KILIMANJARO CHRISTIAN MEDICAL CENTER (KCMC)
AIDS RESEARCH & TREATMENT CENTER
POLICIES & PROCEDURES

TITLE: General Operating Procedure for Essential Regulatory Documents	Policy # 0.1

PURPOSE: The purpose of this standard operating procedure (SOP) is to provide consistent processes/procedures to be followed for regulatory management/maintenance. Regulatory documents are those documents that individually and/or collectively permit the conduct of a clinical trial. These documents are generated throughout the various stages of a clinical trial, including, before the trial begins, during the conduct of the trial, and after completion or termination of the trial.

Regulatory documents serve to ensure the compliance of the investigator with the standards of good clinical practice (GCP) and with all applicable regulatory requirements. These documents ensure the rights and welfare of prospective subjects are protected, that pertinent laws, regulations, and institution procedures and guidelines are observed, that all research involving human subjects receives IRB review and approval before commencement of the research, compliance with all IRB decisions, conditions, and requirements, that protocols receive timely continuing IRB review and approval, reporting unexpected or serious adverse events to the IRB, and IRB review and approval is obtained before changes are made to approved protocols or consent forms

SCOPE

This SOP is based upon: 1) the Code of Federal Regulations (CFR), 2) guidances that apply to the involvement of human subjects in clinical research, 3) standards for GCP, and (4) references to procedures/processes/policies to be followed. This SOP is applicable to Clinical Research Sites conducting therapeutic, vaccine, or prevention studies on human subjects, both domestic and internationally.

POLICY: The clinical research coordinator assigned to the Protocol Office will maintain essential documents for each protocol within the Protocol Office area and ensure compliance with applicable guidelines and regulations of Good Clinical Practice, Code of Federal Regulations, sponsors, Duke University Health System (DUHS), KCMC Ethics Committee and National Institute for Medical Research (NIMR).

RESPONSIBILITY:

1. Clinical Research Coordinator (CRC) is educated and trained to ensure that essential documents are maintained as stated in this SOP.

INSTRUCTIONS

- Regulatory documents in this SOP include 1) a description of the purpose and/or requirements of each document, 2) the location where the document should be filed (central file or protocol file) 3) a reference to the pertinent instructions/forms/SOPs
- It is acceptable to consolidate some of the documents centrally (Central files): CV, Medical License, Laboratory certificates, Lab normal ranges, IND safety letter/memos, IB, Package Inserts, Key Personnel Signature Log, Ethics training, old protocol version filed by protocol.

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Prepared by: Janet Mueller	

- Separate regulatory files must be maintained for each clinical trial protocol (Protocol file). Individual elements must be readily identifiable and filed in date order:

FOLDER TABS, ORDER OF TABS AND CONTENTS WITHIN FOLDERS:

Protocol

- current protocol version
- clarification memos
- administrative letters
- Letters of amendments

Site Registration(Essential documents)

- Site Registration/Site Approvals
- 1572
- Financial disclosure
- Site monitor log
- Delegation of Responsibilities Log/ Signature Log
- IRB board roster that approved protocol and memo of abstention of PI if sits on board that voted
- Sponsor correspondence: Any written or electronic correspondence related to the protocol (For Industry sponsored studies may want separate file due to large volumes of correspondence)

New Submission

- Copies of documents sent to KCMC, NIMR, DUHS IRB, NIH
- New Submission approval
- Amendments/Approvals related to the protocol during the first year

Renewal 1

- copies of all documents associated with the renewal submission
- any amendment submission to the protocol during that renewal year
- associated approvals

Add renewal years as appropriate i.e. Renewal 2 etc.

Consent Forms

- all approved consent forms with consent form stamp

KCMC SAEs

- submission and approval

IB and package Insert

- submission/acknowledgement

Protocol Violation/Deviations

- submission/acknowledgement

- (It is acceptable for Duke University Health System (DUHS) to maintain regulatory files for KCMC as necessary on Sharepoint.
- DUHS will provide oversight, coordination and applicable administrative support for KCMC.
- All of the documents addressed in this SOP must be available for audit/inspection by the sponsor and regulatory authorities.
- All local, institution, and/or institutional review board (IRB)/independent ethics committee (IEC) policies/regulations will be followed including any procedures that are more stringent than NIH SOPs.
- Destruction or retention of Informed consents and regulatory documents will be in accordance with Federal regulations and local institution/IRB/IEC policies and procedures.

General Files: See second bullet under "INSTRUCTIONS" page 1 of this SOP

Document	Requirement / Purpose	File	Instructions/Forms/SOP
Assent Form	• IRB has determined 6 years of age for obtaining assent **PEDIATRIC RISK ASSESSMENT FORM** - required for all IRB protocols involving subjects less than 18 years of age	• Protocol file Consent folder	• **http://irb.mc.duke.edu/**
Assurance Number IRB Roster	The Institution is responsible for obtaining and maintaining a current Health & Human Services (HHS) Assurance through the Office for Human Research Protections (OHRP). ➢ DUHS: M0116 ➢ KCMC: FWA # 00002153 Keep on file the Assurance number and expiration date. Note: A copy of the actual Assurance document must be on file with the Institution and/or IRB/IEC. Copies of IRB roster who voted on protocol and documentation of PI abstention from voting if sits on IRB board.	Central file Protocol file Essential documents folder	http://irb.mc.duke.edu/
Certificate of Confidentiality	To protect the privacy of research subjects by withholding their identities from all persons not connected with the research. Contacts for Information on Certificates of Confidentiality are on the IRB website	Central file and Protocol file Essential	http://irb.mc.duke.edu/ ohrp@od.nih.gov

Document	Requirement / Purpose	File	Instructions/Forms/SOP
		documents folder	
Communications	1. All relevant communications, other than site visits, to document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting, etc. For example: Letters, Meeting notes, Notes of telephone calls, Email messages 2. Includes communications to and from the Sponsor and/or the protocol team. 3. Save electronic media, originals, and/or certified copies, Fed-X, fax receipts etc.	• Protocol file Sponsor Correspondence folder	
Curriculum Vitae (CV)	The site must have on file CVs and/or other relevant documents evidencing qualifications and eligibility to conduct the trial and/or provide medical supervision of subjects. Includes all key personnel 1. Update to reflect significant changes: Affiliation, Education, Responsibilities 2. Dated and Initialed within 2 years	• Central file	
Final Study Report	Final report to the IRB/IEC, and PRO deregistration. Include the following information: • Disposition of subjects, number of patients screened, number enrolled (gender and race), serious adverse experiences since last IRB approval, preliminary finding if any.	• Protocol file Essential documents folder	• **http://irb.mc.duke.edu/**
FDA 1572 Form	1. Required for each initial protocol registration submission of a new protocol with an IND. 2. Update as study personnel and/or other data on the form changes. Updated forms must be signed and dated by the IOR. 3. The original version and any updated forms must be submitted to RCC or sponsor for submission to the FDA. A copy of the forms must be kept on file at the site.	• Protocol file Essential documents folder	• **http://irb.mc.duke.edu/**
Financial Disclosure	1. To document financial aspects of the trial and the financial agreement between the investigator / institution and the sponsor for the trial. 2. Applies to investigators and subinvestigators and pharmacist if listed on 1572	• Protocol file Essential documents folder	
Investigator's Brochures (IBs) ***Package Inserts***	1. To document that relevant and current scientific information about the investigational drug/agent has been provided to the investigator.	• Central file	

Document	Requirement / Purpose	File	Instructions/Forms/SOP
	2. Keep on file a copy for EACH of the study drugs/agents used within the protocol. 2. file all versions		
Information Given to Trial Subject	Must be submitted to the IRB to document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent and to document that recruitment measures are appropriate and not coercive. Includes the following: Informed consent form, All applicable translations, Advertisement for subject recruitment (if used), Education materials (protocol specific), Any other written information such as patient diaries, questionnaires, drug warning cards etc.	• Protocol file New Submission folder or appropriate annual renewal folder	**http://irb.mc.duke.edu/**
Informed Consent Form	1. Create new version date for each revision, must have active IRB stamp and PRO approval before implementation 2. Non-English speaking subjects must be consented in a language they can understand. • Save all written translations and backtranslation, must submit translators qualifications to IRB 3. To document revisions of consent form that take effect during trial, save all versions submitted and approved by IRB/IEC 4. Continual reviews are annual may or may not have revisions but must have active IRB stamp if still open to accrual Changes in consent forms due to protocol amendments and important safety information are at the directive of the IRB/IEC and/or DAIDS.	• Protocol file Consent folder	• **http://irb.mc.duke.edu/**
IRB/IEC Approvals	1. Copies of all materials submitted to the IRB/IEC, including any local committees as required by the IRB/IEC, for example but not limited to: • Clinical Research Center Committee • Radiation Safety Committee • Maternal Fetal Committee • Other Hospital Committees per IRB/IEC requirements 2. Dated proof of submission and IRB/IEC approval of the following for both initial submissions and revisions (if any). Revised documents must be labeled (e.g., date and/or version number) to differentiate them from previous versions. • Advertisements – to document that recruitment measures are appropriate and not coercive. • Continuing/interim review of trial • Informed consent form • Protocol • Protocol Amendments and/or Letters of Amendment • Protocol-specific education materials • Subject compensation • Any other documents receiving IRB/IEC approval or their favorable opinion.	• Protocol file New Submission folder or appropriate Renewal folder	• **http://irb.mc.duke.edu/**

Document	Requirement / Purpose	File	Instructions/Forms/SOP
	• Any other written information to be provided to subjects, to document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent. • Any other pertinent communications with IRB/IEC or documentation required by the IRB/IEC. • Clarification memos *if it requires consent form changes* 3. Dated proof of IRB/IEC submission of the following for both initial submissions and revisions (if any). Revised documents must be labeled (e.g., date and/or version number) to differentiate them from previous versions. • IND Safety Reports, Safety Memos, and Safety Alerts • Investigator's Brochures Proof of IRB/IEC receipt if required by sponsor		
Protocol Registration Approvals	1. The process of completing and submitting the informed consent, IRB/EC approval letter, FDA 1572 Form, and Principal Investigator C.V. is called Protocol Registration. Protocol registration may occur more than once during the course of the protocol. Subsequent protocol registrations are called amendment registrations 2. **Prior to implementing the protocol and enrolling participants, a site must receive approval from Sponsor** **3.** International sites must submit all protocol registration documents in English. Translation requirements for each document are included in the sections that follow.	Protocol file Essential documents folder	
IRB Requirements for credentialing to perform research with human subjects	To comply with federal authorities, research personnel at Duke University Health System (DUHS) must complete basic training in research ethics before conducting research involving human subjects and key research personnel must receive additional ethics training each year to remain credentialed. The IRB will not grant final approval of a new protocol unless required ethics training has been completed. *Research Personnel* are individuals who have any direct or indirect involvement in a research endeavor that involves human subjects or their protected health information. The DUHS IRB requires all research personnel to complete general research ethics training. *Key research personnel* are research personnel who are directly involved in conducting research with human subjects, or who are directly involved with the handling of protected health information related to those subjects in the course of a research project, regardless of the source of the research funding. Key personnel must complete general ethics training and annual ethics training to remain credentialed. Students are considered key personnel if they meet these criteria.	• CTU file	**http://irb.mc.duke.edu/certification.htm**

Document	Requirement / Purpose	File	Instructions/Forms/SOP
Laboratory	1. To document competence of local, central, or Network laboratories to perform protocol required tests and support reliability of results of medical/laboratory/standardized procedures/tests, one of the following must be on file: **Laboratories located in the United States** • CLIA Certification of Compliance • CLIA Certification of Accreditation AND the agency certificate (e.g., CAP Certification of Accreditation) **Laboratories located outside the United States** • Results of established quality control and/or external quality assessment (e.g., DAIDS VQA program) • Other validation 1. To document current competency, updated files when: • Existing certification/accreditation/validation expires. • A new laboratory is added or replaces an existing laboratory. 2. Document normal values/ranges for medical/laboratory/ standardized procedures/tests included in the protocol. • Update when they are revised during the trial. • Does not apply to tests that do not have established normal values/ranges. 3. The preceding (1-3) do NOT apply to laboratories that test protocol specimens but do NOT report any subject-specific results for the diagnosis, treatment or assessment of the health of subjects.	• CTU file • Network-supported central laboratories documents may be filed on Network web sites. • Normal values/reference ranges may be filed in subject records (e.g., on lab report)	
Protocol	To document investigator and sponsor agreement to the protocol and amendments; and, to document revisions of trial-related documents that take effect during trial: • Initial version that the site was registered to by RCC • Amendments and Letters of Amendment • Subsequent versions • Clarification memos	• Protocol file Protocol folder	
Protocol deviations/violation/waiver **Serious Adverse Events (SAE) and Safety Reports**	1. Notification by originating investigator to sponsor of serious adverse events, related reports, and other safety information. 2. Notification by sponsor to investigators of safety information. 3. Notification by study coordinator to sponsor of deviation/violation/waiver 4. Where applicable, notification by sponsor or investigator to regulatory authorities and IRB/IEC: • Unexpected serious adverse drug reactions • Unexpected serous adverse deviation or violation of protocol • Other safety information	• IND Safety memos and letters Central file • Protocol file KCMC SAE SAE folder KCMC protocol violation/waiver/deviation Deviation/violation folder	• http://irb.mc.duke.edu/

Document	Requirement / Purpose	File	Instructions/Forms/SOP
Signature Key/Log	1. To document the signatures of individuals using initials in place of a full signature to sign CRFs and source documents. 2. To document the signatures and initials of all persons authorized to make entries and/or corrections on CRFs. Include all site staff working on a study, such as: • Clinicians, Physicians, Pharmacists, Data personnel, Regulatory personnel • Any other individuals authorized to make entries and/or corrections on CRFs. 3. Key/log must include: • Initials • Printed Signature • Legal Signature, including first and last name • Credentials (if appropriate)	• CTU file	