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

Policy for Facilitating FDA Inspections

Table of Contents

Purpose

This policy defines the process for facilitating a FDA inspection occurring at the Helen Diller Family Comprehensive Cancer Center (HDFCCC). The facilitation process includes the pre-inspection preparation with the Principal Investigator (PI) and the study team, as well as assisting the study team both during and after completion of the inspection.

Scope

This policy applies to all studies approved by the Protocol Review and Monitoring Committee (PRMC) that may be inspected by the FDA.

Definitions

New Drug Application (NDA): the process in which sponsors formally propose that the FDA approves a new pharmaceutical for sale and marketing. The goal of the NDA is to provide enough information to permit FDA reviewers to establish the complete history of the candidate drug.

Pre-Marketing Approval (PMA): Premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices.

FDA 482 Form: A FDA Form 482 is a Notice of Inspection issued at the start of the inspection by the FDA Inspector.

FDA 483 Form: A FDA Form 483 is issued at the conclusion of an inspection when an FDA investigator(s) has observed conditions that, in their judgment, may constitute violations of the Food Drug and Cosmetic (FD&C) Act.

Background

Routine FDA inspections are typically conducted at clinical sites to determine compliance with federal regulations and study protocol in order to verify the validity and integrity of clinical data submitted in applications for approval (i.e., New Drug Application (NDA) for investigational products (IP) for drugs or Pre-Marketing Application (PMA) for devices), and to assure that the rights and welfare of study participants have been protected.

For cause FDA inspections are typically conducted if there are significant issues with the conduct of clinical trials at the institution.

Procedures

1.0 Notification

Upon receipt of notification from the FDA of an inspection, the PI or delegate will immediately notify the Data and Safety Monitoring Committee (DSMC) Director or designee, who will then notify the following UCSF and HDFCCC staff:

- Chair/Vice Chair of the DSMC
- Clinical Research Support Office (CRSO) Medical Director
- CRSO Director
- CRSO Associate Directors
- CRSO Clinical Research Manager (CRM)
- CRSO Clinical Research Operations Director
- Associate Director, Clinical Sciences
- UCSF Human Research Protection Program (HRPP) /Institutional Review Board (IRB) Director
- UCSF Investigational Drug Services (IDS) Manager and IDS Pharmacist (if applicable)
- UCSF Office of Legal Affairs (OLA) Director
- UCSF Office of Ethics and Compliance (OEC) Regulatory Support Manager

It is best for the PI to be available in person during the inspection period. If the PI is not available, then the PI will need to arrange for a Co-Investigator to be present for the inspection. If possible, the PI could be available remotely via Zoom for the Introductory Meeting with the Inspector and to answer any questions that arise during the inspection.

2.0 Preparing for the Inspection

2.1 Documents

Please confirm with the Inspector if he/she would like to have either electronic or paper copies of applicable documents.

The following documents must be prepared, by a study staff, prior to the inspection:

2.1.1 Study Coordination Documents:

- All paper or electronic Research Charts (including screen failures)
    - Clinical Research Coordinator (CRC) and back-up CRCs should be familiar with the layout of the charts and can guide the Inspector through the charts, if requested. It is recommended to have a table of contents for the research charts so the Investigator can refer to it during the inspection.
- Logs/Lists
    - Enrollment Logs
        - Total number of participants screened, enrolled, discontinued, and completed trial
    - Protocol Violations
    - Adverse Events and Serious Adverse Events (SAEs)
- Consent tracker document (i.e., list of consents and reconsents signed by participants)
- Completed verbal notification tracker document as per HDFCCC guideline
- Original signed Informed Consent Forms (ICFs), HIPAA, and California Experimental Subject's Bill of Rights documents
- Screen Failure files, including completed consent package and documentation of the reason for screen failure
- Documentation of workflows (guidelines or standard operating procedures) e.g., consenting process, RECIST measurements, etc.

2.1.2 Regulatory Documents:

- List of all trials the PI has been involved in as both a PI and Co-I over the past 5 years – this list must include:
    - Protocol number
    - Protocol title (including the product name)
    - Research or marketing permit number (if available)
    - Name of sponsor (including government agencies and commercial sponsors)
    - IRB of record, and key study dates (e.g., IRB approval, open to accrual, closed to accrual).
- IRB of record: Chair Name and address of each IRB Panel
- Organization Chart for HDFCCC and the Site Committee (SC) of the trial being inspected
- Summary of Institutional Review Board (IRB) Submissions (snapshot from iRIS)
- Summary of Protocol Amendments
- Summary of approved ICFs (Note where re-consent was required and key changes in ICFs)
- All versions of the Protocol and Informed Consent Forms
- Summary of study timeline (e.g., IRB approval date, first participant consented, first participant enrolled, last participant consented, etc.)
- Completed FDA Form 1572
- Financial Disclosure Forms (FDF) for each investigator listed on the DOA log – each FDF should be completed and signed/dated by the Investigator
- Delegation of Authority (DOA) Log. This log should be updated for each investigator and staff member involved in the trial and all procedures conducted in the trial should be indicated on this log. Ensure that all procedures are delegated to the appropriate staff member.

- Training documents for the Site Initiation Visit (SIV), as well as all versions of the protocol for study members listed on the DOA Log
- HDFCCC Polices and Guidance
- DSMC Policies, Roster, and Data and Safety Monitoring Plan (DSMP)
- Pharmacy Records (i.e., Drug Accountability Record Forms (DARFs), shipment records with TempTales, temperature logs for storage of the Investigational Product (IP), etc.)

2.2 Logistics

2.2.1 CRSO Responsibilities

- The CRSO, along with the DSMC, will help facilitate the inspection. In most cases, the assigned program's Associate Director (AD) will be the CRSO contact for the inspection. If there is no AD assigned, the CRSO Director will designate a contact for the inspection. The CRSO will:
    - Secure a room(s) for the expected duration of the inspection. Ideally the room can be locked so files can be secured at the end of the day.
    - Ensure that all clinical research staff who have workstations in the vicinity of the inspection room are informed of the inspection. This includes cleaning up workstations, assigning someone to remove faxes from photocopier, locking all PHI, ensuring all doors are closed appropriately, and reminding staff to not talk about PHI, the FDA inspection or any trials outside of closed doors.
    - Notify non-HDFCCC UCSF staff who work in the area of the inspection of the inspection dates and reminders about confidentiality, etc.
    - Ensure that the Clinical Research Manager (CRM) for the program has notified the sponsor of the inspection.
    - Book appropriate space for the Sponsor (if they will be present for the inspection).
    - Schedule FDA Liaisons for the inspection room (1/2-day shifts), ready room and on-call. The schedule should be shared with the PI, DSMC Director, DSMC Monitor Supervisor, CRSO Director, AD, CRM, Protocol Project Manager (PPM), and CRC.
    - Send a separate meeting invitation for opening and closing meetings with the FDA Inspector.
    - Identify a "ready room" near inspection location as the "command center" for the inspection.

2.2.2 DSMC Director or Designee Responsibilities

- The DSMC Director or designee will reach out to the assigned FDA Inspector to provide information on accommodations as well as the meeting time and location of the first day of the inspection.
- Send a contact list to all who are involved in the inspection (PI, CRM, PPM, CRC, all FDA Liaisons, CRSO Director, and ADs). Include name, title, role on study (if applicable), email, office number and cell number.
- Prepare the inspection notes in Microsoft Teams for the FDA Liaisons to complete for each day of the inspection.
- Prepare the study team for the inspection, including providing a preparatory meeting with the PI and the study team to go over the logistics of this inspection.

- Audit the participants' charts, regulatory and pharmacy documents in order to identify any findings and assist the study team with the corrective and preventative action plans (CAPAs) for these issues.
- Provide the study team with 1 unencrypted flash drive (if FDA Box file is not utilized) to be used for providing records to the FDA Inspector.

3.0 Conducting the Inspection

- The FDA Liaison will meet with the Inspector and will ensure that he/she signs in with security.
- The FDA Liaison will ensure that the Inspector is aware of the fire/emergency evacuation procedures for the building in which the inspection is taking place.
- The PI or designee will obtain the FDA 482 form (Notice of Inspection) from the Inspector and verify the Inspector's credentials.
- The FDA Liaison will document attendance (both in-person and virtual) at the opening meeting. The attendance list will include name and title.
- The PI or designee will provide a brief overview of the trial to the Inspector at the introductory meeting.
- The study team (i.e., PI, CRC, etc.) will be on 'stand-by' for the duration of the inspection. They are only required to go into the inspection room at the request of the Inspector. The FDA Liaison will notify the study staff member when the Inspector would like to meet with them.

3.1 FDA Liaison Responsibilities

- Document all questions in the daily folder on Microsoft Teams and locate the study team staff who can answer the questions.
- Create an e-mail chain each day to update everyone as noted in section 1.0 above on the status of the inspection and if there are any outstanding questions that need to be answered or documents that need to be retrieved.
- Review all documents provided by the study team before they are provided to the Inspector.
- Provide the requested records to the Inspector via an unencrypted flash drive if they are not provided in the FDA Box files.
- Accompany the Inspector if they leave the designated room.
- Document the name and title of staff members who are interviewed by the Inspector, along with the date and time of the interview, and all questions asked and the provided response.
- Travel with the Inspector and a study staff member when touring the clinic and meeting with the IDS Pharmacist to take notes.

3.2 Interacting with the Inspector

- The FDA Liaison will prep the PI or study team before talking to the FDA Inspector by sharing the questions from the FDA Inspector ahead of time. The PI or study team member should review any relevant document or workflow that will be discussed prior to meeting with the FDA Inspector.

3.3 Interacting with the Sponsor

Any questions from the FDA Inspector outside the scope of activities completed by the study team should be directed to the sponsor.

Many sponsors request a written summary or close-out call at the end of every day. The

FDA Liaison will facilitate this communication based on the notes taken during the inspection.

4.0 Post-Inspection

On the last day of the inspection, the PI, essential members of the study team (at minimum the CRC, CRM, and PPM), FDA Liaison, and the Administrative Director or designee from DSMC and the Director and Associate Director of the CRSO will have a close out meeting with the FDA Inspector to review the summary of findings from the inspection. The FDA Liaison will document attendance similar to the opening meeting. If there aren't any significant observational findings, then an Establishment Inspection Report (EIR) will be sent to the PI after the inspection is completed and reviewed by the appropriate parties at the FDA. The EIR will be sent to the PI via secure e-mail within 3-6 months after completion of the Inspection. If there are significant observational findings, then a FDA Form 483 will be issued to the PI at the close out meeting. The FDA Form 483 will be forwarded to the DSMC, Sponsor, IRB, OEC, and the OLA by the PI and study team.

If the PI receives a FDA Form 483, the PI should consult with the DSMC, CRSO, Sponsor, OEC, and OLA to develop a response letter with a CAPA to the FDA. Refer to instructions from the FDA Inspector regarding timelines for response.

- The response letter will address the CAPA for each of the findings on the FDA Form 483 and will include attachments to support each of the items noted on this report, along with the FDA Form 483. If attachments are included, please ensure to add a listing of these attachments at the end of the response letter.
- The study team will be responsible for the development of the response letter, with the DSMC and OEC involved with assistance of questions that come up with the development of the content for the response letter.
- Please ensure that the PI's letterhead is included in the response letter.
- The PI will sign the final version of the letter via DocuSign.
- The response letter will be submitted to the FDA via e-mail with attachments (if applicable). The attachments must not be embedded within the response letter.
- The total size of the e-mail with attachments must be no larger than 120 MB.
- The content of the e-mail will note exactly what is being submitted to the FDA (i.e., response letter, attachments (if applicable), FDA Form 483, and any other pertinent documents). The e-mail will be sent from the PI.
- The e-mail will be sent to the FDA contact provided by the inspector(s).
- The FDA contact(s) will send a response email (or automated email if out of the office) to note that the response letter has been received.
    - The PI should send a separate follow-up e-mail to the FDA contact(s) if the response email has not been sent to the PI by the deadline.
    - The Response Letter will also need to be forwarded to the Sponsor (if Industry Sponsored study), UCSF IRB, and the UCSF OEC representative.

Alternate Procedures

There are no alternate procedures to this guidance document.

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
- Part 812 Title 21 CFR part 812 (Investigational Device Exemptions), part 812.140 - Records and Reports for Device Trials
- FDA Compliance Program Guidance Manuals 7348.811 – Clinical Investigators and 7348.810 – Sponsors, Contract Research Organizations and Monitors
- FDA Investigations Operations Manual

Policy Approval

This policy document was approved by the following personnel on the following dates:

DocuSigned by:
Rahul Aggarwal
E870F084A5CA4CC...

3/28/2025

Rahul Aggarwal
Associate Director Clinical Sciences
Helen Diller Family Comprehensive Cancer Center

Date

Signed by:
Kate Shumate
80D38159E89D41B...

3/30/2025

Kate Shumate, MPH
Director, Administration and Planning
Helen Diller Family Comprehensive Cancer Center

Date

DocuSigned by:
Katie Kelley
7F538467F93949B...

3/27/2025

Katie Kelley, MD
Chair, Data and Safety Monitoring Committee Helen Diller Family Comprehensive Cancer Center

Date

Policy Contact:

John McAdams
DSMC Director
John.McAdams@ucsf.edu

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

Policy Revision Summary of Changes

Policy Title: Policy for Facilitating FDA Inspections
Version Date: 27Mar2025
Version Number: 5
Number: 1

Notes: Page number corresponds to page number in updated version (Revision 3).
New text in modified paragraphs is shown as ***bold italics*** and deleted text is shown as ~~strikethrough~~.

Page No.: 2		**Section**: Purpose, Scope, Background, Procedures
Original Text	See original document	
New Text	**6.0 Notification** • UCSF Office of Ethics and Compliance Regulatory Support Manager	
Reason for Change	To update the title of the Office of Ethics and Compliance position	
Page No.: 3-4		**Section**: Procedures
Original Text	See original document.	

New Text	**7.0 Preparing for the Inspection** • The following documents must be prepared, by a study staff, prior to the inspection (confirm with the Inspector if he/she would like to have either electronic or paper copies of applicable documents): Study Coordination Documents: • All paper or electronic Research Charts (including screen failures) o Ensure that the Clinical Research Coordinator (CRC) and back-up CRCs are familiar with the layout of the paper or electronic charts and can subsequently guide the Inspector through the charts, if requested. It is recommended, but not required, to have a table of contents for the participant charts so the Investigator can refer to it during the inspection. • Enrollment Logs (including total number of participants screened, enrolled, discontinued, and completed trial). • Listing of all Protocol Violations. • Listing of all Adverse Events. • Listing of all Serious Adverse Events (SAEs). • Original signed Informed Consent Forms (ICFs),HIPAA, and California Experimental Subject's Bill of Rights documents. • Screen Failure Charts, including documentation reason for screen failure. • Study processes such as consenting process, RECIST measurements, etc. • Consent Tracker document (i.e., list of all consents signed by all participants). Regulatory Documents: • PI Listing of Trials over the past 5 years – this list must include: o Protocol number o Protocol title (including the product name) o Research or marketing permit number (if available) o Name of sponsor (including government agencies and commercial sponsors), o IRB of record, and key study dates (e.g., IRB approval, open to accrual, closed to accrual). • Chair of the IRB Panel reviewing the trial, along with the address of each IRB Panel. **Organization Chart for HDFCCC and the Site Committee (SC) of the study program for the trial being inspected.**

Reason for Change	To update the language in this policy as per the FDA inspection process.
Page No.: 5	**Section**: Procedures
Original Text	See original document.
New Text	• specific time in everyone's calendar. • Identifying a "ready room" near inspection location as the "command center" for the inspection. • Reminding everyone attending the opening meeting to bring their business card and will ensure that there is an opening meeting. <u>DSMC Director or Designee Responsibilities</u> • Sending a contact list to all who are involved in the inspection (PI, CRM, PPM, CRC, all FDA liaisons, CRSO Director, and ADs). Include name, title, role on study (if applicable), email, office number and cell number. • Preparing the inspection notes in Microsoft Teams for the FDA Liaisons to complete for each day of the inspection. • Preparing the study team for the inspection, including providing a preparatory meeting with the PI and the study team to go over the logistics of this inspection. • Auditing the charts, regulatory and pharmacy documents in order to identify any findings and assist the study team with the CAPAs for these issues. • Providing the study team with 2 flash drives to be utilized for providing records to the FDA Inspector. **8.0 Conducting the Inspection** • The FDA Liaison will meet with Inspector and will ensure that he/she signs in with security. • The FDA Liaison will ensure that the Inspector is aware of the fire/emergency evacuation procedures for the building in which the inspection is taking place. • The PI or designee will obtain the FDA 482 form (Notice of Inspection) from the Inspector and verify the Inspector's credentials. • The PI or designee will provide a brief overview of the trial to the Inspector at the initial meeting. All staff at this meeting will sign the sign-in sheet and will provide their business cards to the Inspector. There will be a Zoom option for this meeting for staff who cannot attend this meeting in person. • The appropriate study staff (i.e., PI, CRC, etc.) will be on 'stand-by' for the duration of the inspection. They are only required to go into the inspection room at the request of the Inspector. The FDA Liaison will let the appropriate study staff member know when the Inspector would like to meet with them.
Reason for Change	To update the language in this policy as per the FDA inspection process.

Page No.: 6	**Section**: Procedures
Original Text	See original document.

New Text	• Providing requested records to the Inspector via an unencrypted flash drive (after review by the Liaison in the "ready room").
	• Accompanying the Inspector if they leave the designated room.
	• Documenting the name and title of staff members who are interviewed by the Inspector, along with the date and time of the interview.
	• Documenting all those in attendance at the initial meeting and close-out meeting.
	• Traveling with the Inspector and a study staff member when touring the clinic and meeting with the IDS Pharmacist to take notes.
	
	<u>Interacting with the Inspector</u>
	• The PI and the study team members will be provided with guidance from the FDA Liaison with answering questions from the FDA Inspector as well as reviewing documents to be provided to the Inspector.
	• For all interactions with the FDA Inspector, please ensure to always:
	  • Be honest at all times.
	  • Be respectful and professional.
	  • Understand the question before answering.
	  • Only answer one question at a time.
	  • Think before you speak.
	  • Answer the question only and don't elaborate.
	  • Don't volunteer information that is not requested.
	  • Don't be afraid to say, "I do not know" and offer to find the answer and get back to the Inspector.
	  • Don't be afraid to ask Inspector to repeat question if unclear.
	  • Don't provide a document to the Inspector until requested by the Inspector and the FDA Liaison has reviewed these documents.
	
	<u>Interacting with the Sponsor</u>
	• Any questions outside the scope of activities completed by the study team should be director to the sponsor.
	• Many sponsors request a written summary or close-out call at the end of every day. The FDA Liaison will facilitate this communication based on the notes taken during the inspection.
	
	9.0 Post-Inspection
	
	• On the last day of the inspection, the PI, study team, FDA Liaison,

	etc. will have a close out meeting with the FDA Inspector to review the summary of findings from the inspection. If there aren't any significant observational findings, then an Establishment Inspection Report (EIR) will be sent via secure e-mail to the PI in 3-6 months after completion of the Inspection. If there are significant observational findings, then a FDA Form 483 Report will be issued to the PI at the close out meeting. 1.
Reason for Change	To update the language in this policy as per the FDA inspection process.
Page No.: 7	**Section**: Procedures
Original Text	See original document.

New Text	• If the PI receives a FDA Form 483 Report:
	  • PI should consult with DSMC, Sponsor, and the UCSF Office of Legal Affairs (OLA) for the response letter with the CAPA to the FDA. This response letter is due to the FDA within 15 business days after the close out visit.
	  • The FDA Form 483 Report will be forwarded to the DSMC, Sponsor, IRB, and the OLA by the PI and study team.
	
	10.0 Ongoing Readiness
	
	Note: While the average notice of inspection falls within a one week to three-week time frame, the rule is to always be audit ready. Additionally, the FDA may choose to not announce their inspection of a trial if there are significant issues (i.e., multiple Serious and Non-Compliance (SNC) Reports from the IRB) (i.e., "for cause" inspection).
	
	<u>Research Study File Maintenance</u>
	  • Keep files organized at all times. Conduct a chart review as per Appendix 1.
	  • Retain all correspondence from sponsor, IRB, monitors, study subjects, letters, e-mails, memos, and phone contacts.
	  • Retain all test article accountability records.
	  • Retain shipping receipts, screening and enrollment logs, and dispensing logs.
	
	<u>FDA Inspection Triggers (increase the chance of a FDA inspection)</u>
	  • Application for a New Drug Application (NDA).
	  • Expedited Submission or Pre-Market Approval (PMA).
	  • Non-compliance or study misconduct.
	  • Protocol violation, Serious Non-compliance (SNC) Reports, high number of deaths reported, high enrollment, and a large number of studies/investigators. 1)

Reason for Change	Removed Chart Review Checklist	
Page No.: 9-10		**Section**: Appendix 1 (Chart Review Checklist)
Original Text	See original document.	
New Text	☐ Deleted this checklist.	

Reason for Change	Updated this information.

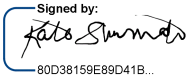
Certificate Of Completion

Envelope Id: 341867EE-23E1-41B9-AB38-05ED20464B87
Status: Completed
Subject: Complete with Docusign: Facilitating FDA Inspections Policy (version 27Mar2025).docx
Source Envelope:
Document Pages: 16
Signatures: 3
Certificate Pages: 2
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
John Mcadams
1855 Folsom St
Suite 601
San Francisco, CA 94103
John.McAdams@ucsf.edu
IP Address: 169.230.248.65

Record Tracking

Status: Original
3/27/2025 6:22:24 PM
Holder: John Mcadams
John.McAdams@ucsf.edu
Location: DocuSign

Signer Events	Signature	Timestamp
Kate Shumate kate.shumate@ucsf.edu Chief of Staff, Director of Administration University of California, San Francisco Security Level: Email, Account Authentication (Optional)	Signed by:  80D38159E89D41B... Signature Adoption: Drawn on Device Using IP Address: 169.230.248.36	Sent: 3/27/2025 6:25:46 PM Viewed: 3/30/2025 11:26:44 AM Signed: 3/30/2025 2:48:58 PM
Electronic Record and Signature Disclosure: Not Offered via Docusign		
Katie Kelley katie.kelley@ucsf.edu MD University of California, San Francisco Security Level: Email, Account Authentication (Optional)	DocuSigned by:  7F538467F93949B... Signature Adoption: Pre-selected Style Using IP Address: 169.230.248.175	Sent: 3/27/2025 6:25:45 PM Viewed: 3/27/2025 9:04:12 PM Signed: 3/27/2025 9:04:42 PM
Electronic Record and Signature Disclosure: Not Offered via Docusign		
Rahul Aggarwal rahul.aggarwal@ucsf.edu Rahul Aggarwal, MD Professor of Medicine University of California, San Francisco Security Level: Email, Account Authentication (Optional)	DocuSigned by:  E870F084A5CA4CC... Signature Adoption: Pre-selected Style Using IP Address: 128.218.42.140	Sent: 3/27/2025 6:25:45 PM Viewed: 3/28/2025 9:14:14 AM Signed: 3/28/2025 9:14:49 AM
Electronic Record and Signature Disclosure: Not Offered via Docusign		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	3/27/2025 6:25:46 PM
Certified Delivered	Security Checked	3/28/2025 9:14:14 AM
Signing Complete	Security Checked	3/28/2025 9:14:49 AM
Completed	Security Checked	3/30/2025 2:48:58 PM

Payment Events	Status	Timestamps