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1. Overview

Purpose

The purpose of this document is to outline the process for the establishment, management and retention of essential documents and regulatory files that are required for clinical research in compliance with good clinical practice (GCP) guidelines. These guidelines apply to all clinical research conducted at, under the purview of, or by a research agent of Drexel University.

2. Definitions

21 CFR Part 11 Compliance: a set of guidelines from the US Food and Drug Administration (FDA) that establishes requirements for electronic records and signatures. The regulations are intended to ensure the security and integrity of electronic data, as well as the authenticity and nonrepudiability of electronic signatures. They also aim to ensure that electronic records and signatures are trustworthy, reliable, and equivalent to paper records with handwritten signatures.

Case Report Form (CRF): an electronic or paper document which is used in a clinical research study to record the protocol required information about each study participant.

eRegulatory: electronic versions of clinical research regulatory binders used to manage essential regulatory documents, e.g., Florence eBinders is a software application designed to support eRegulatory management.

Essential Documents: documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced

Good Clinical Practice (GCP): an international ethical and scientific quality standard for designing, conducting, recording and reporting research studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of research participants are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical research data are credible.

Investigator's Brochure: a document that summarizes clinical and non-clinical data about an investigational product (IP) or study drug. It includes the pre-clinical data such as chemical, pharmaceutical, toxicological, pharmacokinetic and pharmacodynamic data in animals and humans as well as the results of earlier research.

Note-to-File: a document written by a research team member to provide additional information or clarification about a research study. Examples include the explanation of the location of a study document, documentation of a discrepancy or problem and the actions taken to address it, or clarification of unclear protocol instructions.

Regulatory Files: a collection of documents that are essential for a clinical research study to comply with regulations and maintain good practices. These documents are often kept in regulatory binders, also known as study files or investigator binders.

Source Documents: original documents, data, and records that document the existence of a research participant and the integrity of the research data collected.

3. General Procedures

During the conduct of the study, key regulatory documents or essential documents are stored as central regulatory files. The regulatory files may be maintained in paper binders and/or in electronic file storage, e.g., Drexel University SharePoint or Drexel-supported eRegulatory systems. Throughout the study, the complete files must be maintained in a secure location and/or in a secure electronic format.

Sponsors may provide a regulatory binder for use. The regulatory binder(s) should be kept up to date and must be made available for review and inspection by the study sponsor or their representatives, the Drexel University Quality Assurance Program, and/or applicable regulatory authorities. Essential regulatory documents may be stored outside of the regulatory files, e.g., signed informed consent forms may be stored with participant files or completed case report forms in an electronic database. At the completion of the study, ensure all essential regulatory files are stored in a central location or the location of all essential documents is otherwise documented and verified and can be made available upon request.

Please note, this guidance follows GCP guidelines for maintenance of essential documents. Some sections may not be applicable to all clinical research studies, e.g., Investigator's Brochure or Investigational Product documents. If conducting an investigator-initiated clinical research study, essential regulatory documents required for the investigator/institution and the sponsor must be maintained by the lead investigator/institution.

4. Regulatory Files Sections and Content

4.1 Investigator's Brochure and Updates

Maintain a copy of all Investigator's Brochures and updates to document that the investigator is aware of relevant information related to the investigational product (IP).

4.2 Protocol and Amendments

Maintain a copy of all protocols and updates, including protocol administrative letters. The protocols and updates should be signed by the investigator to document acknowledgment of the protocol.

4.3 Informed Consent Forms/Information Given to Participants*

Maintain copies of all versions of the IRB-approved consent forms, other written information for participants, and advertisements used for participant recruitment. Signed informed consent forms must be maintained after the study start.

4.4 Financial Agreements and Financial Disclosures*

Maintain copies of the financial agreements, e.g., study budget and applicable financial disclosures of essential study personnel.

4.5 Insurance Statement*

If applicable, maintain a copy of the insurance statement/agreement related to participant compensation for study-related injuries.

4.6 Signed Agreement(s) Between Involved Parties*

Maintain copies and amendments of signed agreements between the investigator/institution and the sponsor or CRO and the investigator/institution and applicable regulatory authorities (e.g., FDA).

4.7 IRB Approvals and Communications

Maintain copies of IRB submissions, communications, and approved documents, including but not limited to the protocol, informed consent forms, information to be provided to participants, advertisements for recruitment, and investigator's brochure.

4.8 IRB Composition/IRB Roster*

Maintain a copy of the IRB Roster to document that the IRB is constituted in agreement with Federal regulations and GCP guidelines.

4.9 Regulatory Authority Approval/Communications and Interim Reports

Maintain copies of all communications, approvals, and interim reports from applicable regulatory authorities, e.g., FDA. This section should include the FDA Form 1572 for applicable studies under an Investigational New Drug (IND) application.

4.10 Copies of Curriculum Vitae (CVs) and Licenses

Maintain copies of current CVs/resumes and licenses for all investigators and co-investigators to document investigator qualifications throughout the duration of the study. CVs/resumes and applicable licenses should all be maintained for personnel directly involved in the performance of the study procedures, including participant recruitment and consent, collection of study data, and maintaining study records.

4.11 Laboratory Documents

For laboratories utilized in the conduct of the study or processing tests included in the protocol, maintain copies of laboratory reference ranges/normal values for tests included in the protocol. Also, maintain documentation of laboratory certification, accreditation, or validation of tests for the duration of the study.

4.12 Investigational Product (IP) Documents

Maintain copies of instructions for the handling of the IP, a sample label for IP containers, shipping records for IP and related materials, accountability records (shipping, dispensation, destruction or return of products), and unblinding procedures.

4.13 Study Initiation Report and Monitoring Visit Reports

Maintain copies of the site initiation report and all interim monitoring visit reports to document oversight and monitoring findings.

4.14 Source Documents*
Maintain all original source documents to substantiate the integrity of the study data.

4.15 Completed Case Report Forms*
Maintain a copy of the signed, dated and completed case report forms (CRFs), including documentation of any CRF corrections made after the initial data was recorded.

4.16 Safety Reports and Adverse Event Reports*
Maintain copies of safety reports and reports of unanticipated problems from the sponsor to the investigators as well as adverse event reports originating from the investigator to the sponsor per protocol reporting requirements.

4.17 Participant Screening and Enrollment Log(s)
Maintain a list of participants entered into pre-screening and chronological enrollment of participants by study number.

4.18 Participant Identification Code List
The investigator must maintain a confidential participant identification code list linking participant names to their study identification number.

4.19 Site Signature and Delegation/Responsibility Log
Maintain a log of personnel signatures and initials for personnel authorized to make entries and corrections on case report forms. The signature sheet is frequently combined with the Delegation of Authority Log (see SOP ORI-612 Delegation of Authority).

4.20 Relevant Communications
Maintain documentation of all relevant communications, including but not limited to meeting notes, letters, notes of telephone calls, email correspondences with the sponsor, CRO, participants, etc.

* Documents as indicated with and asterisk (*) above may standardly be stored outside of the regulatory binder or electronic regulatory files, as detailed below. Consider including a note to file in your regulatory binder to document the storage location(s) of any essential documents stored outside of the regulatory binder, and ensure all essential documents are accounted for at the time of study completion.

- Signed informed consent forms may be stored in participant study files.
- Financial agreements (including the study budget), insurance statements, and signed agreements may be stored in an external file with limited, secured access.
- The IRB composition information may be maintained and available on the IRB's website or available upon request from the IRB.
- Source Documents may be stored in participant study files or electronic medical records.
- Completed Case Report Forms are frequently stored within a secure electronic database. At the completion of the study, a final dataset or data disc is often provided by the study sponsor.

- Safety and Adverse Event Reports may be stored within specific participant files if the adverse event has occurred at the local study site. External site safety reports are often provided de-identified and are stored within the regulatory files.

5. Responsibilities

5.1 Office for Research & Innovation Responsibilities

The Office for Research & Innovation is responsible for maintaining this guidance document, applicable tools, and monitoring. For inquiries regarding these procedures, please contact the Associate Vice Provost for Research Compliance and Regulatory Affairs, as part of the Office for Research & Innovation (ORI).

5.2 Principal Investigator Responsibilities

The Principal Investigator retains overall responsibility for the study and maintenance of study documents in accordance with this guidance. The PI must maintain and review study documents as specified by the regulatory authorities and in GCP.

5.3 Study Personnel Responsibilities, as delegated by the PI

Study personnel, as delegated by the PI, are responsible for assisting the PI in maintaining up to date regulatory files. Designated personnel should review the regulatory files for completeness and ensure documents comply with federal, state and local regulations.

6. Resources

- ICH E6 R2 Guidance for Industry Good Clinical Practice
- 21 CFR, Part 312: Investigational New Drug Application
- 21 CFR, Part 812: Investigational Device Exemptions

7. Revision and Workgroup Members

7.1 Revision

Version 001/Effective Date 1/24/2025 – Original Document: Maintenance of Regulatory Files

7.2 Workgroup & Advisory Members

The Office for Research and Innovation appreciates the following individuals who served as Workgroup and Advisory Members:

Workgroup & Advisory Members	
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