QA-601– FDA Inspections

1. **PURPOSE:**
   To outline the process of an inspection by the US Food and Drug Administration (FDA) and describe activities required to facilitate the inspection. An FDA inspection is typically conducted at sites to determine compliance with federal regulations and adherence to guidelines, to verify the validity and integrity of clinical data submitted in applications for market clearance of medical devices, drugs, or biologics and to assure that the rights and welfare of subjects have been protected.

2. **SCOPE:**
   This SOP applies to all personnel involved in the implementation and coordination of a clinical investigation.

3. **RESPONSIBLE INDIVIDUALS:**
   The responsible personnel include the Principal Investigator (PI) and, when delegated by the PI, Sub-Investigators, Research Coordinators, and other staff involved in the conduct of clinical research.

4. **RELATED TERMS AND DEFINITIONS:**
   Clinical Investigation/Clinical Research
   Food and Drug Administration (FDA)
   Inspection
   Inspectional Observations (FDA Form 483)
   Investigational Device Exemption (IDE)
   Investigational New Drug
   Investigator Initiated Research
   Notice of Inspection (FDA Form 482)
   Principal Investigator
   Sponsor-Investigator

   Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**

PIs and their research study teams will prepare for and respond to all FDA inspections. The Office of Clinical Research (OCR), Associate Vice President for Research Operations and the Executive Director of Research Compliance will be notified in advance of the inspection and will provide support throughout the inspection process.

6. PROCEDURES:

6.1 Receiving notification of an inspection

6.1.1 When the FDA contacts the investigational site to schedule an inspection, begin completing the FDA Inspection Checklist and obtain the following information:

- FDA inspector name and contact information.
- Number of inspectors expected and additional inspector information, if applicable.
- The name of the PI being inspected.
- Which protocol(s) is/are being inspected.
- The specific personnel to be made available.
- The specific documents to be made available.
- Duration of the inspection.
- Date of the inspection.

6.1.2 Document any telephone conversation(s) that occur between the FDA inspector and study staff.

6.1.3 The FDA inspector will usually request that the inspection take place within 10 days.

6.2 Notify the appropriate parties of the impending inspection.

Include the name(s) of the protocol(s), IRB number(s), and date of the inspection for all protocols to be inspected when notifying the following parties of the impending inspection:

- PI and all study staff
- Staff in the facility where the inspector's tour will be given
- Staff in areas where the research has been conducted
- Sponsor (if applicable) if the PI is not the sponsor-investigator of the investigational new drug application (IND), or investigational device exemption (IDE)
- Research Finance Specialists and Post Award/Revenue Cycle
- UTRGV Office of Clinical Research
- UTRGV Executive Director of Research Compliance
- Associate Vice President for Research Operations
- Health Information Services (medical records)
- Remind staff to limit idle conversation during the inspection

6.3 Preparing for the inspection

6.3.1 Request access for the auditor(s) to the medical records for all subjects enrolled in the study. Inform the Medical Records Department and/or Electronic Health Information Services that this is for an FDA inspection and all records need to be available upon the first day of the inspection.

6.3.2 Begin the access process for Florence, if applicable, for the study(ies) being audited.

6.3.3 If the FDA requests that identifiers remain on the records, the HIPAA Privacy Rule at 45 CFR 164.512(b)(1)(iii) permits this.

6.3.4 If the FDA does not require identifiers on records, research staff should redact identifiers.

6.3.5 Reserve a room for the proposed number of days in a private area with the ability to access the necessary EMR for the inspection. The room should not contain files or records that do not pertain to the inspection.

6.3.6 A copy machine should be located close to the room.

6.3.7 FDA inspectors should not be located in/around patient care and research staff workspace areas during the inspection.

6.3.8 Identify a person on the study staff who will serve as an escort and oversee the inspection. The escort will serve as a guide and general study contact person. The escort will need to be readily available to the inspector(s) at all times.

6.3.9 Create a written list of all the PI's clinical studies and/or trials. The list should include protocol title, start, and stop date.

6.3.10 Prepare a general overview of the study. This should include: a summary of the study, adverse events, deaths, violations, and deviations. This is to be kept as a reference for the PI and study staff.

6.3.11 Ensure that all study documentation including informed consent forms, source documents, case report forms (CRFs), regulatory documents and sponsor correspondence are available for review by the inspector(s).

6.3.12 Review agreements/contracts for specific details regarding FDA inspections.

6.3.13 Review study documentation for:

- Comprehensiveness, accuracy, and compliance
- Weakness/gaps (and correct those that can be corrected [i.e., file violations, draft notes-to-file, locate missing documents, etc.])
- Unresolved or outstanding issues (and develop a corrective action plan for any unresolved/outstanding issues)

6.3.14 Keep all study documents and records ready and accessible so you are prepared for requests to provide information.

6.4 During the inspection

6.4.1 The PI or the PI's designee must be available to meet with the inspector and receive and sign the FDA Form 482 "Notice of Inspection", which will be

provided by the inspector. Preparation of the "Notice of Inspection" officially begins the inspection. Email a copy of the 482 to the local PI, the study sponsor (if applicable), Office of Clinical Research and the Director of Research Compliance.

6.4.2 The FDA inspector should present their credentials upon arrival at the site. If he/she does not, ask to see identification prior to allowing access to confidential records. Failure to ask for the inspector's credentials and Form 482 can be noted as a deficiency in the inspector's report.

6.4.3 The FDA inspector will request a tour of the facility areas where the research took place. Notify staff in the study areas so they will be prepared for the visit and possible questions. The FDA inspector must be accompanied by research staff **at all times** during the tour.

6.4.4 Research study staff will need to be available at all times to the FDA auditors. All staff should answer questions directly and honestly. Listen carefully to the question and answer what was asked. If unclear of the question, ask the inspector to repeat or rephrase the question. Respond to queries promptly. It is acceptable to defer to the PI or other study staff if you don't know the answer.

6.4.5 The standard procedure is that the inspector will request files for review. Provide the inspector with files that have been requested. Keep a "shadow binder" with a copy of every record or document that is provided to the inspector during the inspection.

6.4.6 The inspector will request copies of some documents. Make a separate copy for yourself of any documents that are requested by the inspector. The inspector's copies should be labelled "Confidential", and your copies should be labelled "Copy". Copies are provided without charge to the FDA.

6.4.7 If the inspector insists on taking photographs or other video or audio recordings, take and retain duplicates at the same time. If the inspector requests to take samples, ask for a receipt of the samples, and pull and retain identical samples at the same time.

6.4.8 The PI should designate an individual to take notes of activities and discussions during the inspection. Keep an exhibit log, a list of all questions asked by the inspector.

6.4.9 The PI must set aside time each day to talk with the inspector, either in person or via phone, and be available for any questions that may arise.

6.5 After the inspection

6.5.1 The FDA inspector will hold an exit interview with the PI at the conclusion of the inspection. The escort, PI, and any other appropriate staff should attend this interview. The purpose of this interview is to review the FDA's findings and deficiencies, if any. Any deficiencies will be noted on the FDA Form 483 and given to the PI. The inspector will give a copy of this report to the PI.

6.5.2 Do not sign any affidavits provided to you by the inspector. If the inspector presents an affidavit for signature, politely decline to sign, and tell the inspector that you are not permitted to sign documents on behalf of the institution, but you will identify the appropriate person and report back. After that contact (1) Office of Clinical Research and (2) UTRGV Legal Counsel and Chief Compliance Officer.

6.5.3 During the exit interview, the escort or designee will document the conversation, specifically noting observations, comments, and commitments.

6.5.4 Maintain all research documentation on site until the Establishment Inspection Report (EIR) is received.

6.5.5 If deficiencies are found during the inspection, a written Inspection Observations (FDA Form 483) will be issued that lists the deficiencies. If no deficiencies are found, then no form will be issued.

6.5.6 Email the exit interview summary to your manager, the PI, the Office of Clinical Research, the Executive Director of Research Compliance and the Associate Vice President for Research Operations.

6.6 Response to the FDA Form 483, if applicable

6.6.1 Contact the Office of Clinical Research for guidance with the response to the FDA Form 483. A response must be submitted for FDA From 483.

6.6.2 The written response should include the following information:

- Determine if a finding was an oversight/single occurrence or if it is a systematic problem requiring a change of procedure/process.
- Describe corrective actions in a Corrective and Preventative Action Form. This should include justification of why the proposed response would correct this problem and prevent it from reoccurring. Include a timeline for the corrective actions.
- The Inspector may provide their own CAPA form or format. If not, use the UTRGV CAPA. (See references)
- Address each specific finding, point by point.
- The response should be sent to the FDA within 15 business days.
- Maintain all inspection documentation on site until the Establishment Inspection Report (EIR) is received.

7. REFERENCES

- 21 CFR 312.68 – Inspection of investigator's records and reports https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.68
- 21 CFR 812.45 – Inspections https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=812.145

- ICH GCP 1.29 Definition: Inspection; https://ichgcp.net/1-glossary/
- ICH GCP 6.10 Direct Access to Source Data/Documents https://ichgcp.net/610-direct-access-to-source-datadocuments/
- Inspections, Compliance, Enforcement, and Criminal Investigations, Compliance Program Manual. Updated August 2010. http://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-manuals/compliance-program-manual
- Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors FDA Inspections of Clinical Investigators. June 2010 http://fda.gov/downloads/RegulatoryInformation/Guidances/UCM126553.pdf
- FDA Form 483 Inspection Observations. Current as of November 2020 https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-observations
- Form 483 Frequently Asked Questions. Current as of January 2020 https://www.fda.gov/inspections-compliance-enforcement-and-criminial-investigations/inspection-references/fda-form-483-frequently-asked-questions
- Reporting to Government and Response to Government Investigations and Accreditation Surveys
- UTRGV GA-105
- UTRGV RA-201
- UTRGV RA-205
- UTRGV DM-502
- UTRGV DM-504
- UTRGV DM-505
- UTRGV QA-602

8. FORMS OR ATTACHMENTS

FDA Inspection Checklist
UTRGV CAPA Template