TITLE: Responsibilities of Investigators		
POLICY #: RCO-102	**Page:** 1 of 11	**Effective Date:** ~~1/31/18~~1/31/19

1. POLICY STATEMENT:

A system using an Overall Principal Investigator (PI), site responsible investigator and subinvestigator is utilized for the conduct of DF/HCC research. The Overall Principal Investigator has the ultimate responsibility for the conduct of the research under his or her name~~, including subject safety, the integrity and validity of the data, delegation of research responsibilities and personal supervision of the research team.~~.

Commented [CC1]: Merged with RCO-206: Overall or Site PI Leave of Absence language below. Additional updates to streamline language and clarify requirements.

2. BACKGROUND:

The Principal Investigator is fully responsible for protocols conducted under his or her name as set out for example on the ~~Form FDA~~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 ~~as documented in medical records and research charts~~; ensuring the research is conducted in accordance with federal, state, and local laws and regulations, institutional policies, protocol requirements and IRB determinations; and ~~accountability for events of data collection that can be reconstructed from source data to demonstrate subjects participated in the research and efficacy/safety parameters support the data collected~~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. Subinvestigator

4. DEFINITIONS:

4.1. ~~**Investigator (Overall **~~**Principal Investigator**~~**):**~~: An individual who actually conducts the research. In the event the research is conducted by a team of individuals, the investigator is the responsible leader of the team. ~~For the research for which they are the Principal Investigator of the overall research project, this applies to all sites at which the research is conducted. For the research for which they are not the Principal Investigator of the overall research project but are the DF/HCC Overall Principal Investigator, this applies to all~~The DF/HCC Overall Principal Investigator is the Principal Investigator for all participating sites within DF/HCC.

4.2. **Site Responsible Investigator:** An individual located at a specific DF/HCC site and designated by the Overall PI to assist with the conduct of the research at that site.

4.3. **Sponsor:** The individual, pharmaceutical company, government agency, academic institution, private organization, or any other organization who takes responsibility for ~~and initiates the research. The sponsor does not have to actually conduct the research.~~ the initiation, management, and/or financing of a trial and holds the IND/IDE when applicable.

4.4. **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.

~~4.4.~~4.5. **Subinvestigator**: Any other member of the research team who will make clinical decisions during the research or make a direct and significant contribution to the data. 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".

5. POLICY:

5.1. This policy applies to both clinical and non-clinical research. ~~Specific~~Where indicated, some requirements ~~apply as applicable. For example, references~~are specific to ~~requirements relating to drugs will not apply to~~certain types of research ~~where no drug is involved~~.

5.2. 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. Qualifications for~~ All active protocols must have a single designated Overall PI and, when applicable, Site Responsible Investigator ~~and Subinvestigator Designation~~

~~5.4.~~5.3. for each participating site. The following individuals may serve as Overall PI or Site Responsible Investigator:

~~5.4.1.~~5.3.1. Active faculty members with privileges at a DF/HCC institution

~~5.4.1.1.~~For research deemed minimal risk by the IRB

~~5.4.1.1.1. Faculty~~only, faculty members without a medical license or privileges at a DF/HCC institution

~~5.4.1.1.2. Nurse~~, nurse researchers with the endorsement of the respective institutional nursing department

~~5.4.2.~~5.3.2. ~~Trainees~~, or trainees and other non-faculty research personnel with the inclusion of a faculty mentor.

~~5.4.3. The following individuals may serve as Site Responsible Investigator:~~

~~5.4.3.1.Active faculty members with privileges at a DF/HCC institution~~

~~5.4.3.2.For research deemed minimal risk by the IRB~~

~~5.4.3.2.1. Faculty members without medical licenses or privileges at a DF/HCC institution and nurse researchers, trainees or other non-faculty research personnel~~

~~5.5.~~5.4. **The following individuals may serve as Subinvestigator:**

~~5.5.1.~~5.4.1. Active faculty members with privileges at a DF/HCC institution

~~5.5.2.~~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

~~5.5.3.~~5.4.3. Other individuals if they will make a significant intellectual or scientific contribution to the development and/or conduct of the research.

~~5.6.~~5.5. **Responsibilities of the Overall PI**

~~5.6.1.~~5.5.1. The Overall PI assumes the responsibility for the conduct of the research and must personally oversee the conduct of the research ensuring that it complies with applicable regulations and institutional policies. These responsibilities include:

~~5.6.2.~~5.5.2. Conducting research according to the signed investigator agreement, the research plan and/or protocol, and applicable regulations and IRB policies.

~~5.6.3.~~5.5.3. When applicable, ensuring that all medical decisions and activities are performed by an individual qualified according to state and local regulatory and licensure requirements.

~~5.6.4.~~5.5.4. When applicable, ensuring access to appropriate medical care for any research related injuries, during and following a subject's participation.

~~5.6.5.~~5.5.5. 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.

~~5.6.6.~~5.5.6. 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 ~~their LAR~~the LAR informed of any new information which may affect the subject's continued willingness to participate.

~~informed of any new information which may affect their continued willingness to participate.~~

~~5.6.7.~~5.5.7. Completing and submitting reports as required by the protocol, regulations, IRB and/or sponsor or funding agency. Specifically, reporting adverse events, all unanticipated problems involving risk to subjects or others, as well as any changes in the IRB approved protocol.

~~5.6.8.~~5.5.8. 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.

~~5.6.9.~~5.5.9. ~~Ensuring~~A signed and dated Statement of Principal Investigator / Statement of Sub-Investigator Form is required to ensure financial disclosure is provided for each research team member contributing data and performing protocol assessments.

~~5.6.10.~~5.5.10. 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.

~~5.6.11.~~5.5.11. 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.

~~5.6.12.~~5.5.12. The Overall PI may have additional responsibilities based on the nature of the research. These may include but are not limited to:

~~5.6.12.1.~~5.5.12.1. Sponsor responsibilities for the research where he or she is also the research sponsor (e.g., ~~IND or IDE holder, PI-initiated research, multi-center research)~~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. Sponsor responsibilities for investigator-sponsored, multi-center trials. See MULTI-100.

~~5.6.12.2.~~5.5.12.3. Registration and ~~subsequent research~~ results reporting ~~for FDA-regulated research to~~in ClinicalTrials.gov, when applicable. See REGIST-200.

~~5.6.12.3.~~5.5.12.4. 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

~~5.6.12.4.~~5.5.12.5. For Research Funded by the Department of Defense (DoD~~): The~~), 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.

~~5.6.12.5. For general information on meeting these requirements, please refer to the OHRS Information Sheet, "Research Funded or Supported by the Department of Defense." Additional information regarding the specific requirements of the DoD Component should be obtained directly from the granting agency.~~

~~5.6.13.~~5.5.13. The Overall PI may choose to delegate significant research-related duties. Delegation ~~of duties~~ does not negate nor replace the obligations and responsibilities of the Overall PI, who remains personally responsible for all research conduct. When delegating duties to others, the Overall PI must ensure that:

~~5.6.13.1. Designated individuals are qualified to perform such tasks.~~

5.5.13.1. Delegation of authority is properly documented as per RCO-203~~0~~.

~~5.6.13.2.~~5.5.13.2. All research personnel~~, including experienced individuals and replacement staff, receive~~ complete required training ~~on how to conduct the delegated duties and are provided with an understanding of the research~~as per EDU-100.

~~5.6.13.3.~~ There is adequate supervision and involvement in the ongoing conduct of the research~~.~~

~~5.6.13.4.~~5.5.13.3. ~~These primary~~ and these oversight responsibilities are not delegated.

~~5.6.14.~~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 eleven elements, to the extent they apply to the research:

~~5.6.14.1.~~5.5.14.1. Routine joint meetings ~~(these can occur by telephone, video, or web conferencing)~~ 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. ~~Meetings will generally occur every 1-4 months, depending on the nature of the research, in order to ensure that the Overall PI is aware in a timely manner of toxicities, dose modifications, serious adverse events, and outcomes data at all sites participating in the research.~~

~~5.6.14.2. Routine meetings with the sponsor's monitors~~

~~5.6.14.3.~~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

~~5.6.14.4.~~5.5.14.3. 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)

~~5.6.14.5.~~5.5.14.4. A procedure for ensuring that source data are accurate, contemporaneous (i.e., documented in real time), and original

~~5.6.14.6.~~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.

~~5.6.14.7.~~5.5.14.6. A procedure for ~~dealing with~~addressing data queries and discrepancies identified by the ~~research~~ monitor, the DF/HCC Office of Data Quality (ODQ), or other individuals responsible for oversight for the research.

~~5.6.14.8.~~5.5.14.7. Procedures for ensuring research personnel comply with the IRB-approved protocol and all adverse event assessment and reporting requirements~~.~~.

~~5.6.15. The Overall PI will establish a regular review schedule, commensurate with the subject population and the nature of the research, to review related reports, decisions and documentation verifying actions taken for those duties that have been delegated. Review activities must be documented.~~

~~5.7.~~5.6. **Responsibilities of a Site Responsible Investigator**

~~5.7.1.~~5.6.1. A Site Responsible Investigator assumes delegated responsibilities that are limited to his or her institution. These responsibilities include:

~~5.7.1.1.Assuming all of the responsibilities outlined in section 5.3.1 for his or her institution~~

~~5.7.1.2.~~5.6.1.1. Promptly communicating information relevant to the conduct of the research to the Overall PI

~~5.7.1.3.~~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.

~~5.7.1.4.~~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~~. Meetings will occur every 1-4 months, depending on the nature of the research, in order to ensure that the Site Responsible Investigator is aware in a timely manner of toxicities, dose modifications, serious adverse events, and outcomes for subjects enrolled at his or her institution.~~ and made available to the Overall PI.

~~5.7.1.5.The Site Responsible Investigator will ensure that minutes from these institution-specific meetings are recorded, and a copy is forwarded to the Overall PI in a timely manner.~~

~~5.8.~~5.7. **Responsibilities of a Subinvestigator**

~~5.8.1.~~5.7.1. Subinvestigators assume delegated responsibility for the daily conduct of the research. These responsibilities include:

~~5.8.1.1.~~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.

~~5.8.1.2.~~5.7.1.2. Adhering to the IRB-approved protocol unless immediate actions are necessary to protect the rights, safety or welfare of subjects.

~~5.8.1.3.~~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.
~~and keeping the subject or their LAR informed of any new information which may affect their 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 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 and no change is necessary.

5.8.2. If the Overall PI or Site Responsible Investigator 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 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. 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 ~~Sample Joint~~Study Team Meeting Agenda
DF/HCC Sample Joint Meeting Communication Record
DF/HCC Supervisory Plan ~~for Clinical and Non-Clinical Research~~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