TITLE: Preparation for Site Close Out		
POLICY #: RCL-100	**Page:** 1 of 4	**Effective Date:** 8/31/16

1. POLICY STATEMENT:

There are procedures that are conducted at the time of site termination or formal close out of research subject to FDA regulations for drugs, biologics and devices during all phases of development. Site termination should take place once enrollment has ceased and all subjects have completed the protocol including the follow-up/data analysis phase of the trial.

2. BACKGROUND:

A close out visit is the final visit a monitor will conduct to formally terminate a site's participation in a research study. Sponsors/Contract Research Organizations (CROs) conduct close out visits to ensure that all data has been collected and verified, to perform the final accounting and disposition of test articles and to verify that the site's files are complete and accurate after all subjects have completed the protocol. Close out visits are usually scheduled after submission of all clinical data from a site and all queries have been resolved. Sponsors may elect to conduct the final monitoring and termination at the same close out monitoring visit.

3. RESPONSIBLE PERSONNEL:

3.1. Overall Principal Investigator (PI)
3.2. Research Nurse
3.3. Study Coordinator

4. DEFINITIONS:

4.1. **Closed Protocol:** A protocol that is permanently closed to enrollment of new subjects. The protocol remains active for treatment or long term follow up/ data analysis.

4.2. **Completed Protocol**: All subjects on protocol have completed the treatment and the follow up/data analysis phase of the trial. No further research takes place (e.g. no subjects are treated or followed; no additional data are collected).

5. POLICY:

5.1. **Sponsor Initiated Trials:**

5.1.1. The sponsor will contact the site to schedule the close out visit once the last subject has completed all scheduled visits associated with the protocol.

5.1.2. The clinical trial monitor should send a close out confirmation letter describing what is expected, what needs to be accomplished before the visit takes place, and other issues that require resolution before the visit.

5.1.3. Ensure that all required monitoring is complete. If all data were entered by computer, determine when hard copies or the CD of all case report forms (CRFs) will be provided to the site.

5.1.4. Ensure that all data queries received to date have been resolved and that the database has been locked.

5.1.5. DF/HCC Lead Site must check-in with all participating DF/HCC non-lead and satellite sites and confirm that all their outstanding data queries have been resolved and all data is complete.

5.1.6. Confirm that all research drug, biologic or device has been returned to the sponsor or destroyed at the site. File copies of drug, biologic or device packing slips and shipment receipts appropriately.

5.1.7. Ensure return or destruction of all other protocol-related materials, such as unused research kits or unused CRFs.

5.1.8. Ensure that any equipment on loan (i.e. EKG machines, holter monitors, blood pressure cuffs) is returned. If the equipment was inspected by Biomedical Engineering, please notify them that the equipment was returned.

5.1.9. Check the status of the final payment from the sponsor.

5.1.10. Review with the clinical trial monitor the responsibilities for reporting serious adverse events and IND safety reports after formal termination of the protocol.

5.1.11. Review with the clinical trial monitor the possibility of a quality assurance (QA) and/or Food and Drug Administration (FDA) audit.

5.1.12. Ensure the site receives a final letter from the clinical trial monitor stating everything has been done and there are no outstanding issues.

5.1.13. Once the final close out monitoring report is received by the Overall PI, notify the Institutional Review Board (IRB) that the protocol is complete by submitting a Study Completion Request. The Study Completion Request

may be submitted at any time or you may wait until the next continuing review is due. The IRB will send an approval for this form that must be filed with the lead site's essential regulatory documents.

5.1.14. Once the protocol is complete, all applicable documents and files (CRFs, research charts, regulatory files and other related data) may be sent to storage per the DF/HCC policy on record retention.

5.2. **PI- Initiated Trials (DF/HCC PI is the sponsor):**

5.2.1. Ensure that the database is complete, clean, and ready for analysis.

5.2.1.1. All CRFs must be completed and submitted to the Office of Data Quality (ODQ), as applicable.

5.2.1.2. All data queries must be answered and resolved.

5.2.1.3. The PI and/or study team must confirm with ODQ that all data cleanup activities are complete, no data is outstanding, and no additional queries will be opened.

5.2.2. Notify the research pharmacy to either dispose of or prepare any unused drug, biologic or device for return to the supplier.

5.2.3. Ensure that any equipment on loan (i.e. EKG machines, holter monitors, blood pressure cuffs) is returned. If the equipment was inspected by Biomedical Engineering, please notify them that the equipment was returned.

5.2.4. Ensure that final payment is received from the funding sponsor, if applicable.

5.2.5. Confirm that www.clinicaltrials.gov record is up to date, including study status and results entry (if required to report results). For clinicaltrials.gov records that are considered applicable to FDAAA-801, results must be posted and accepted without comment from the Clinicaltrials.gov QA department.

5.2.6. Once the protocol is deemed complete by the Overall PI, a Study Completion Request is submitted to the IRB as the final protocol report. The Study Completion Request may be submitted whenever the protocol is ready to be completed or at the time the next continuing review is due. The IRB

will send an approval for this form that must be filed with the lead site's essential regulatory documents.

5.2.7. Once the protocol is complete and no further research takes place, all applicable documents and files (CRFs, research charts, regulatory files and other related data) may be sent to offsite storage per the RCL-101.

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 – Human Subject Protections
FDA Industry Guidelines and Information Sheets
FDA Compliance Policy Guidance Programs: 7348.809, 7348.810, and 7348.811
Clinical Trials Agreement

7. RELATED REFERENCES:

International Conference on Harmonisation – E6

8. RELATED RESOURCES:

DF/HCC Sample Research Close Out Checklist
DFCI IRB Study Completion Request Form