

Section Clinical Research Center

Date Created/Modified: November 1<sup>st</sup>, 2010

Title: Regulatory Binder

Date Reviewed: April 1, 2019

SOP Number: SOP-27

Version Number: 4

**PURPOSE:** The purpose of this standard operating procedure (SOP) is to ensure all Clinical Research Center (CRC) personnel are familiar with the documents that must be maintained in a regulatory binder.

**SCOPE:** This SOP applies to most documents maintained in the Regulatory binder (electronic or paper). These documents are referred to as Essential documents. Essential documents serve to show compliance of an investigator and sponsor with the regulatory requirements of the study.

**PERSONNEL RESPONSIBLE:** Principal Investigator, Sub-investigators, Study Coordinator, Regulatory Coordinators and/or other pertinent staff should be familiar with the content and the location of the regulatory binder.

**DEFINITIONS:**

- **College of American Pathologists (CAP)** – sets quality, accuracy, and consistency standards for laboratory accreditation.
- **Clinical Laboratory Improvement Amendments (CLIA)** – Regulations that establish quality standards for laboratory testing performed on specimens from humans, such as blood, body fluid, and tissue, for the purpose of diagnosis, prevention, or treatment of disease, or assessment of health.
- **Essential Documents** - Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.
- **Financial Disclosure Form (FDF)** - Official legal document that the FDA requires sponsors to certify the absence of certain financial arrangements between an investigator and/or disclose those financial interests when the sponsor has submitted a marketing application of a new investigational product in the United States.
- **Food and Drug Administration (FDA)** - Department within the United States Department of Health and Human Services. Enforces Food, Drug and Cosmetics Act and related federal public health laws.
- **Good Clinical Practice (GCP)** -A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of research that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of subjects are protected.
- **Institutional Review Board (IRB)** - An independent group made up of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by reviewing and approving the clinical protocol, informed consent forms, and the methods and materials used in the trial.

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- **Investigational Product (IP)** - A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, when used for an unapproved indication, or when used to gain further information about an approved use.
- **Investigator's Brochure (IB)** - Relevant clinical and non-clinical data compiled on the investigational drug, biologic or device being studied in human subjects.
- **Laboratory reference ranges** - A set of values used by a health professional to interpret a set of medical laboratory test results from blood, urine or other body fluid samples.
- **Protocol** - A document that describes how a clinical trial will be conducted to include the objective(s), design, methodology, statistical considerations and organization. It works to ensure the safety of study participants and integrity of the data collected.
- **Protocol Amendment**--A change(s) to or formal clarification of a protocol.
- **Statement of Investigator, Form FDA 1572** - an agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic.

### **PROCEDURES:**

- For all studies, the regulatory binder documentation will be established at the beginning of a trial and kept in a three-ring binder or electronically, once that is established as secure. Paper binders will be locked in a cabinet when not in use.
- Typically, for industry studies, the regulatory binder is provided by the sponsor. If the regulatory binder received has tabs to file documents but they are stored elsewhere, a Note to File stating where that information can be found (e.g., "Subject Logs are maintained in the coordinators office in the Subject log folder/binder") should be inserted into the regulatory binder.
- In order to demonstrate compliance of the investigator, sponsor, and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements, the regulatory binder must contain the following essential documents, when applicable:
  - Investigator's Brochure and all updates
  - Signed protocol and amendments. The outdated protocols will be marked as outdated to reduce confusion.
  - Documents evidencing qualifications for all site personnel, as required, include:
    - CV's
    - Professional Licenses
    - CITI Training certificates
  - Sample Case Report Forms (CRF) and any updated versions

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- Signed Form FDA 1572 and any signed revisions (for drug or biologic studies only). All previous signed copies must be retained including the original.
- Information given to study subjects and any revisions of these items:
  - Informed consent document
  - Any other written information (e.g., Subject Visit Items: Questionnaires, ID Cards, Treatment Diaries)
  - Advertisement for subject recruitment
- Initial IRB approval letter, dated and to reference the following items:
  - Protocol and any amendments
  - CRF (if applicable)
  - Informed consents
  - Any other written information provided to the subjects
  - Advertisement for subject recruitment
  - Subject compensation (if any)
  - Any other approved documents
- Dated, documented IRB approval of protocol amendments, revisions of the consent forms, written materials, advertisements, any other documents and continuing review (annual report) of the study
- IRB membership list
- Medical/Lab/technical procedures/test certifications, accreditation or established quality control assessment or other validation and any updates
- CLIA Certificates
- CAP
- Normal values/ranges and all updates for medical/lab/technical procedures/tests included in the protocol
- Instructions for handling of the IP and study-related materials
- Decoding procedures for blinded studies
- Study (Site) Initiation Monitoring report/letter
- Notification by originating investigator of Serious Adverse events and related reports (only if reportable to the IRB)
- Notification by sponsor/investigator, where applicable, to regulatory authorities and IRBs of unexpected SAEs (only if reportable to the IRB)
- Notifications by sponsor of safety information (only if reportable to the IRB)
- Relevant communications other than site visits regarding trial administration, protocol violations, trial conduct, AE reporting (letters, meeting notes, notes of phone calls)
- Blank templates of the following documents are maintained in the regulatory binder. Completed copies are kept and maintained by the pharmacy or nurse coordinator:

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- Subject Screening log
- Subject Identification code list
- Subject enrollment log
- Shipping records for IP and study-related materials
- IP accountability at the site
- If applicable, record of banked human biological material
- Documentation of IP Destruction or returns to sponsor
  - Final completion report submitted to IRB
  - Delegation of authority/Site signature log
- Other study-specific documents included in the regulatory binder, if provided by the Sponsor, include:
  - Training documentation
  - Notes to File
  - Sponsor newsletters or other written correspondence
  - Site-visit (Monitor) log
- Documents should be organized in reverse chronological order, i.e. the most current one on top.
- The regulatory binders will be made available for monitoring and audit visits
- At study close-out and packaging for long-term storage, a paper or electronic copy of the regulatory binders will be included with all corresponding source documents and case report form copies

#### **RESOURCES:**

ICH, Guideline for Good Clinical Practice (GCP) – E6, Section 8

Information Sheet Guidance for Sponsors, Clinical Investigators and IRB; FAQs Statement of Investigator (Form FDA 1572)

#### **Staff Accountability:**

Developed By: Director of Clinical Research Operations, Clinical Research Center  
Associate Vice Chancellor for Clinical Research, Clinical Research Center

Reviewed By: Regulatory Coordinators, Clinical Research Center

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### Department Approval

Signed   
Director of Clinical Research Operations

Signed   
Medical Director of Clinical Research Center