

## Policy for Facilitating FDA Inspections

### Table of Contents

Purpose .....	1
Scope .....	1
Background .....	2
Procedures .....	2
1.0 Notification .....	2
2.0 Preparing for the Inspection .....	2
3.0 Conducting the Inspection .....	5
4.0 Post-Inspection .....	6
5.0 Ongoing Readiness.....	6
Alternate Procedures .....	7
References .....	7
Appendix I: Chart Review Checklist .....	9
Policy Revision Summary of Changes .....	11

### **Purpose**

This policy defines the process for facilitating a FDA inspection occurring at the Helen Diller Family Comprehensive Cancer Center (HDFCCC). This includes the pre-inspection preparation of 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 are reviewed and regulated by the FDA.

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 the trial's conduct.

### **Definitions**

**New Drug Application (NDA):** the process in which sponsors formally propose that the FDA approve 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 483 Form:** A FDA Form 483 is issued at the conclusion of an inspection when an FDA investigator(s) has observed any conditions that, in their judgment, may constitute violations of the Food Drug and Cosmetic (FD&C) Act.

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## **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 (or Vice Chair) of the Data Safety Monitoring Committee (DSMC)
- Clinical Research Support Office (CRSO) Medical Director
- CRSO Director
- CRSO Associate Directors
- CRSO Clinical Research Operations Director
- Protocol Review and Monitoring Committee (PRMC) Chair
- PRMC Manager
- 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 Director
- UCSF Office of Ethics and Compliance Director

The DSMC Director or designee will reach out to the assigned FDA Inspector to provide information on parking, lunch options, hotels, etc. as well as the meeting time and location of the first day of the inspection. It is best practice for PI to be available in person and this should be arranged when the FDA inspector contacts the PI to schedule this inspection. If PI is not available or is out of town, 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**

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):

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**2.1.1 Study Coordination Documents:**

- All paper or electronic Research Charts (including screen failures)
  - Ensure that the Clinical Research Coordinator (CRC) and back-up CRCs are familiar with the layout of the paper or electronic charts and can 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)
- Consent tracker document (i.e., list of all consents signed by all participants)
- Original signed Informed Consent Forms (ICFs), HIPAA, and California Experimental Subject's Bill of Rights documents
- Screen Failure Charts, including 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 study program for 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.)
- FDA Form 1572s for each Investigator (ensure that all Investigators with a FDA Form 1572 are listed on the Delegation of Authority (DOA) log)
- 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 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.

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- Training documents for the Site Initiation Visit (SIV) and for all versions of the protocol for all staff members listed on the DOA Log. There should be a separate training document signed off by all members of the team for each new version of the protocol.
- HDFCCC Policies and Guidances, as well as Data and Safety Monitoring Committee (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, other ADs, 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.
  - Remind everyone attending the opening meeting to bring their business card.

### **2.2.2 DSMC Director or Designee Responsibilities**

- 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.

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- Audit the 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 2 flash drives to be utilized for providing records to the FDA Inspector.

### **3.0 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.

#### **3.1 FDA Liaison Responsibilities:**

- Document all questions and locate the study team staff who can answer the questions. The Liaison will create an e-mail chain each day to update everyone 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 (note: all documents provided to the inspector should be saved on the second flash drive so the HDFCCC has record of what was provided).
- 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 (along with the provided response).
- Document all those in attendance at the initial meeting and close-out meeting.
- 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.
- Anyone interacting with the FDA inspector should:
  - Be honest at all times
  - Be respectful and professional
  - Understand the question before answering

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- 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 the documents

### **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, 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 within 3-6 months after completion of the inspection. If there are significant observational findings, then a FDA Form 483 form will be issued to the PI at the close out meeting.

If the PI receives a FDA Form 483 form, the 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 form will be forwarded to the DSMC, Sponsor, IRB, and the OLA by the PI and study team.

## **5.0 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).

### Research Study File Maintenance

- 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.

### FDA Inspection Triggers (increase the chance of a FDA inspection)

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- 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.
- 
- If any of the above triggers apply to your study, contact the DSMC if you are informed by the sponsor that the investigational drug or device has been submitted for an NDA or PMA. Advance preparation is recommended in case your study is selected for an inspection.
  - In order to be audit ready, please use Attachment 1 (Chart Review Checklist) for the review of each of your study participant charts.

### **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](#)

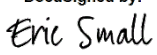
### **Appendices**


Appendix I: Chart Review Checklist

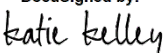
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Policy Approval

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

<div style="border: 1px solid black; padding: 2px; display: inline-block;"><small>DocuSigned by:</small>  <small>7FCB32D327E3438...</small></div> <hr/> <p>Eric Small, MD Deputy Director Helen Diller Family Comprehensive Cancer Center</p>	<p>2/23/2023</p> <hr/> <p>Date</p>
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<div style="border: 1px solid black; padding: 2px; display: inline-block;"><small>DocuSigned by:</small>  <small>80D38159E89D41B...</small></div> <hr/> <p>Kate Shumate, MPA, CCRP Director, Administration and Planning Helen Diller Family Comprehensive Cancer Center</p>	<p>2/22/2023</p> <hr/> <p>Date</p>
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<div style="border: 1px solid black; padding: 2px; display: inline-block;"><small>DocuSigned by:</small>  <small>7F538467F93949B...</small></div> <hr/> <p>Katie Kelley, MD Chair, Data and Safety Monitoring Committee Helen Diller Family Comprehensive Cancer Center</p>	<p>2/22/2023</p> <hr/> <p>Date</p>
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Policy Contact:

John McAdams  
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**Appendix I: Chart Review Checklist**

Study CC#:

Study Title:

Study Status:

Subject ID:

Subject Status:

Chart Review Completed by:

Date:

☐ Review Bill of Rights <sup>(1)</sup> HIPAA <sup>(2)</sup>, and ICF <sup>(3)</sup> to ensure that these documents were obtained properly as per the ICF Policy and CRC Guideline and were completed prior to any procedures occurring for the trial. Also, review to ensure this process has been documented in the patient's chart.

- Patient and Investigator signed same date (if by telephone consent, documentation is on hand to explain process. Also, ensure that the original ICF is present with wet signatures filed in the chart and that this process is documented).
- Ensure all ICFs are scanned into APeX.
- Investigator listed on FDA 1572, IRB application section 3.2, DOA, and FDF.
- For new risks, ensure that the verbal notification form has been completed and signed by the Investigator and was completed within the timeline for the verbal notification of the new risk(s) (as per the Verbal Notification Policy).
- For re-consents, ensure that the patient and Investigator signed same date as above and that there is clear discussion of this process (or consent documentation form) in the patient's chart.

☐ Review Medical History/Baseline Conditions for completeness and Investigator signature(s).

☐ Review Eligibility Criteria for completeness and Investigator signature(s).

- PI signed and dated each page, and this date is prior to the patient's first dose of IP (enrollment in trial). Also, CRM and CRC have signed the last page of this document and this date is prior to first dose of IP.
- Ensure that the EC document matches the EC in the protocol verbatim.
- # on checklist corresponds to # tabbed on source doc
- Source document on file to support each inclusion/exclusion criteria
- PI signed/dated all sources docs (Source docs include Study ID/MRN and CC#/Study Name)
- Sources docs are tabbed to correspond with corresponding Inclusion/Exclusion
  - For example: if labs are inclusion criteria #4, the source doc labs should be signed off and dated by PI and tabbed #4

☐ Review Adverse Events and Concomitant Medications forms for completeness and Investigator signatures. Review all SAEs to ensure that they have been submitted to the Sponsor, IRB, FDA, etc. (as applicable) and per timelines in the protocol and as per regulations.

☐ Review for any Patient Eligibility Exceptions, Protocol Violations, Notes to File, etc. in patient files.

☐ Review all MD Dictations for medical history items, adverse events, and concomitant medications not captured in these forms.

☐ Review all labs, scans, etc. for Investigator review and signatures.

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- Signed and dated day of infusion
- Abnormal values are graded using CTCAE and indicated as CS or NCS by PI.
- CS events are documented as AE on AE log

☐ Ensure restaging scans were completed per protocol specifications, if completed outside window: follow up with PI to determine if this is Protocol Deviation vs Protocol Violation.

☐ Review all PI orders to ensure that these were completed.

☐ Ensure that GCP is followed throughout chart (i.e., cross-outs are initialed and dated) (paper chart).

☐ Ensure that chart is organized chronological for the Auditor to review and that the chart is properly tagged for visits, labs, ICF, etc. (paper chart only)

☐ Ensure that OnCore is updated to accurately reflect patients' visits, study status, including SAEs, and Protocol Violations

☐ Ensure Off-Study Treatment form is complete and signed/dated by PI (if applicable)

☐ Ensure that the documentation for Screen Failure (SF) patients is complete (i.e., completed and signed EC checklist for all SF patients).

Follow up Items to be completed by Study CRC:

**Action Item:**

**Comment:**

**Completed  
(Yes/No and  
Date)**

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**Policy Revision Summary of Changes**

**Policy Title:** Policy for Facilitating FDA Inspections  
**Version Date:** 18Jan2023  
**Version** 4  
**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 ~~strike through~~.

Page No.: 2		Section: Purpose, Scope, Background, Procedures
Original Text	See original document	
New Text	<b>6.0 Notification</b> <ul style="list-style-type: none"><li>• 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:<ul style="list-style-type: none"><li>• Chair (or Vice Chair) of the Data Safety Monitoring Committee (DSMC)</li><li>• Clinical Research Support Office (CRSO) Medical Director</li><li>• CRSO Director</li><li>• CRSO Associate Directors</li><li>• Protocol Review and Monitoring Committee (PRMC) Chair</li><li>• PRMC Manager</li><li>• Human Research Protection Program (HRPP) /Institutional Review Board (IRB) Director</li><li>• Clinical Research Operations Director</li><li>• Investigational Drug Services (IDS) Manager and IDS Pharmacist (if applicable)</li><li>• UCSF Office of Legal Affairs Director</li><li>• UCSF Office of Ethics and Compliance Director</li></ul></li></ul>	
Reason for Change	To update the language in this policy as per the FDA inspection process.	
Page No.: 3-4		Section: Procedures
Original Text	See original document.	

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<p><b>New Text</b></p>	<p><b>7.0 Preparing for the Inspection</b></p> <ul style="list-style-type: none"> <li>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):</li> </ul> <p><u>Study Coordination Documents:</u></p> <ul style="list-style-type: none"> <li>All paper or electronic Research Charts (including screen failures) <ul style="list-style-type: none"> <li>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.</li> </ul> </li> <li>Enrollment Logs (including total number of participants screened, enrolled, discontinued, and completed trial).</li> <li>Listing of all Protocol Violations.</li> <li>Listing of all Adverse Events.</li> <li>Listing of all Serious Adverse Events (SAEs).</li> <li>Original signed Informed Consent Forms (ICFs), HIPAA, and California Experimental Subject's Bill of Rights documents.</li> <li>Screen Failure Charts, including documentation reason for screen failure.</li> <li>Study processes such as consenting process, RECIST measurements, etc.</li> <li>Consent Tracker document (i.e., list of all consents signed by all participants).</li> </ul> <p><u>Regulatory Documents:</u></p> <ul style="list-style-type: none"> <li>PI Listing of Trials over the past 5 years – this list must include: <ul style="list-style-type: none"> <li>Protocol number</li> <li>Protocol title (including the product name)</li> <li>Research or marketing permit number (if available)</li> <li>Name of sponsor (including government agencies and commercial sponsors),</li> <li>IRB of record, and key study dates (e.g., IRB approval, open to accrual, closed to accrual).</li> </ul> </li> <li>Chair of the IRB Panel reviewing the trial, along with the address of each IRB Panel.</li> </ul> <p style="text-align: right;"><b><u>Organization Chart for HDFCCC and the Site Committee (SC) of the study program for the trial being inspected.</u></b></p>
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<b>Reason for Change</b>	To update the language in this policy as per the FDA inspection process.	
<b>Page No.: 5</b>	<b>Section:</b> Procedures	
<b>Original Text</b>	See original document.	
<b>New Text</b>	<ul style="list-style-type: none"> <li>• specific time in everyone's calendar.</li> <li>• Identifying a "ready room" near inspection location as the "command center" for the inspection.</li> <li>• Reminding everyone attending the opening meeting to bring their business card and will ensure that there is an opening meeting.</li> </ul> <p><u>DSMC Director or Designee Responsibilities</u></p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• Preparing the inspection notes in Microsoft Teams for the FDA Liaisons to complete for each day of the inspection.</li> <li>• 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.</li> <li>• Auditing the charts, regulatory and pharmacy documents in order to identify any findings and assist the study team with the CAPAs for these issues.</li> <li>• Providing the study team with 2 flash drives to be utilized for providing records to the FDA Inspector.</li> </ul> <p><b>8.0 Conducting the Inspection</b></p> <ul style="list-style-type: none"> <li>• The FDA Liaison will meet with inspector and will ensure that he/she signs in with security.</li> <li>• 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.</li> <li>• The PI or designee will obtain the FDA 482 form (Notice of Inspection) from the Inspector and verify the Inspector's credentials.</li> <li>• 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.</li> <li>• 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.</li> </ul>	
<b>Reason for Change</b>	To update the language in this policy as per the FDA inspection process.	

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<b>Page No.:</b> 6	<b>Section:</b> Procedures
<b>Original Text</b>	See original document.

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<p><b>New Text</b></p>	<ul style="list-style-type: none"> <li>• Providing requested records to the inspector via an unencrypted flash drive (after review by the Liaison in the “ready room”).</li> <li>• Accompanying the Inspector if they leave the designated room.</li> <li>• Documenting the name and title of staff members who are interviewed by the Inspector, along with the date and time of the interview.</li> <li>• Documenting all those in attendance at the initial meeting and close-out meeting.</li> <li>• Traveling with the Inspector and a study staff member when touring the clinic and meeting with the IDS Pharmacist to take notes.</li> </ul> <p><u>Interacting with the Inspector</u></p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• For all interactions with the FDA Inspector, please ensure to always: <ul style="list-style-type: none"> <li>• Be honest at all times.</li> <li>• Be respectful and professional.</li> <li>• Understand the question before answering.</li> <li>• Only answer one question at a time.</li> <li>• Think before you speak.</li> <li>• Answer the question only and don’t elaborate.</li> <li>• Don’t volunteer information that is not requested.</li> <li>• Don’t be afraid to say, “I do not know” and offer to find the answer and get back to the Inspector.</li> <li>• Don’t be afraid to ask Inspector to repeat question if unclear.</li> <li>• Don’t provide a document to the Inspector until requested by the Inspector and the FDA Liaison has reviewed these documents.</li> </ul> </li> </ul> <p><u>Interacting with the Sponsor</u></p> <ul style="list-style-type: none"> <li>• Any questions outside the scope of activities completed by the study team should be directed to the sponsor.</li> <li>• 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.</li> </ul> <p><b>9.0 Post-Inspection</b></p> <ul style="list-style-type: none"> <li>• On the last day of the inspection, the PI, study team, FDA Liaison,</li> </ul>
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	<p>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.</p> <p>1.</p>
<b>Reason for Change</b>	To update the language in this policy as per the FDA inspection process.
<b>Page No.: 7</b>	<b>Section: Procedures</b>
<b>Original Text</b>	See original document.
<b>New Text</b>	<ul style="list-style-type: none"> <li>• If the PI receives a FDA Form 483 Report: <ul style="list-style-type: none"> <li>• 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.</li> <li>• The FDA Form 483 Report will be forwarded to the DSMC, Sponsor, IRB, and the OLA by the PI and study team.</li> </ul> </li> </ul> <p><b>10.0 Ongoing Readiness</b></p> <p><i>Note:</i> 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).</p> <p><u>Research Study File Maintenance</u></p> <ul style="list-style-type: none"> <li>• Keep files organized at all times. Conduct a chart review as per Appendix 1.</li> <li>• Retain all correspondence from sponsor, IRB, monitors, study subjects, letters, e-mails, memos, and phone contacts.</li> <li>• Retain all test article accountability records.</li> <li>• Retain shipping receipts, screening and enrollment logs, and dispensing logs.</li> </ul> <p><u>FDA Inspection Triggers (increase the chance of a FDA inspection)</u></p> <ul style="list-style-type: none"> <li>• Application for a New Drug Application (NDA).</li> <li>• Expedited Submission or Pre-Market Approval (PMA).</li> <li>• Non-compliance or study misconduct.</li> <li>• Protocol violation, Serious Non-compliance (SNC) Reports, high number of deaths reported, high enrollment, and a large number of studies/investigators. 1)</li> </ul>



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**Helen Diller Family Comprehensive Cancer Center**

<b>Reason for Change</b>	To update the language in this policy as per the FDA inspection process.	
<b>Page No.:</b> 9-10	<b>Section:</b> Appendix 1 (Chart Review Checklist)	
<b>Original Text</b>	See original document.	
<b>New Text</b>	<p><input type="checkbox"/> Review Bill of Rights <sup>(1)</sup> HIPAA <sup>(2)</sup>, and ICF <sup>(3)</sup> to ensure that these documents were obtained properly as per the ICF Policy and CRC Guideline and were completed prior to any procedures occurring for the trial. Also, review to ensure this process has been documented in the patient's chart.</p> <ul style="list-style-type: none"> <li>○ Patient and Investigator signed same date (if by telephone consent, documentation is on hand to explain process. Also, ensure that the original ICF is present with wet signatures filed in the chart and that this process is documented).</li> <li>○ Ensure all ICFs are scanned into APeX.</li> <li>○ Investigator listed on FDA 1572, IRB application section 3.2, DOA, and FDF.</li> <li>○ For new risks, ensure that the verbal notification form has been completed and signed by the Investigator and was completed within the timeline for the verbal notification of the new risk(s) (as per the Verbal Notification Policy).</li> <li>○ For re-consents, ensure that the patient and Investigator signed same date as above and that there is clear discussion of this process (or consent documentation form) in the patient's chart.</li> </ul> <p><input type="checkbox"/> Review Medical History/Baseline Conditions for completeness and Investigator signature(s).</p> <p><input type="checkbox"/> Review Eligibility Criteria for completeness and Investigator signature(s).</p> <ul style="list-style-type: none"> <li>○ PI signed and dated each page, and this date is prior to the patient's first dose of IP (enrollment in trial). Also, CRM and CRC have signed the last page of this document and this date is prior to first dose of IP.</li> <li>○ Ensure that the EC document matches the EC in the protocol verbatim.</li> <li>○ # on checklist corresponds to # tabbed on source doc</li> <li>○ Source document on file to support each inclusion/exclusion criteria</li> <li>○ PI signed/dated all sources docs (Source docs include Study ID/MRN and CC#/Study Name</li> <li>○ Sources docs are tabbed to correspond with corresponding Inclusion/Exclusion <ul style="list-style-type: none"> <li>○ For example: if labs are inclusion criteria #4, the source doc labs should be signed off and dated by PI and tabbed #4</li> </ul> </li> </ul> <p><input type="checkbox"/> Review Adverse Events and Concomitant Medications forms for completeness and Investigator signatures. Review all SAEs to ensure that they have been submitted to the Sponsor, IRB, FDA, etc. (as applicable) and per timelines in the protocol and as per regulations.</p> <p><input type="checkbox"/> Review for any Patient Eligibility Exceptions, Protocol Violations, Notes to File, etc. in patient files</p>	

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<b>Reason for Change</b>	Updated this information.	
<b>New Text</b>		

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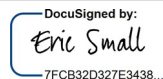
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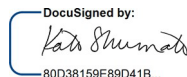
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