

Title: **REGULATORY DOCUMENTATION**

1.0 OBJECTIVE:

- 1.1 This Standard Operating Procedure (SOP) describes the methods for the collection and storage of complete, organized, and accurate regulatory documentation.
- 1.2. This procedure is intended to meet FDA (Food and Drug Administration) and DHHS (Department of Health and Human Services) regulations, GCP (Good Clinical Practice) guidelines, state regulations and MCG Health System regulations regarding regulatory documentation for clinical research.

2.0 DEFINITIONS

- 2.1 Note-to-File: A description of the protocol-specific method of accomplishing a process. This document can also be used to describe the reason for a discrepancy, missing data or missing documentation and can include information regarding the location of central files.
- 2.2 Investigator's Brochure: This document contains a collection of all relevant information known prior to the start-up of a clinical research study involving an investigational 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 trials.

3.0 RESPONSIBILITIES:

**The PI may delegate certain responsibilities to another qualified member of the research team. The delegation of responsibility should be clearly documented. The PI retains full responsibility for to the procedures described in this standard operating procedure.*

- 3.1 The Principal Investigator (PI) shall maintain all required documentation for clinical research studies conducted at the Medical College of Georgia, Medical College of Georgia Health, Inc and the Augusta Veterans Affairs Medical Center.
- 3.2 The Principal Investigator shall obtain and store all required regulatory documents for each study.
- 3.3 The Principal Investigator shall maintain records of study administrative activities and data from each study subject.

4.0 PROCEDURES

- 4.1 Original documents relating to clinical research studies must be kept in a regulatory file.
- 4.2 When a study is being planned, a regulatory file should be started so that regulatory documentation can begin to be collected properly for the study.
- 4.3 Regulatory documents should be stored in a well organized manner and in a readily available format, preferably a ringed binder with the appropriate tabs.
- 4.4 Regulatory documents should be kept in a secure, locked area.
- 4.5 Financial documents pertaining to the study (i.e. budgets, contracts, etc...) should be stored separately from the items listed in Section 5.0
- 4.6 As the study progresses, the PI is responsible for the retention of documents received in the appropriate sections of the regulatory file as described in Section 5.0.
- 4.7 The regulatory file should be reviewed for accuracy. Missing documents should be retrieved and inserted, and discrepancies should be noted by creating a Note-to-File. If the document cannot be found or replaced, a Note-to- File explaining why the document is missing should be placed in the regulatory file. In the event that a document is temporarily stored outside of the regulatory binder, a note-to-file should be created indicating the document's location.
- 4.8 After the study is completed and all applicable committees have been notified, the regulatory file can be stored. It should be stored in a safe place and made available in the event of a regulatory audit.
 - 4.8.1 MCG policies require the retention of regulatory files for three years past completion of the research activity or at least three years after termination of the last IRB approved period for research activity, whichever is later.
 - 4.8.2 Refer to the sponsor/funding agency's contract/agreement to determine the required regulatory document retention guidelines.

5.0 DOCUMENT REQUIREMENTS

- 5.1 The following items should be filed in the regulatory files. All studies will not require all the documentation listed.

5.1.1 Original Protocol

A copy of the IRB-approved protocol should be kept with the PI's signature. If the protocol is modified during the course of the study, a copy of each amended and revised protocol should be added to the file. Each protocol should be dated for clarity and copies maintained in chronological order. The most current version of the IRB approved protocol should be clearly separated from outdated versions.

5.1.2 IRB Submissions

To document any submissions to the IRB, this section should include, but is not limited to, the Description of Research Proposal (local protocol), amendments, Investigational New Drug Application, change in research personnel, delegation of duties, continuations, response to stipulations, and terminations.

5.1.3 Informed Consent/Children's Assent Documents

The original informed consent/children's assent document (ICD/CAD) with the IRB approval stamp should be filed in this section. If there are amendments to the ICD/CAD, the originals should be accurately dated and maintained in chronological order. Careful attention should be given to the process to ensure that subjects are given the correct version of the ICD/CAD when they are enrolled in the study.

5.1.4 IRB Correspondence

All correspondence with the IRB including letters of initial approval, amendment approvals, continuations,

terminations, stipulations, and e-mail correspondence should be filed in this section.

5.1.5 IRB Membership Rosters

IRB rosters are required to be filed to document the IRB's composition is constituted in agreement with GCP guidelines, OHRP, and FDA regulations. The IRB will notify researchers of any changes to IRB membership. The PI is responsible for filing and maintaining copies of current and archived rosters.

5.1.6 FDA 1572

This form is required for clinical research involving investigational drugs. It is the investigator's agreement to perform the study according to applicable federal regulations. If the study is an investigational device study, the Device Agreement should be filed in this section. Each version of the FDA Form 1572 or Device Agreement should be filed in chronological order.

5.1.7 Staff Signature Log

This log should contain the names and delegated roles of all research team members. It should consist of each person's printed name and their signature (See Appendix I). The sponsor's staff signature log can be used, if provided by the sponsor.

5.1.8 Training and Education Records

This section should contain the training records/certifications for all research team members.

5.1.9 Drug/Device Accountability

The drug/device accountability records may be kept in another location during the active study period. If the study involves a drug, a signed and dated Note-to-File should be placed in this section discussing the drug's maintenance at the Clinical Research Pharmacy (See SOP 03- Investigational Drug Handling). At the conclusion of

the study, the drug/device accountability records should be placed in this section of the regulatory file.

5.1.10 Investigator's Brochure or Package Insert

A copy of the investigator's brochure should be filed in this section. If the investigational drug is approved by the FDA, a copy of the package insert should be filed in this section in lieu of the Investigator's Brochure.

5.1.11 Laboratory Certification, Accreditation or Validation

This section should be included in the regulatory files to document the competence of the facility performing the protocol-specified laboratory tests. Copies of the laboratory certifications for all labs involved with the study should be included in this section. Expired certifications should be replaced with current certifications and filed in chronological order.

5.1.11.1 Laboratory Director's Curriculum Vitae and Medical License (if applicable)

A copy of the laboratory director(s)' CV and medical license should be maintained in this section. Expired CV's and medical licenses should be replaced with current copies and filed in chronological order.

5.1.12 Range of Normal Lab Values

In the event that lab work is required, the range of normal values for the laboratory performing the analyses should be included in this section. A current copy of this listing should be maintained. Older versions of the listing should be filed in chronological order.

5.1.13 IATA Shipping Certification

This section should contain the IATA shipping certification for all research team members involved in the shipment of infectious and diagnostic specimens.

5.1.14 Screening Log

This section should include a list of all subjects who signed the ICD/CAD and were screened to be a participant in the study. Notation should be made as to whether the subjects were found to be eligible or a screen failure for the study. In the event that the subject is ineligible, the reason for the subject's ineligibility should be recorded (See Appendix II). The sponsor's screening log can be used, if provided by the sponsor.

5.1.15 Enrollment Log

This section should include a list of all subjects who were enrolled into the study (See Appendix III). The sponsor's enrollment log can be used, if provided by the sponsor.

5.1.16 Monitoring/Auditing Log and Reports

This section should contain records of all monitoring or auditing visits and all notifications thereof. All monitoring/auditing correspondence should also be placed in this section, including e-mail correspondence (See Appendix V).

5.1.17 Sponsor/Funding Source Correspondence

All correspondence between the sponsor/funding source and PI pertaining to the conduct of the study should be included in this section, including e-mail correspondence.

5.1.18 Advertisements

All IRB-approved research subject recruitment materials should be included in this section.

5.1.19 Curriculum Vitae (CV)/Licenses

This section should include the CV and medical licenses of all research team members. CVs should be updated annually and filed in chronological order. Medical licenses

must be kept current and filed with expired medial licenses in chronological order.

5.1.20 Adverse Events

Copies of all correspondence related to the reporting of adverse events and serious adverse events to the IRB, study sponsor/funding source and applicable regulatory authority should be maintained in this section. All documentation pertinent to the AE/SAE should be filed in this section as well as in the individual subject's research record.

5.1.21 Case Report Forms

A sample copy of all data capture forms or case report forms should be maintained in this section.

6.0 Study Subject Data Requirements

The study site should maintain an adequate and accurate record for each research subject screened and enrolled in the study. These records should be filed separately from the regulatory documentation described in section 5.0. These records may include, but are not limited to:

- case report forms
- medical history records
- physical exam results
- laboratory and diagnostic test results
- clinic notes pertinent to the research study

APPENDIX I
Regulatory File Checklist

- Original Protocol (s)
- IRB Submissions
- Informed Consent/Children's Assent Document(s)
- IRB Correspondence
- IRB Membership Rosters
- FDA 1572/Device Agreement
- Staff Signature Log
- Training and Education Records
- Drug/Device Accountability
- Investigator's Brochure/Package Insert
- Laboratory Certification, Accreditation or Validation
- Range of Normal Values
- IATA Shipping Certification
- Screening Log
- Enrollment Log
- Monitoring/Auditing Log and Reports
- Sponsor/Funding Source Correspondence
- Advertisements
- Curriculum Vitae/Licenses
- Adverse Events
- Case Report Forms

APPENDIX II
Staff Signature Log

Study Title: _____

Name	Role	Signature	Initials	Date Trained	Authorization	Dates of Involvement
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:

* The above personnel have been authorized to perform the following study functions:

1.	Collect study data	9.	Perform physical exams/study procedures
2.	Communicate with Sponsor	10.	Review medical records/access PHI
3.	CRF entries/corrections	11.	Sign CRFs
4.	Dispense study medications	12.	Subject selection/screening
5.	Drug Accountability	13.	Other: _____
6.	Drug Return Procedures	14.	Other: _____
7.	IRB approved to obtain informed consent	15.	Other: _____
8.	Obtain study measurements	16.	Other: _____

By signing this form, I, the Principal Investigator for this study, agree to take responsibility of the day-to-day conduct of the study, to delegate only when appropriate, and to delegate to qualified individuals who have met institutional research education requirements and have been adequately trained in the protocol and their study-related duties and functions before any involvement in the study. I confirm that it is my responsibility to ensure that any new staff added during the course of the study will also sign this form and be adequately trained before they become involved in any study-related duties.

By signing this agreement, I agree to conduct this study according to FDA regulations, MCG institutional policies, and IRB/OHRP policies and procedures. I further agree to internal and external auditing of this study.

Signature of Principal Investigator

Date

APPENDIX III
Subject Screening Log

Study Title: _____

Study Screening Number	Date	Met Criteria?		If no, why not?	Consented?		If no, why not?
		Yes	No		Yes	No	
001							
002							
003							
004							
005							
006							
007							
008							
009							
010							
011							
012							
013							
014							
015							

APPENDIX IV
Enrollment Log

Study Title: _____

Date of Consent	Date Randomized	Sex (M/F)	DOB	Study #	Follow-up Date	Comments

