1 PURPOSE
This procedure describes the process for conducting business with representatives of the FDA before, during, and after an inspection of FDA-regulated human subject or other related research within the Memorial Healthcare System.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES
a) The Investigator and all study personnel are responsible for fully cooperating with all FDA requests and personnel engaged in the inspection.

b) The Investigator may request the Office of Human Research (OHR) assist with the details regarding preparation, coordination and scheduling directly with the FDA.

c) The Investigator is responsible for carrying out all follow-up actions and responses with consultation from the OHR, if necessary.

d) The Investigator is responsible for maintaining the FDA inspection files, to include copies of the Form 482 (Notice of Inspection), Form 483 (Inspectional Observations) if issued, copies of all documents provided to the FDA Inspector, response letter(s) to the Form 483, the FDA Establishment Inspection Report (EIR), and inspection classification correspondence. The investigator will ensure copies of these records will be provided to the OHR and MHS Legal (if applicable) when contract notifications to Sponsors are needed.

3 SPECIFIC PROCEDURES
3.1 Before the Inspection
a) If contacted by the FDA to schedule an inspection, the Investigator should immediately inform the OHR, the IRB of record and the Sponsor (if required by contract) of the
2.2 During the inspection

a) On the first day of the inspection, and upon arriving to the site, the Principal Investigator or designee must ask to see the FDA Inspector's credentials (identification with photograph).

b) The inspection must not begin until the FDA Inspector has provided the Form FDA 482, Notice of Inspection, to the Investigator and the purpose of the inspection has been ascertained. The Investigator is required to sign the Form FDA 482.

c) The Investigator or designee will assemble other applicable individuals for the inspection.

d) The Investigator will provide the FDA Inspector with adequate space to review documents and records. The Inspector should be taken to a private room to conduct the audit and provided with the relevant files – Regulatory binder, ICF, subject binders, Accountability logs, etc. for the designated study.

e) Documents that the FDA may not inspect (except when Investigator provides them voluntarily) include but are not limited to:
   - Financial data
   - Personnel data (other than that needed to establish the qualifications of technical and professional personnel performing functions as defined by their roles in the delegation log)
   - Internal Monitoring and Compliance visit records (written certification may be provided that these visits are performed)

h) The following are forbidden (unless they are part of an IRB approved research protocol, or part of Memorial Healthcare System approved media coverage):
   - Still or video cameras, or voice recording apparatus as part of an audit.
   - If an FDA Inspector has such equipment, he/she should be asked to store the equipment in his/her car or in a secured location on the premises.
   - If the FDA Inspector insists on using such equipment, the Investigator, in consultation with OHR and Memorial Healthcare System’s Legal department should decide whether this request should be honored.

i) The FDA Inspector may request to view electronic data files on a computer, and to make copies of electronic data files on a flash drive to be provided to him/her as part of the inspection document collection process. The Investigator and other institutional officials should be prepared to respond to that request as appropriate.
Investigator Standard Operating Procedures

j) The Investigator will designate an individual to take notes of activities and discussions during the inspection.

k) The Investigator will designate an individual to make copies and obtain documents and records as requested.

l) The Investigator must approve all FDA requests for copies of documents and records, and review the copies of documents and records before handing them to the FDA Inspector. He/She must first be satisfied that appropriate measures have been taken to ensure the protection of proprietary or confidential information contained in those documents and records. If the Investigator is unsure if such a request is appropriate, the Investigator can consult with the OHR for advice.

m) The Investigator or his/her designee will ensure that the FDA Inspector is not left unattended at any time and arrange for him/herself and/or appropriate study staff be available to answer questions, retrieve documents, and facilitate completion of audit.

n) The Investigator or designee should document all relevant discussion and requests.

o) The designee will make two copies of every document that is requested by the FDA Inspector, one for the FDA and one for the site’s inspection file.

p) The Investigator will review the copies to redact any proprietary or confidential information before the copy is given to the FDA.

q) The Investigator should request an opportunity to immediately correct objectionable observations.

r) The Investigators and/or designees should respond to the FDA Inspector’s questions as they occur and request additional time to respond if necessary.

s) The Investigator and/or designee should permit the FDA Inspector to speak with other study personnel, as requested (e.g. Pharmacy, Regulatory, Study Coordinator, etc).

l) If the FDA Inspector asks to inspect an area or document that is outside the “legally permissible” scope of the current inspection, contact the OHR for further discussion.

u) Under no circumstances may an FDA Inspector remove an original document or record from MHS premises, nor may an FDA Inspector make any copies him/herself nor make any marks on original documents and records.

3.3 Concluding the Inspection

a) At the conclusion of the inspection, the FDA inspector will summarize any objectionable observations on Form FDA 483, Inspectional Observations, and will typically review the findings with the PI and study staff.

b) If certain observations can be corrected before the end of the inspection, the PI should attempt to do so, and the FDA Inspector may annotate the Form FDA 483 to document that the observation was corrected or a corrective process put into place.

c) The signed Form FDA 483 will be provided to the Principal Investigator.

d) At any time during the inspection, if the FDA Inspector requests that an affidavit or any other document be signed (with the exception of the FDA 482), initialed or otherwise ratified, the Investigator or other representatives should not comply until the OHR, and/or MHS Legal has been consulted.
e) All relevant personnel should be reconvened for the close-out meeting with the FDA Inspector.

f) The PI's inspection team should review the Form FDA 483 (if one is provided) carefully and confirm that corrected items are either not listed, or the Form FDA 483 is annotated to show a correction was implemented.

g) The PI should request such deletions or annotations of the Form FDA 483 if they are not already present.

h) During the discussion, the PI should ask the FDA Inspector to clarify any items and provide as much detail as appropriate for items that need clarification.

i) The Investigator should express explanations or disagreements about any items or issues clearly, assertively, and respectfully.

j) The Investigator should advise the FDA Inspector that a written response to the Form FDA 483 will be sent to the office/address the FDA Inspector specifies.

a) The Investigator and/or designees should meet with all relevant study personnel to discuss and summarize the day's events after the FDA Inspector has departed. He/She will ensure that all promised corrective actions are carried out expeditiously and within promised timeframes.

k) With assistance from the OHR and MHS Legal, the Investigator will submit a full, written response to the Form FDA 483, item by item, within 10 days of the inspection's conclusion, indicating all corrective actions taken to date, and summarizing actions yet to be taken, within a proposed time frame for conclusion.

l) Thirty days after the inspection, the Investigator should send a written request to the FDA for a copy of his/her Establishment Inspection Report (EIR).

m) If a letter from the FDA officially classifying the inspection (No Action Indicated, Voluntary Action Indicated, Official Action Indicated) is not received within 45 days of the inspection, the Investigator or designee should contact the FDA office and request the status of the letter.

n) The Investigator will confer with the OHR about reporting FDA inspection occurrence/results to other relevant regulatory authorities or funding sponsors.

4 REFERENCES TO OTHER APPLICABLE SOPS

- None

5 ATTACHMENTS

None

6 APPLICABLE REGULATIONS AND GUIDELINES

- Inspection of Sponsor's Records and Reports (21 CFR 312.58)
- Inspection of Investigator's Records and Reports (21 CFR 312.68)
- Inspections (21 CFR 812.145)
Investigator Standard Operating Procedures

- The Principles of ICH (ICH E6, Section 2.0)
- Investigators’ Qualifications and Agreements (ICH E6, Section 5.1)
- Quality Assurance and Quality Control (ICH E6, Section 5.1)
- Record Access (ICH E6, Section 5.15)
- FDA Compliance Program Guidance Manual, 7348.811 Clinical Investigators
- www.fda.gov