DANA-FARBER / HARVARD CANCER CENTER
POLICIES FOR HUMAN SUBJECT RESEARCH

TITLE: Preparation for Site Close Out		
POLICY #: RCL-100	**Page:** 1 of 6	**Effective Date:** ~~8/31/16~~

1. POLICY STATEMENT:

~~There are procedures that are conducted~~Certain steps must be taken at the time ~~of site~~ or, or prior to, the 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~~at a site or IRB completion of a research protocol.. These can only occur after enrollment has ceased ~~and,~~ all subjects have completed the protocol including ~~the~~ any follow-up~~/~~ activities, and all data ~~analysis phase of the trial~~collection is complete.

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~~ will perform close out ~~visits~~activities 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~~These activities 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~~during an onsite close out monitoring visit. DF/HCC sponsor-investigators are responsible for conducting close out activities with each participating site prior to completion of the protocol with the IRB.

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 has ended. No further research takes place (e.g. no subjects are treated or followed; no additional data are collected).

5. POLICY:

Version: ~~6~~7
Effective Date: ~~8/31/16~~
Last Reviewed Date: ~~6/30/16~~

Commented [CC1]:
Updated to encompass all DF/HCC research, rather than FDA-specific

Updates to clarify requirements for externally-sponsored vs. investigator-sponsored

5.1. ~~**Sponsor Initiated**~~**Externally-Sponsored Trials:**

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

5.1.2. ~~The~~For on site monitoring visits, 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.~~5.1.3. The DF/HCC Lead Site must ~~check in~~confirm 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.~~that the following have occurred:

5.1.3.1.~~Confirm that all~~All required data entry is complete and all data queries have been answered and resolved.

~~5.1.5.1.~~5.1.3.2. All research drug, biologic or device ~~has~~products have been returned to the sponsor or destroyed at the site~~. File~~, and copies of ~~drug, biologic or device~~all related documentation, including packing slips and shipment receipts, are filed appropriately.

~~5.1.5.2.~~5.1.3.3. ~~Ensure return or destruction of all~~All other protocol-related ~~materials~~supplies, such as unused research kits or unused CRFs~~.~~, have been returned or destroyed.

~~5.1.5.3.~~5.1.3.4. ~~Ensure that any~~Any equipment on loan (i.e. EKG machines, holter monitors, blood pressure cuffs) ~~is~~has been returned~~. If the equipment was inspected by~~ and Biomedical Engineering~~, please~~

~~notify them that the equipment was returned.~~ has been notified.

~~5.1.5.4.~~5.1.3.5. ~~Check the status of the final payment~~ All expected payments from the sponsor~~.~~ have been received.

5.1.4. ~~Review~~After close out activities have been completed, the Lead Site confirms the following items with the ~~clinical trial monitor the~~sponsor:

5.1.4.1.When hard copies or the CD of all case report forms (CRFs) will be provided to the site.

~~5.1.5.5.~~5.1.4.2. Any ongoing responsibilities for reporting ~~serious adverse events and IND~~ safety ~~reports~~information after formal termination of the protocol.

~~5.1.5.6.~~5.1.4.3. ~~Review with the clinical trial monitor the~~The possibility of a quality assurance (QA) and/or Food and Drug Administration (FDA) audit and process to notify the sponsor should these occur.

~~5.1.5.7.~~5.1.4.4. ~~Ensure the site receives~~ Receipt of a final report or letter from the ~~clinical trial monitor~~sponsor (or representative) stating ~~everything has been done and~~ that there are no outstanding issues and DF/HCC may complete the study with the IRB.

~~5.1.6.~~5.1.5. Once the final close out ~~monitoring~~letter or 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.~~

~~5.1.7.~~5.1.6. Once the protocol is IRB complete, ~~all~~no further research activities may take place. All applicable documents and files (CRFs, research charts, regulatory files and other related data) ~~may~~must be ~~sent to storage per the~~ maintained and stored according to DF/HCC policy ~~on record retention~~RCL-101.

5.2. ~~**PI-Initiated**~~**DF/HCC Investigator-Sponsored Trials** ~~(~~**:**

~~5.2.~~ The 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. ~~All data queries~~ investigator must ~~be~~ensure completion of the following activities prior to IRB closure of each participating site:

5.2.1.1.All monitoring and quality control activities (including ODQ review of the data for InForm trials) are complete and all outstanding issues have been resolved.

5.2.1.2.All required data entry is complete and all data queries have been 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.~~

~~5.2.1.4.~~5.2.1.3. ~~Notify the research pharmacy to either dispose of or prepare any unused~~All research drug, biologic or device ~~for return to the supplier.~~products have been returned or destroyed appropriately.

~~5.2.2. 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.~~

5.2.1.4.~~Ensure that~~ Any loaned equipment or devices have been returned, as applicable.

5.2.1.5.All subject registration information is up to date with final ~~payment is~~subject status.

5.2.1.6.All research samples have been shipped and received, as applicable.

5.2.1.7.All required regulatory documents have been collected and filed.

5.2.1.8.All expected payments have been received from ~~the~~ funding collaborators and paid out to participating sites.

~~5.2.3.~~ For protocols registered on ClinicalTrials.gov, the responsible party (usually the sponsor~~, if applicable.~~

~~5.2.4.~~5.2.2. ~~Confirm that www.clinicaltrials.gov~~ investigator) must confirm that the 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.

5.2.3. ~~Once~~After all of the ~~protocol is deemed~~above are complete ~~by,~~ the DF/HCC Overall PI~~,~~ or designated research staff member will submit a Study Completion Request ~~is submitted~~ to the IRB ~~as~~. When applicable, the sponsor-investigator may also need to provide a final ~~protocol~~study report~~. The Study Completion Request may be submitted whenever~~ to the ~~protocol is ready to be completed or at the time the next continuing review is due. The~~FDA and/or funding sources.

~~5.2.5.~~ Following IRB ~~will send an~~ approval for ~~this form that must be filed with the lead site's essential regulatory documents.~~

~~5.2.6.~~5.2.4. ~~Once the protocol is complete and~~the study completion, no further research ~~takes~~activities may take place~~, all~~. All applicable documents and files (CRFs, research charts, regulatory files and other related data) ~~may~~must be ~~sent~~maintained and stored according to ~~offsite storage per the~~DF/HCC policy 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