TITLE: Reporting of Protocol Deviations, Exceptions and Violations		
POLICY #: RCO-205	**Page:** 1 of 5	**Effective Date:** 1/31/19

1. POLICY STATEMENT:

All protocol deviations, exceptions and violations must be recorded and reported to the sponsor, Institutional Review Board (IRB) and, when required, to the appropriate regulatory authorities.

2. BACKGROUND:

Federal regulations specifically require the IRB of record to review proposed changes in a research activity, and to ensure that such changes in approved research are not initiated without prospective IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject [45 CFR Part 46.103(b)(4)(iii) and 21 CFR Part 56.108(a)(4)].

Research activity includes all aspects of the conduct of the research (e.g., recruitment methods, informed consent process, drug administration, data collection, procedures used to protect privacy and confidentiality, etc.) and all of the information outlined in the IRB application and/or protocol reviewed and approved by the IRB.

Investigators are also responsible for conducting human subject research in accordance with:

- Institutional Review Board (IRB) reviews, determinations, policies and procedures
- DFCI IRB Policies and Procedures for the Protection of Human Subjects in Research
- DF/HCC Policies and Operations
- DF/HCC Guide to Human Research Activities (GHRA)
- Office of Data Quality (ODQ) requirements
- All applicable Regulatory sponsor requirements

Non-compliance with IRB reviews, determinations, policies and procedures, DFCI IRB Policies and Procedures for the Protection of Human Subjects in Research, ODQ requirements, DF/HCC Policies or sponsor requirements during the conduct of a research study constitutes a deviation, violation or exception.

3. RESPONSIBLE PERSONNEL:

3.1. Overall Principal Investigator (PI)
3.2. Site Responsible Investigator
3.3. Subinvestigator
3.4. Research Nurse
3.5. Study Coordinator

4. DEFINITIONS:

4.1. **Major Deviation/Violation/Exception:** A deviation or violation that impacts the risks and benefits of the research; may impact subject safety, affect the integrity of research data and/or affect a subject's willingness to participate in the research.

4.2. **Minor Deviation/Violation:** A deviation or violation that does not impact subject safety, compromise the integrity of research data and/or affect a subject's willingness to participate in the research.

4.3. **Deviation:** Any prospective departure from the defined procedures set forth in the IRB-approved protocol.

4.4. **Exception:** Any protocol deviation that relates to the eligibility criteria, e.g., enrollment of a subject who does not meet all inclusion/exclusion criteria.

4.5. **Violation:** Any protocol deviation that was not prospectively approved by the IRB prior to its initiation or implementation.

4.6. **Research Activity:** All aspects of the conduct of the research study outlined in the protocol submission and reviewed and approved by the IRB, e.g., recruitment methods, consent process, treatment plan, data collection, procedures used to protect privacy and confidentiality, etc.

5. POLICY:

5.1. Except in emergency situations, a protocol exception or deviation request must be reported to the Overall PI and requires prior IRB and sponsor approval. Prior Food and Drug Administration (FDA) approval may be required for applicable research, if the exception or deviation request may affect the scientific soundness of the plan or the safety, rights or welfare of subjects.

5.2. In an emergency, a protocol deviation may be implemented to eliminate or reduce an apparent immediate hazard to a subject. Prior IRB approval is not required, but the deviation must be promptly reported to the IRB for review and to the sponsor, according to the protocol or contract requirements, and possibly to the FDA or other regulatory agency as appropriate depending on the nature of the research.

5.3. Source documents within the medical records or research charts must explain all deviations, exceptions and violations.

5.4. When a research team member learns that a deviation or exception is necessary, or a violation has occurred, he/she will contact the Overall PI who will assess the event and determine the required reporting. It is the responsibility of the Overall PI to determine whether an event is a major or minor event and to ensure proper reporting to the IRB.

5.5. Promptly report non-compliance that occurs during the course of the research to the sponsor and IRB, according to the protocol and/or contract requirements and the IRB of Records reporting policy. Note: The above definitions may not match the sponsor's definitions or expectations.

5.5.1. Major Deviation/Violation/Exception reports (also known as non-compliance reports) should include:

5.5.1.1. IRB protocol number

5.5.1.2. What was violated, e.g. protocol requirement, IRB policy, procedure, law or regulatory requirement that was not followed

5.5.1.3. Description or manner in which the event deviated from the protocol or failed to comply with the requirement

5.5.1.4. Reason for the departure

5.5.1.5. Date the sponsor was notified of the incident

5.5.1.6. Overall PI assessment regarding the major deviation / violation / exception effect on the subject's risk

5.5.1.7. Description of the implemented corrective action plan to prevent recurrence

5.5.2. The Overall PI must maintain a comprehensive log of all minor deviations and violations that occur during the course of the research inclusive of events occurring at participating sites. The minor deviation / violation log must be reported to the IRB at least annually at the time of continuing review submission. Report these events to the sponsor according to the protocol or contract requirements. Note: The above definitions may not match the sponsor's definitions or expectations.

5.6. Subjects' failures to follow the research design or procedures are considered protocol violations and must be reported to the Overall PI and the IRB. The Overall PI must determine if subject non-compliance results in either a major or minor protocol violation.

5.7. Reporting Investigators are responsible for knowing and adhering to the reporting requirements to their institutional risk management department.

5.8. The DFCI does not consider scheduling delays due to state or federal holidays, inclement weather, or circumstances beyond the control of the research team and/or the subject to be either non-compliance or unanticipated problems requiring reporting to the IRB of Record.

5.8.1. All scheduling delays, regardless of IRB reporting requirements, must be explained in the subject's medical record or research chart.

5.8.2. Conflicts with a subject's work schedule or planned vacation are generally considered non-compliance, or an unanticipated problem, and must be reported to the Overall PI and the IRB of Record per the IRB's reporting requirements. The Overall PI must determine if a subject' scheduling delays require reporting to the IRB of Record.

5.8.3. These situations may not match the sponsor's expectations.

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 New Device Exemptions
45 CFR 46 – Human Subject Protections
FDA Industry Guidelines and Information Sheets
FDA Compliance Policy Guidance Programs: 7348.809, 7348.810, and 7348.811

7. RELATED REFERENCES:

International Conference on Harmonisation – E6
OHRS Info Sheet – Policy: Deviation/Violation/Exception and Other Event Reporting to DFCI IRB

8. RELATED RESOURCES:

DFCI IRB Major Deviation/Violation/Exception/Other Event Reporting Form
DFCI IRB Minor Deviation/Violation Log
DF/HCC Guidance on Reviewing Protocol Departures and Developing Corrective Actions