TITLE: Responsibilities of Investigators		
POLICY #: RCO-102	**Page:** 1 of 10	**Effective Date:** 1/31/~~19~~2020

1. POLICY STATEMENT:

~~A~~DF/HCC research is conducted under a system ~~using an Overall Principal Investigator (PI),~~where a single core site ~~responsible~~functions as a regulatory coordinating center, but a principal investigator ~~and subinvestigator~~ is ~~utilized for the conduct of~~designated at each participating DF/HCC ~~research.~~ institution. The ~~Overall Principal Investigator has the ultimate~~principal investigator takes responsibility for the conduct and oversight of ~~the~~ research ~~under his or her name.~~ at their site(s). The principal investigator at the core site has some additional responsibilities.

Commented [SC1]: Significant updates throughout to remove old terminology, and clarify the responsibilities of the PI at each participating DF/HCC site, including additional responsibilities that all under the Core Site.

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. ~~Overall~~ Principal Investigator (PI)
~~3.2. Site Responsible Investigator~~
~~3.3.~~3.2. Subinvestigator

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. ~~The DF/HCC Overall Principal Investigator is the Principal Investigator for all participating sites within DF/HCC.~~

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

4.3. **Subinvestigator**: 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 subinvestigator 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. ~~Investigators~~All PIs and subinvestigators 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 ~~single~~ designated ~~Overall PI~~core site and, when applicable, ~~Site Responsible Investigator~~ a separate PI for each other participating DF/HCC site. The following individuals may serve as ~~Overall~~a PI ~~or Site Responsible Investigator~~:

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, 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 subinvestigator:**

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 ~~Overall~~ PI:**

5.5.1. The ~~Overall~~ 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:

~~5.5.2.0.~~5.5.1.1. Conducting research according to the signed investigator agreement, the research plan and/or protocol, and applicable regulations and IRB policies.

~~5.5.3.0.~~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.

~~5.5.4.0.~~5.5.1.3. When applicable, ensuring access to appropriate medical care for any research related injuries, during and following a subject's participation.

~~5.5.6.0.~~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.

~~5.5.7.0.~~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.

~~5.5.8.0.~~5.5.1.6. ~~Completing and submitting reports~~Regulatory reporting specific to the PI's institution as required by the protocol, regulations, IRB and/or sponsor or funding agency. ~~Specifically,~~This includes reporting adverse events, all unanticipated problems involving risk to subjects or others, protocol violations, as well as any ~~changes in~~requests to deviate from the IRB approved protocol.

~~5.5.9.0.~~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.

~~5.5.9.1.~~5.5.1.8. ~~A signed~~PIs and ~~dated Statement of Principal Investigator / Statement of Sub-Investigator Form is required~~subinvestigators will each complete an attestation form to ensure financial disclosure is provided ~~for each research team member contributing data and performing protocol assessments~~.

~~5.5.10.0.~~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.

~~5.5.11.0.~~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. ~~The Overall~~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.

~~5.5.12.~~5.5.2. A PI may have additional responsibilities based on the nature of the research. These may include but are not limited to:

~~5.5.12.1.~~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 ~~and RCO-101~~, when applicable.

~~5.5.12.2.~~5.5.2.2. Sponsor responsibilities for investigator-sponsored, multi-center trials. See MULTI-100.

~~5.5.12.3.~~5.5.2.3. Registration and results reporting in ClinicalTrials.gov, when applicable. See REGIST-200.

~~5.5.12.4.~~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.

~~5.5.12.5. For Research Funded by the Department of Defense (DoD), the Principal Investigator is responsible for ensuring that all obligations for the research are fulfilled as required by the specific DoD Component. See OHRS Information Sheet – Research Funded or Supported by the Department of Defense.~~

~~5.5.13.~~5.5.3. The ~~Overall~~ PI may choose to delegate significant research-related duties. Delegation does not negate nor replace the obligations and responsibilities of the ~~Overall~~ PI, who remains personally responsible for all research ~~conduct.~~conducted at their site. When delegating duties to others, the ~~Overall~~ PI must ensure that:

~~5.5.13.1.~~5.5.3.1. Delegation of authority is properly documented as per RCO-203.

~~5.5.13.2.~~5.5.3.2. All research personnel complete required training as per EDU-100.

~~5.5.13.3.~~5.5.3.3. There is adequate supervision and involvement in the ongoing conduct of the research and 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.

~~5.5.14. The Overall PI must develop a written supervisory plan for each new clinical and non-clinical project application submitted on or after September 17, 2012, regardless of the research sponsor. The plan must be in place prior to the first subject accrual. The initial plan and any prospective changes to the plan must be maintained in the regulatory files. These documents are not subject to IRB review or approval. The supervisory plan must include the following seven elements, to the extent they apply to the research:~~

~~5.5.14.1. Routine joint meetings with site responsible investigators across all DF/HCC sites to review research progress, adverse events, changes to the protocol or other procedures, issues with subject or staff compliance. The date, content, and attendees for these meetings must be recorded.~~

~~5.5.14.2. A procedure for the timely correction and documentation of problems identified by research personnel, outside monitors or auditors, or other parties involved in the conduct of the research~~

~~5.5.14.3.1.1.1.1.~~ ~~A procedure for 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)~~

~~5.5.14.4. A procedure for ensuring that source data are accurate, contemporaneous (i.e., documented in real time), and original~~

~~5.5.14.5. A procedure for 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.~~

~~5.5.14.6. A procedure for addressing data queries and discrepancies identified by the monitor, the DF/HCC Office of Data Quality (ODQ), or other individuals responsible for oversight for the research.~~

~~5.5.14.7. Procedures for ensuring research personnel comply with the IRB-approved protocol and all adverse event assessment and reporting requirements.~~

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

5.6.1. ~~A~~The Core Site ~~Responsible Investigator~~ assumes ~~delegated~~additional responsibilities ~~that are limited to his or her institution.~~related to the coordination of the protocol across DF/HCC. These responsibilities include:

~~5.6.1.1.Promptly communicating information relevant to the conduct of the research to the Overall PI~~

~~5.6.1.2.Participating in the joint research meetings scheduled by the Overall PI. When it is not possible for him or her to participate in the meeting, he or she will ensure that a delegate is able to participate.~~

~~5.6.1.3.Coordinating routine meetings with research personnel within the Site Responsible Investigator's institution. Content will focus on safety and compliance topics (e.g., research progress, adverse events, changes to the protocol or other procedures, issues with subject or staff compliance, etc.). The date, content, and attendees for these meetings must be documented and made available to the Overall PI.~~

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 Subinvestigator**

5.7.1. Subinvestigators 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 ~~Site Responsible Investigator and the Overall~~ PI of adverse events and unanticipated problems involving risk to subjects or others during the course of the research.

5.8. **Leaves of Absence**

5.8.1. ~~If the Overall PI or Site Responsible Investigator~~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 ~~Overall PI or Site Responsible Investigator~~PI and no change is necessary.

5.8.2. If ~~the Overall PI or Site Responsible Investigator~~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 months**,** a qualified on-site alternate must be formally appointed to assume their responsibilities on each protocol.

5.8.2.1. The new ~~Overall~~ PI ~~or Site Responsible Investigator~~ 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.

5.8.2.2. The 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 replacement must be selected from within the institution hosting the IND/IDE, and~~ the Sponsor-Investigator must promptly inform the FDA of any planned IND/IDE holder change via a transfer of IND/IDE letter.

~~5.8.3. The Overall PI must prospectively report a planned change in Overall PI or Site Responsible Investigator to the funding agency, sponsor, and/or the FDA, as applicable. In addition, the Overall PI must promptly notify the IRB of any changes in Overall PI or Site Responsible Investigator according to the IRBs submission requirements.~~

~~5.8.3.1.When research is sponsored or funded by the National Institute of Health (NIH) or National Cancer Institute (NCI), notify the respective Grants and Contracts office of any planned change to Overall PI.~~

~~5.8.3.2.When research is sponsored by industry, notify the respective Grants and Contracts office of any planned changes to Overall PI or Site Responsible Investigator. Additionally, notify the sponsor of the Overall PI change by submitting the following information:~~

- ~~A revised Form FDA 1572, as applicable~~
- ~~Current Curriculum Vitae~~
- ~~Medical License, as applicable~~
- ~~Financial Disclosure Form~~

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:

OHRS Information Sheet: Overall PI or Site Responsible Investigator Leave of Absence
DF/HCC Study Team Meeting Agenda
DF/HCC Sample Joint Meeting Communication Record
~~DF/HCC Supervisory Plan Template~~
~~Guidance on Developing a Supervisory Plan for Clinical and Non-Clinical Research~~
OHRS Change of Principal / Site Responsible Investigator / External Investigator Form
OHRS Statement of Principal Investigator Form
OHRS Statement of Sub-Investigator Form
OHRS Outside Interests Log Sheet
OHRS Request to Add/Remove Site