UCSF Helen Diller Family Comprehensive Cancer Center

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

Policy for Clinical Research Essential Regulatory Documents

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Purpose

This policy outlines the requirements for the collection and maintenance of essential regulatory documents for clinical research studies conducted at the UCSF Helen Diller Family Comprehensive Cancer Center (HDFCCC).

Scope

This policy applies to all clinical research studies conducted in the HDFCCC, unless otherwise specified throughout this document.

For the purpose of this policy, signatures which require use of a 21 CFR part 11 compliant system will be referred to as “Part 11 compliant” or “Part 11 compliant system”. 21 CRF part 11 compliant systems used in the HDFCCC include, but are not limited to, Complion and the 21 CFR part 11 compliant version of DocuSign.

Definitions

Essential regulatory documents: documents which individually and collectively permit evaluation of the conduct of a clinical trial and the quality of the data produced. These documents serve to demonstrate compliance with standards of good clinical practice (GCP) and all applicable regulatory requirements. (ICH-GCP: E6R2)

Background

As per ICH-GCP: E6R2, all clinical research studies must create and maintain a Trial Master File (TMF) with applicable essential regulatory documents. While ICH-GCP: E6R2 defines which documents are required, this policy outlines how to complete and maintain these documents based on HDFCCC and UCSF institutional requirements, procedures and information. Essential regulatory documents not listed in this policy do not have HDFCCC or UCSF completion or maintenance considerations and will be filed in the TMF according to requirements listed in ICH-GCP: E6R2 and any applicable sections of the FDA Code of Federal Regulations.

Study teams are responsible for keeping and maintaining the appropriate TMF and the files will be made available to the study sponsor or HDFCCC DSMC, as per the HDFCCC Clinical Research Policy for External Study Related Visits.

Procedures

Essential study regulatory documents are stored in the study’s regulatory binder which may be physical or electronic.

1.0 Accessing External Sponsor-Specific Portals

HDFCCC does not access external (i.e. non-UCSF portals) portals or platforms for any study documents [protocols, investigator brochures, Informed Consent Form (ICFs), participant materials, etc.]. For essential clinical research documents, quality assurance and compliance measures require person-to-person transfer of documents and communication via email.

2.0 Essential Regulatory Documents

2.1 FDA Form 1571

The Form FDA 1571, Investigational New Drug (IND) Application, is completed per Clinical Research Support Office (CRSO) protocol development workflows. Questions about IND applications may be directed to crsoind@ucsf.edu.

2.2 Delegation of Authority Log

Refer to the Policy for Delegation of Authority Log.

2.3 Form FDA-1572

The Form FDA-1572 will be completed prior to the study opening for interventional studies under an Investigational New Drug application (IND) or Investigational Device Exemption (IDE) application.

Individuals making direct and significant contributions to the clinical data may be designated by the Principal Investigator (PI) as sub-investigators (sub-Is) on the 1572. Sub-Is must be licensed clinical professionals considered appropriate experts to investigate the intervention(s) and potential adverse events related to the clinical investigation.

Clinical Research Coordinators (CRCs) in the HDFCCC do not perform critical study functions nor make direct and significant contributions to the data, and, do not meet the definition of a sub-I according to the FDA Information Sheet Guidance for Sponsors, Clinical Investigators and IRBs. The HDFCCC exercises its judgment by not listing CRCs as sub-Is for studies conducted in the HDFCCC.

PI signature on the FDA-1572 will be completed via wet-ink signature or a Part 11 compliant system. If the PI signs via wet ink, the original will be retained in a physical binder and the document will be scanned and uploaded to the study's electronic TMF.

In the event of a PI or sub-I addition, the Form FDA-1572 will be updated in real time. Other form updates will be communicated to the sponsor, documented in study records, and included in a subsequent Form FDA-1572 update.

Laboratories and other clinical facilities, including imaging and EKGs, listed on the 1572 will be limited to those performing protocol specified research-only tests/procedures. Laboratories performing tests/procedures for a participant's conventional/standard care for their disease may not be required as the data is obtained as a result of a medical record review. Additionally, local labs used for emergency care, SAE assessment or follow-up, or in exceptional circumstances (e.g. participant on vacation or cannot go to their regular lab) will not be included in the form FDA-1572 form.

Addresses listed on the form FDA-1572 will be the recorded as the relevant site's primary mailing address. Room and floor numbers may only be indicated if the site only consists of a portion of a building (i.e., rented office space).

2.4 Investigator Qualifications and Credentials

The PI and delegated sub-Is (as per the Form FDA-1572 or Delegation of Authority Log) will file their curriculum vitae (CV), medical license (ML), and any certifications applicable to the study, in the TMF. The CV on file in the TMF will be current within 2 years of the start of the study (defined as when the PI signs the delegation of authority log or the Form FDA-1572 – whichever is first). CVs do not expire. The CV and medical license for the lab director is described in section 2.7.

FDA regulations do not require a CV to be signed and dated. The investigator's dated signature on the Form FDA-1572 is sufficient to attest to the accuracy of the CV or other statement of qualifications submitted with the Form FDA-1572.

2.5 Pharmacy Documents

The study's lead investigational pharmacist will maintain Investigational Drug Service (IDS) Policies, pharmacy manuals, blinding procedure documentation, Investigational product (IP) shipping records, and IP accountability and destruction records. Pharmacy documents are maintained by the UCSF IDS and available by contacting the IDS pharmacy directly.

2.6 Financial Disclosure Forms (FDFs)

Each clinical investigator (PI, sub-Is) listed on the Form FDA-1572 will file an FDF (FDA form 3454 or 3455) for each study. Each FDF will be signed by its respective investigator via wet ink or a Part 11 compliant system. If wet ink is used, the original will be retained in a physical binder and the document will be scanned and uploaded to the study's electronic regulatory binder. An updated form will only be filed in the event of a relevant change through one year following completion of the study.

2.7 Laboratory Documents

Relevant certifications/accreditations (e.g., CAP, CLIA, TJC) and laboratory directors' CVs and medical license will be filed for each laboratory listed on the Form FDA-1572. In the event of a delay between the expiration date and renewed certification documentation, the study team will file placeholder documentation provided by the laboratory. If no placeholder documentation is provided, email communication between the study team and the laboratory may be used in its place.

Normal values/ranges will be filed for tests and procedures included in the protocol.

2.8 Training Logs

Protocol and protocol amendment training will be documented via attendance at a meeting where the protocol training occurred (e.g., site committee or site initiation visit) or via individual training attestations for all individuals on the Delegation of Authority Log. If training on a protocol amendment is not necessary (or not necessary for specific roles), a note to file explaining the rationale for not training will be filed in the TMF.

Any additional study-specific training or attestation requested by the sponsor must be provided and documented by the sponsor (e.g., study platform or electronic data capture system training, study manual review, etc.).

Human Subjects Protection (HSP) Training (CITI GCP and HSP or equivalent training) certificates will be filed in the TMF for each individual listed on the Delegation of Authority log.

IATA Safe Shipping training certificates will be filed in the TMF for individuals delegated the task of shipping biospecimens.

2.9 Participant Screening Log

Participants who have not signed informed consent will not be included on the screening log unless specified in the protocol and approved by the Institutional Review Board (IRB) of record.

2.10 Informed Consent Forms (ICFs)

Refer to the Policy for Obtaining Informed Consent of Potential Participants for Oncology Research.

2.11 UCSF Health equipment and facility records

UCSF Health Medical Center standard of care facilities and equipment are maintained per UCSF Health policies. Regular maintenance records for UCSF Health equipment (which may also be used on UCSF Health non-research patients) such as calibration logs are not available, unless requested by Federal Regulatory Agencies (e.g., FDA).

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Policy Exemptions

If a laboratory is used to test specimens in a manner which does not impact research participants' clinical care (i.e., results are not used for diagnosis, treatment, prevention, or assessment of participants' health), CAP/CLIA/TMJ certifications are not relevant and do not need to be filed.

Interim/temporary PI – In the event of a PI's temporary leave (e.g., medical leave), an interim PI will be established. The interim PI holds all the responsibilities of PI while appointed, and they will sign a new Form FDA-1572. The permanent PI will then submit a new form FDA-1572 upon their return. A Note-to-File will be filed with the regulatory documents to indicate the effective dates and explain the circumstances of the temporary leave. Changes to the Delegation of Authority log during the temporary leave will be signed by the interim PI. If possible, the permanent PI will designate the interim PI in the DOA log prior to their leave, closing out any secondary delegation line for the individual serving as interim PI. Upon return, the permanent PI will complete the interim PI delegation and, if appropriate, initiate a new entry for the outgoing interim PI's subsequent role in the study (e.g., subinvestigator).

References

21 CFR 312
21 CFR 312 Subpart B – IND Application
21 CFR 312 Subpart D – Responsibilities of Sponsors and Investigators
21 CFR 312.53 – Form FDA 1572
21 CFR 54 - Financial Disclosure by Clinical Investigators
42 CFR 493.3 – Laboratory Requirement Applicability
ICH GCP E6 Guidelines
Information Sheet – Form FDA 1572
Instructions – Form FDA 1572
Good Clinical Practice Inquiries

Policy Approval

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

DocuSigned by:
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Helen Diller Family Comprehensive Cancer Center

6/21/2024
Date

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6/21/2024
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DocuSign

Certificate Of Completion

Envelope Id: AD666E22CFD8447486BBDF3740630DE2
Status: Completed
Subject: Complete with Docusign: Regulatory Documents Policy_FINAL_v1_2024JUN21.pdf
Source Envelope:
Document Pages: 7
Signatures: 3
Certificate Pages: 2
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Andrea Skafel
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IP Address: 128.218.42.98

Record Tracking

Status: Original
6/21/2024 11:28:40 AM
Holder: Andrea Skafel
andrea.skafel@ucsf.edu
Location: DocuSign

Signer Events	Signature	Timestamp
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Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Katherine Shumate kate.shumate@ucsf.edu Chief of Staff, Director of Administration University of California, San Francisco Security Level: Email, Account Authentication (Optional)	DocuSigned by: Kate Shumate 80D38159E89D41B... Signature Adoption: Uploaded Signature Image Using IP Address: 128.218.42.202	Sent: 6/21/2024 11:30:06 AM Viewed: 6/21/2024 1:31:56 PM Signed: 6/21/2024 1:32:18 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: Rahul Aggarwal E870F084A5CA4CC... Signature Adoption: Pre-selected Style Using IP Address: 128.218.42.167	Sent: 6/21/2024 11:30:06 AM Viewed: 6/21/2024 12:04:32 PM Signed: 6/21/2024 12:04:39 PM
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
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Certified Delivered	Security Checked	6/21/2024 12:04:32 PM
Signing Complete	Security Checked	6/21/2024 12:04:39 PM
Completed	Security Checked	6/28/2024 9:09:13 AM

Payment Events	Status	Timestamps