

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

**FACILITATING FDA INSPECTIONS**

**PURPOSE**

To outline the process for an FDA sponsor or clinical investigator inspection, and describe activities that should be done to facilitate the inspection.

**SCOPE**

Applies to all Helen Diller Family Comprehensive Cancer Center (HDFCCC) faculty and staff involved in the implementation and coordination of clinical investigations (defined to include any FDA-regulated clinical trials).

Personnel responsible: The Principal Investigator (PI) is ultimately accountable for the performance and supervision of a clinical investigation. While the PI may delegate some required tasks to sub-investigators and other research staff, the PI remains at all times accountable for their conduct. If the PI also files an investigational new drug application (IND) which is approved by the FDA, the PI has additional responsibilities as Sponsor.

**BACKGROUND**

FDA inspections are typically conducted at clinical sites to determine compliance with federal regulations and adherence to guidelines, to verify the validity and integrity of clinical data submitted in applications for approval, and to assure that the rights and welfare of subjects participating in clinical studies have been protected.

**REFERENCES**

Title 21 CFR part 11 - Electronic Records; Electronic Signatures  
Title 21 CFR parts 50 (Protection of Human Subjects), 56 (Institutional Review Boards)  
Title 21 CFR part 312 (Investigational New Drug Application),  
part 312.62 - Investigator Record Keeping and Record Retention for Clinical Drug or  
Biological Trials  
Title 21 CFR part 812 (Investigational Device Exemptions),  
part 812.140 - Investigator Record Keeping and Record  
Retention for Device Trials  
ICH GCP Consolidated Guideline - Part 4.9 Records and Reports  
ICH GCP Consolidated Guideline - Part 5.15 Record Access  
FDA Compliance Program Guidance Manuals 7348.811 – Investigators and 7348.810 –  
Sponsors/CROs/Monitors  
FDA Investigations Operations Manual

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

**PROCEDURES**

In order to be well prepared for FDA inspections (alternatively known as surveys or audits) on an ongoing basis, it is very important to maintain well-organized and robust research files for all studies at UCSF. In addition, the research file must match all true original source documents for each subject found in paper or EMR patient charts. FDA Inspectors (alternatively known as surveyors, auditors or investigators) will request original source documentation during the FDA inspection.

**A. NOTIFICATION**

1. Upon receipt of notification from the FDA of an inspection or site survey, the PI will immediately notify the following UCSF Officials, Offices, and Sponsors (refer to Appendix A):
  - a) the Director of the HDFCCC Clinical Research Support Office (CRSO) in the Investigational Trials Resource (ITR) who will immediately inform the Associate Vice Chancellor (AVC) of Compliance and Ethics;
  - b) the Manager of the HDFCCC Research Personnel Office in the ITR;
  - c) the Director of the Human Research Protection Program (HRPP), also known as Committee on Human Research (CHR), which serves as the UCSF IRB;
  - d) the UCSF Office of Legal Affairs (OLA);
  - e) the sponsor, if applicable, as they will likely want to review the study files prior to the site inspection; and
  - f) the Chair of the HDFCCC Data Safety Monitoring Committee (DSMC).
2. A copy of any inspection letter will be forwarded to the Director of the CRSO and the Manager of the Research Personnel Office.
3. The PI will ensure that his/her research staff immediately begin to retrieve and assemble any requested trial-related records.
  - a) The Lead Study Coordinator will immediately forward the list of study participants to be included in the inspection to the Director of the CRSO who will then request each study participant's complete medical record, including original hospital and clinic charts and/or access to e-Medical Records from UCSF Medical Records (Health Information Management Services or HIMS).
  - b) HIMS will receive a written request from the Director of the CRSO for all applicable charts to be available for pickup by the research staff within two (2) business days of the request. If the inspection is

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

to occur sooner than two days after notification, HIMS will need to make the records available within one (1) business day or less, as needed.

- c) The Lead Study Coordinator will immediately communicate any difficulty in obtaining charts from HIMS to the PI and the Director of the CRSO so that issues are resolved immediately and collection of required materials is completed in the desired timeframe.
  - d) The Lead Study Coordinator will immediately send an email notification to the following study-delegated personnel about the date/time and occurrence of the FDA inspection:
    - Principal Investigator
    - Sponsor contact for the study
    - Protocol Project Manager for the research unit
    - Manager of the CRSO regulatory team
    - Director of the HRPP
    - Investigational Pharmacist.
4. The PI must be available in person during the FDA inspection. If the PI is unavailable during the proposed date of the audit, and the date must be rescheduled, the PI or designee may contact the FDA investigator to request rescheduling at a mutually convenient time. This request and response should be made in a timely fashion and should be documented together with the agency's response. If a new date is agreed upon, the rescheduled inspection must be communicated to all involved, as noted above including but not limited to CSRO, AVC, OLA, HIMS.

*Note: FDA can and in the past has been known to perform an inspection without the PI present during all or a portion of the inspection. This can be problematic as the PI can often clear up misunderstandings more efficiently and effectively than staff, thus potentially avoiding unnecessary citations. At a minimum, the PI should make every effort to be physically available during the entrance and exit interviews. Note that FDA has cited some sites for supervision deficiencies where a PI has been unavailable in person for any extended period during which a new PI has not been named.*

**B. PREPARING FOR THE INSPECTION**

1. UCSF faculty and staff must cooperate with any FDA inspection. All study personnel will be available to answer questions for which they have direct knowledge.
2. The Lead Study Coordinator or Protocol Project Manager will be responsible for securing a room for the entire inspection process that can be locked if the inspection is expected to span longer than one day.

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

3. The Lead Study Coordinator will designate a “documents” person to assist and support him/her to obtain any requested items for the FDA inspector.
4. In preparation for the audit, the Lead Study Coordinator, designee or Protocol Project Manager will retrieve and assemble all study-related records including:
  - a) SOPs
  - b) Regulatory records – CHR approvals, enrollment logs, signed and dated consents (including screen failures), protocols, investigator brochure, and correspondence.
  - c) CRFs, monitoring reports.
  - d) Source records – clinic charts, hospital records, x-rays, lab reports, subject’s diaries, referrals.
  - e) Test article accountability records.
5. The Lead Study Coordinator will organize all study-related files, arrange logistics and prepare for the audit according to the FDA Inspector’s request.
6. The PI along with the Director of the CRSO and the Manager of the Research Personnel Office will function as the liaison/escort for the FDA Inspector (s) and will facilitate all document requests or requests for personnel interviews with the Lead Study Coordinator.

**C. CONDUCTING THE INSPECTION**

1. The liaison (Director of CRSO or Manager of the Research Personnel Office) and the PI will:
  - a) Greet the FDA Inspector (s) and verify identification/credentials. The FDA will provide the PI with the FDA 482 (Notice of Inspection). FDA regulations generally require the FDA Investigator to give the FDA 482 to the most responsible individual. This may not occur in certain situations, for example in connection with a criminal investigation. **If FDA does not provide the 482, notify OLA immediately.**
  - b) Provide a tour of the facility. The FDA Inspector may request a tour of the facility where the research took place. Staff will have been notified in advance and be prepared for the visit and possible questions.
  - c) Provide requested records. The liaison or designee will make two (2) copies of each record requested by FDA; one for FDA, and one for retention on site following the inspection.

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

- d) Assist in ensuring that each question is answered by person(s) most knowledgeable of the issue.
- e) Accompany FDA Inspector (s) at all times other than when they are in the designated conference room reviewing documents. FDA inspectors should not be allowed to enter patient care areas or research staff workspace areas unescorted at any point during the inspection.
- f) Assist the FDA Inspector (s) as needed
- g) Arrange for follow-up as required for any unanswered questions or outstanding document reports.

*Note: FDA Compliance Program Guidance Manual 7348.811 provides a list of information that will be requested during every inspection. This reference is very helpful in preparing for the inspection.*

2. The designated liaison will:

- a) Take notes concerning the progress of the inspection. A form may be used to assist in this task, with spaces for the FDA Inspector's name (if a team inspection), documents requested, date and time of request, date and time delivered.
- b) Provide requested records and make photocopies for the FDA and clinical site. Any copies of CRFs or medical records requested by the FDA Inspectors will be made in duplicate for retention at the site.
- c) Arrange any interviews requested by the FDA Inspector, and escort the FDA Inspector if they request to go to the pharmacy, HRPP, etc.
- d) Document any line of questioning pursued by the PI and the FDA Inspector, including issues that could not be resolved and steps taken during the inspection to resolve the issue.
- e) Document the name and title of all persons interviewed by the FDA, and the date (and time if possible) of the interview.

**D. POSTINSPECTION**

- 1. The PI or liaison should request an end of day discussion during each day of the inspection with the FDA Inspector to review any preliminary findings.
- 2. The liaison will document any questions whose answer could not be provided, along with appropriate follow-up to obtain the requested information.

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

3. If the PI receives a Form FDA 483 (report of observations) after the audit, he/she should consult OLA on how to respond and provide the sponsor with an opportunity to assist in the response. A copy of the 483 must be forwarded to the Director of the CRSO, along with OLA.
4. The PI or designee must send a copy of the Form FDA 483 to the Study Sponsor's project manager, the Office of Ethics and Compliance, CHR, and the Cancer Center DSMC.
5. The PI must arrange a meeting to discuss the findings with CRSO, OLA, CHR, and other offices as necessary or determined by the findings.
6. The PI will prepare a written response with input from CRSO, OLA, CHR, and appropriate persons to any observations noted in the Form FDA 483, and send the response to the FDA within the time specified by FDA, typically within 15 days. The written response should:
  - a) Address each observation and explain what steps have been implemented or will be implemented to remedy the observation, and prevent future occurrences of similar observations.
  - b) The response should be factual and the tone should be respectful, professional and cooperative.

*Note: FDA sometimes will extend the deadline for response depending on the circumstances. Such a request should be made, if at all, as soon as possible. The PI should contact the Director of the CRSO to discuss reason for delay and OLA can assist in facilitating such a request.*

7. The PI or designee should attempt to obtain a copy of the official FDA investigator's field audit report [**Establishment Inspection Report (EIR)**] under the Freedom of Information Act (FOIA Request). This request can be made at the conclusion of the 483 response; alternatively, OLA can assist with a separate request. FDA typically will not respond to an EIR request until the matter is formally closed.

*Note: The PI or designee should not contact the FDA Inspector directly without first consulting with CRSO, OLA, or the Office of Ethics and Compliance.*

**University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center**

**FDA Inspections Guidance**

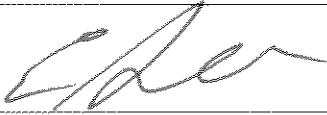
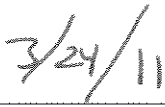
**E. ON-GOING READINESS**

*Note: While the average notice of inspection falls within a two-day to twenty-four-day timeframe, it may be more or less than this timeframe. The rule is to always be audit ready!*

1. Research Study File Maintenance
  - a) Keep files organized at all times.
  - b) Retain all correspondence from sponsor, CHR, monitors, study subjects, letters, faxes, e-mails, memos, and phone contacts.
  - c) Retain all test article accountability records.
  - d) Retain Shipping receipts, screening and enrollment logs, dispensing logs.
  
2. FDA Inspection Triggers (increase the chance of an FDA audit):
  - a) Studies with a high enrollment, where test article approval is pending.
  - b) Studies with few or no adverse events.
  - c) PIs who have received an FDA Form 483 in the past.  
Studies where other sites have had problematic inspections.
  
3. If any of the above triggers apply to your study, contact the Director of the HRPP once the study is closed to enrollment. Advance preparation is recommended in case your study is selected for an inspection.

\* \* \*

This guidance was approved by the following individuals on the date listed.

	
Eric Small, MD Director of Investigational Trials Resource ( ITR) Helen Diller Family Comprehensive Cancer Center	Date

University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center

FDA Inspections Guidance

APPENDIX A

**PHONE CONTACT FOR INSPECTION SUPPORT AND PREPARATION**

Director of Clinical Research Support Office:

Nicole G. Lama, MS (415) 885-7399 Office  
(415) 215-6665 Cell

Manager of Research Personnel Office:

Bev Fein, RN, MSN (415) 353-9607 Office  
(415) 513-3006 Cell

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