5.1.1. Conducting research according to the signed investigator agreement, the research plan and/or protocol, and applicable regulations and IRB policies.

5.5.1.2. When applicable, ensuring that all medical decisions and activities are performed by an individual qualified according to state and local regulatory and licensure requirements.

5.5.1.3. When applicable, ensuring access to appropriate medical care for any research related injuries, during and following a subject's participation.

5.5.1.4. Ensuring no changes to the current written approved protocol are made unless previously approved by the IRB and the sponsor of the research or as necessary to protect the rights, safety or welfare of subjects as defined by IRB policy.

5.5.1.5. Obtaining and documenting the effective informed consent of the subject or the subject's legally authorized representative (LAR) prior to altering an individual's care for the purposes of research or initiating any research specific procedures and keeping the subject or the LAR informed of any new information which may affect the subject's continued willingness to participate.

5.5.1.6. Regulatory reporting specific to the PI's institution as required by the protocol, regulations, IRB and/or sponsor or funding agency. This includes reporting adverse events, all unanticipated problems involving risk to subjects or others, protocol violations, as well as any requests to deviate from the IRB approved protocol.

5.5.1.7. Recruiting subjects in a fair and equitable manner while weighing the potential risks and vulnerability of the subjects with the potential benefits of the research.

5.5.1.8. PIs and sub-investigators will each complete an attestation form to ensure financial disclosure is provided.

5.5.1.9. Controlling the use of any investigational or commercially available product, biologic or test article including maintaining adequate records of the use, disposition and storage of the product in compliance with applicable federal laws and institutional policies. Retaining records required for drug or device research in accordance with federal regulations and DF/HCC policy.

5.5.1.10. Ensuring that subject records and documentation are compiled, maintained and held in accordance with the research protocol, applicable regulations, institutional and DF/HCC policies, privacy laws, and that research documentation and records are available for inspection or audit.

5.5.1.11. Ensuring timely correction and documentation of data queries or other problems identified by research personnel, the Office of Data Quality, outside monitors or auditors, or other parties involved in the conduct of the research.

5.5.1.12. Documenting or reviewing the performance of delegated tasks in a satisfactory and timely manner and, where appropriate, verifying findings (e.g., observation of the performance of selected assessments or independent verification by repeating selected assessments).

5.5.1.13. Ensuring that source data are accurate, contemporaneous (i.e., documented in real time), and original. Ensuring collected data are supported by information in the source documents, and that information in source documents is accurately captured on the data collection forms, case report forms (CRFs), or elsewhere as appropriate for the research.

5.5.2. A PI may have additional responsibilities based on the nature of the research. These may include but are not limited to:

5.5.2.1. Sponsor responsibilities for the research where he or she is also the research sponsor (e.g., investigator holds an Investigational New Drug [IND] application or Investigational Device Exemption [IDE]). See RCO-100, when applicable.

5.5.2.2. Sponsor responsibilities for investigator-sponsored, multi-center trials. See MULTI-100.

5.5.2.3. Registration and results reporting in ClinicalTrials.gov, when applicable. See REGIST-200.

5.5.2.4. Obtaining sponsor permission prior to sharing and publication of research results. Submission of final peer-reviewed journal manuscripts that arise from National Institutes of Health (NIH) funds to digital archive PubMed Central upon acceptance for publication.

5.5.3. The PI may choose to delegate significant research-related duties. Delegation does not negate nor replace the obligations and responsibilities of the PI, who remains personally responsible for all research conducted at their site. When delegating duties to others, the PI must ensure that:

5.5.3.1. Delegation of authority is properly documented as per RCO-203.

5.5.3.2. All research personnel complete required training as per EDU-100.

5.5.3.3. There is adequate supervision and involvement in the ongoing conduct of the research by the PI and that these oversight responsibilities are not delegated. This should include regular and documented meetings and communication to review research progress, adverse events, changes to the protocol or other procedures, and issues with subject or staff compliance.

5.6. **Additional Responsibilities of the Core Site PI (or designee):**

5.6.1. The Core Site assumes additional responsibilities related to the coordination of the protocol across DF/HCC. These responsibilities include:

5.6.1.1. Submission of all amendments, administrative modifications, continuing reviews, protocol changes, and consent changes to SRC/IRB. The Core Site will keep other participating DF/HCC sites informed of the status of these submissions.

5.6.1.2. Tracking overall enrollment for DF/HCC and setting overall DF/HCC enrollment goals.

5.7. **Responsibilities of a Sub-investigator**

5.7.1. Sub-investigators assume delegated responsibility for the daily conduct of the research. These responsibilities include:

5.7.1.1. If applicable, maintaining license in the state for which they are enrolling subjects and/or credentials in the institution where the research is conducted.

5.7.1.2. Adhering to the IRB-approved protocol unless immediate actions are necessary to protect the rights, safety or welfare of subjects.

5.7.1.3. If applicable, obtaining and documenting the effective informed consent of the subject or LAR prior to altering an individual's care for the purposes of research or initiating any research specific procedures and keeping the subject or the LAR informed of any new information which may affect the subject's continued willingness to participate.

5.7.1.4. Promptly informing the PI of adverse events and unanticipated problems involving risk to subjects or others during the course of the research.

5.8. **Leaves of Absence, Departures and Transfer of PI Role**

5.8.1. If any PI will be taking a leave of absence for more than one month, but no more than three months, and will remain reachable by telephone or email, he or she may remain the PI and no change is necessary.

5.8.2. If any PI will be taking a leave of absence and will not be reachable by telephone or email, or the leave of absence will exceed three consecutive months, the PI must transition active research projects to a new, appropriately qualified principal investigator.

5.8.3. Any investigator or sub-investigator who will no longer be primarily employed at a DF/HCC institution, regardless of role, must adhere to applicable institutional policies that may restrict or prohibit ongoing research participation, access to confidential information, and/or the use of research data and specimens.

5.8.4. PIs who will no longer be primarily employed at a DF/HCC institution must complete and close out all active research projects with the IRB and OHRS or transition active research projects to a new, appropriately qualified principal investigator. Departing PIs of interventional, treatment studies must complete and close out projects or transition to a new PI. Departing PIs

of interventional, non-treatment and noninterventional studies who wish to continue participation in research after departure should verify that this is allowed by their institution and confer with the disease program leader to determine whether this is appropriate. Departing PIs will not have continued access to OncPro due to institution's confidentially agreements. OHRS must review all such requests and will ensure protocols are amended where necessary.

5.9. **PI Changes**

5.9.1. The current PI must prospectively report a planned change in PI to the Core Site, and any institutional offices as applicable. The Core site will notify the IRB, funding agency, sponsor, and/or the FDA, as applicable. For studies where a DF/HCC investigator holds an IND/IDE, the Sponsor-Investigator must promptly inform the FDA of any planned IND/IDE holder change via a transfer of IND/IDE letter.

5.9.2. In all cases, the new PI must be selected from the same institution and assume all responsibilities for the role, complete any required trainings prior to execution of the new role, and disclose any outside interests.

5.9.3. In the event a PI change submission cannot be practicably submitted and approved by the IRB prior to the current PI becoming unavailable, the regulatory files must indicate a qualified sub-investigator that will provide temporary oversight of the research and the reason why IRB approval was not prospectively obtained. The amendment to formally change the PI should be submitted as soon as possible.

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 Exemptions
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

7. RELATED REFERENCES:

International Conference on Harmonisation – E6

8. RELATED RESOURCES:

None